IOMERON- iomeprol injection injection, solution
BRACCO DIAGNOSTICS INC

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

IMPORTANT DRUG INFORMATION
may be found at the following link:
https://imaging.bracco.com/us-en/products/ct-ct-colonography/iomeron

July 6, 2022

Subject: Temporary importation of Iomeron® (iomeprol injection) to address drug shortage issues

Dear Healthcare Professional,

Due to the current critical shortages of Omnipaque™ (iohexol injection), Visipaque™ (iodixanol injection), and Ultravist (iopromide injection) in the U.S. market, Bracco Diagnostics Inc. (hereafter "Bracco") is coordinating with the U.S. Food and Drug Administration (FDA) to increase the availability of iodinated contrast media indicated for intravascular use.

Accordingly, Bracco has initiated temporary importation of Iomeron® (iomeprol injection), an intravascular iodinated contrast medium, into the U.S. market. This product will be used in adult patients by intravenous or intraarterial route of administration only during the shortage. FDA has not approved Iomeron (iomeprol). Iomeron (iomeprol) drug product is manufactured by BIPSO GmbH in Germany and Patheon Italia S.p.A. in Italy. These facilities are also used to manufacture Bracco's FDA-approved intravascular iodinated contrast medium Isovue (iopamidol injection).

FDA's regulatory discretion for the importation and distribution of Iomeron (iomeprol) is limited to Bracco during the critical U.S. shortages of Omnipaque, Visipaque, and Ultravist.

Effective immediately, and during this temporary period, Bracco will offer the following presentations of Iomeron (iomeprol) to the U.S. market:

Product Description	Iodine Concentration (mg iodine/mL)	Package Size	Lot Number	Label Language	NDC Number	UK SmPC
Iomeron (iomeprol injection) 250	250	56 X 100 mL	2C42685	French	0270-7250-10	Iomeron 300 UK SmPC SD
Iomeron (iomeprol injection) 300	300	56 X 100 mL	2C43416 KP1552A	French	0270-7300-10	Iomeron 300 UK SmPC SD
Iomeron		10 X 200			0270	Iomeron 300 UK

(iomeprol injection) 300	300	10 X 200 mL	KP2701F	English	0270-7300-20	300 UK SmPC SD
Iomeron (iomeprol injection) 300	300	6 X 500 mL	KP2804A	Spanish	0270-9300-06	Iomeron 300 UK SmPC MD
Iomeron (iomeprol injection) 350	350	56 X 100 mL	LP1566C	Russian	0270-7350-10	Iomeron 350 UK SmPC SD
Iomeron (iomeprol injection) 350	350	30 X 150 mL	2C42507	French	0270-7350-15	Iomeron 350 UK SmPC SD
Iomeron (iomeprol injection) 350	350	10 X 200 mL	LP2705A	English	0270-7350-20	Iomeron 350 UK SmPC SD
Iomeron (iomeprol injection) 350	350	6 X 500 mL	LP2807A	Spanish	0270-9350-06	Iomeron 350 UK SmPC MD
Iomeron (iomeprol injection) 350	350	9 X 500 mL	LP2810B	English	0270-9350-09	Iomeron 350 UK SmPC MD
Iomeron (iomeprol injection) 400	400	56 X 100 mL	MP1577A	Russian	0270-7400-13	Iomeron 400 UK SmPC SD
Iomeron (iomeprol injection) 400	400	10 X 100 mL	MP2561C	Portuguese	0270-7400-10	Iomeron 400 UK SmPC SD
Iomeron (iomeprol injection) 400	400	56 X 100 mL	MP2556A	Polish	0270-7400-16	Iomeron 400 UK SmPC SD
Iomeron (iomeprol injection) 400	400	30 X 200 mL	MP2702C	Slovenian	0270-7400-20	Iomeron 400 UK SmPC SD
Iomeron (iomeprol injection) 400	400	9 X 500 mL	MP2807C	English	0270-9400-01	Iomeron 400 UK SmPC MD
Iomeron (iomeprol	400	6 X 500 mL	MP2806A	English	0270-9400-06	Iomeron 400 UK SmPC

injection) 400		mL			9400-06	SmPC MD
Iomeron (iomeprol injection) 400	400	9 X 500 mL	MP2807A	Portuguese	0270-9400-03	Iomeron 400 UK SmPC MD

The imported Iomeron (iomeprol) was originally labelled for use in countries outside the United States. The bottle and box labels will display the text used when marketing Iomeron (iomeprol) in those countries. Note that:

- The prescribing information will be provided with each bottle of Iomeron (iomeprol), in the form of the appropriate Summary of Product Characteristics (SmPC) document approved for the U.K., which is written in English, and is representative of all Iomeron (iomeprol) SmPCs for that presentation.
- Copies of the U.K. SmPCs accompany this letter, along with images of the U.K. bottle and box labels that will be imported.
- The Iomeron (iomeprol) U.K. SmPCs are available on-line at: https://imaging.bracco.com/us-en/products/ct-ct-colonography/iomeron
- For those bottles and box labels not in English, English translations of these labels are available on-line at: https://imaging.bracco.com/us-en/products/ct-ct-colonography/iomeron

There are differences among the currently marketed nonionic, low-osmolar iodinated contrast media in their physico-chemical properties, as can be seen in the below table that compares them at the concentration of 300 mg iodine/mL (except for Visipaque, for which the nearest concentration is 320 mg iodine/mL):

Table of Physico-chemical Properties of Iomeron (iomeprol) vs. Comparable U.S. Marketed Products (using a concentration of 300 mg iodine/mL or nearest equivalent)

	Viscosity (CP)		Osmolality (mOsm/kg water)	Density	pH
Product	**20°C**	**37°C**	**37°C**	**37°C**	
Iomeron (iomeprol injection) 300	8.1	4.5	521	1.334	6.5 – 7.2
Iomeron (iomeprol injection) 300	8.8	4.7	616	1.339	6.5 – 7.5
Omnipaque (iohexol injection) 300	11.8	6.3	672	1.349	6.8 – 7.7
Optiray (ioversol injection) 300	8.2 (25°C)	5.5	651	1.352	6.0 – 7.4
Visipaque (iodixanol injection) 320	26.6	11.8	290	1.356	6.8 – 7.7
Ultravist (iopromide injection) 300	9.2	4.9	607	1.322	6.5 – 8.0

Iomeron multi-dose container’s administration:

The 500 mL presentations of Iomeron are multi-dose containers. The U.K. SmPC states that the Iomeron multi-dose bottle stopper should be pierced only once, and that proper

withdrawal cannulas for piercing the stopper and drawing up the contrast medium should be used. For those injectors in which the Iomeron container would be directly inserted (i.e., there would be no use of a transfer set), the injector manufacturer's procedures for insertion should be followed, keeping in mind that the bottle stopper should be pierced only once.

Microbial contamination studies were performed where Iomeron solutions in multi-dose containers were inoculated with micro-organisms. These studies demonstrated that Iomeron solutions are bacteriostatic, with microbial growth not observed over the 10-hour period of the studies. Based upon these studies, when the 500 mL multi-dose container is used to draw up or administer separate doses of Iomeron, any unused product remaining in the bottle after 10 hours from the stopper being pierced must be discarded.

Please see Appendix 1 of this letter for tables showing the differences among the FDA-approved intra-arterial and intravenous indications for Omnipaque (iohexol), Visipaque (iodixanol), Ultravist (iopromide) and Isovue (iopamidol) vs. the intra-arterial and intravenous indications for Iomeron (iomeprol) approved in the U.K.

Iomeron (iomeprol) will be available only by prescription in the U.S. However, the imported lots do not have the statement "Rx only" on their labeling. **Please refer to the Iomeron (iomeprol) U.K. SmPC for the product's full prescribing information. In addition, please note the following comments and recommendations:**

- There are differences between indications for Iomeron (iomeprol) approved in the U.K. and approved indications for iodinated contrast media (ICM) in the US. Tables comparing indications for selected FDA approved ICM and Iomeron (iomeprol) are provided in Appendix 1.
- We recommend that imported Iomeron (iomeprol) be administered only by intravenous and intra-arterial routes.
- We recommend that imported Iomeron (iomeprol) be used only in adult patients. Iomeron (iomeprol) adult dosing per the U.K. SmPC is provided in Appendix 2.
- Obtain a history of allergy, hypersensitivity, or hypersensitivity reactions to iodinated contrast agents and always have emergency resuscitation equipment and trained personnel available prior to Iomeron administration. Monitor all patients for hypersensitivity reactions.
- Use the lowest necessary dose of Iomeron (iomeprol) in patients with renal impairment or with congestive heart failure.
- Avoid angiocardiography whenever possible in patients with homocystinuria because of the risk of inducing thrombosis and embolism.
- Thyroid storm has occurred after the intravascular use of iodinated contrast agents in patients with hyperthyroidism, or with an autonomously functioning thyroid nodule. Evaluate the risk in such patients before use of any iodinated contrast agent.
- Administer iodinated contrast agents with extreme caution in patients with known or suspected pheochromocytoma. Inject the minimum amount of contrast necessary, assess the blood pressure throughout the procedure, and have measures for treatment of a hypertensive crisis readily available.
- Severe cutaneous adverse reaction severity may increase and time to onset may decrease with repeat administration of contrast agents; prophylactic medications may not prevent or mitigate severe cutaneous adverse reactions. Avoid administering

Iomeron to patients with a history of a severe cutaneous adverse reaction to Iomeron.

- Stop metformin at the time of, or prior to, Iomeron (Iomeron) administration in patients with an eGFR between 30 and 60 mL/min/1.73 m2; in patients with a history of hepatic impairment, alcoholism or heart failure; or in patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure and reinstitute metformin only after renal function is stable.
- Administration of iodinated contrast agents may interfere with thyroid uptake of radioactive iodine (I-131 and I-123) and decrease therapeutic and diagnostic efficacy in patients with carcinoma of the thyroid. The decrease in efficacy lasts for 6 to 8 weeks.
- Renal toxicity has been reported in a few patients with liver dysfunction who were given an oral cholecystographic agent followed by intravascular iodinated contrast agents. Administration of any intravascular iodinated contrast agent should therefore be postponed in patients who have recently received a cholecystographic contrast agent.

The Iomeron (iomeprol) barcode may not register accurately on U.S. barcode scanning systems. Institutions should manually input the product into their systems and confirm that their systems do not provide incorrect information when the product is scanned. Alternative procedures should be followed to assure that the correct drug product is being used and administered to individual patients.

To place an order for Iomeron (iomeprol), please contact Bracco Customer Service at 1-877-272-2269 or at Bracco.otc@diag.bracco.com. Hours of operation: Monday-Friday 8:30 AM – 6:00 PM EDT, excluding holidays.

To report adverse events associated with the use of this product, please contact Bracco Drug Safety at 1-800-257-5181, option 1, or at adverse.events@diag.bracco.com.

To report quality problems, or if you have any questions about the information contained in this letter or the use of Iomeron (iomeprol), please contact Bracco Professional Services at 1-800-257-5181, option 2, or at services.professional@diag.bracco.com.

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm
- **Regular Mail or Fax**: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178 (1-800-332-0178)

Sincerely,

Alberto Spinazzi

Alberto Spinazzi, MD
Senior Vice President
Chief Medical and Regulatory Officer
Bracco Group

Attachments:
Iomeron (iomeprol) U.K. SmPCs
Images of Iomeron (iomeprol) U.K. Bottle and Box Labels

Appendix 1. Comparisons of approved uses for iodinated contrast media in shortage and those manufactured by Bracco.

Table of Approved Intra-arterial Uses for Iodinated Contrast Media in Shortage, and for Those Manufactured by Bracco					
POPULATION/ INDICATION	**OMNIPAQUE (iohexol) mg iodine/mL**	**VISIPAQUE (iodixanol) mg iodine/mL**	**ULTRAVIST (iopromide) mg iodine/mL**	**ISOVUE (iopamidol) mg iodine/mL**	**IOMERON* (iomeprol) mg iodine/mL**
ADULTS					
Intra-arterial digital subtraction angiography	140	270, 320			250, 300
Aortography	300, 350		370		350, 400
Angiocardiography	350	320	370	370	300, 350, 400
Visceral arteriography	300, 350	320	370	370	300, 350, 400
Cerebral arteriography	300	320	300	300	250, 300
Peripheral arteriography	300, 350	320	300	300	300, 350, 400
*Approved uses for Iomeron (iomeprol) are from the U.K.					

Table of Approved Intravenous Uses for Iodinated Contrast Media in Shortage, and for Those Manufactured by Bracco					
POPULATION/ INDICATION	**OMNIPAQUE (iohexol) mg iodine/mL**	**VISIPAQUE (iodixanol) mg iodine/mL**	**ULTRAVIST (iopromide) mg iodine/mL**	**ISOVUE (iopamidol) mg iodine/mL**	**IOMERON* (iomeprol) mg iodine/mL**
ADULTS					
CT head	240, 300, 350	270, 320	300, 370	250, 300	250, 300, 350
CT body	300, 350	270, 320	300, 370	250, 300	250, 300, 350, 400
Intravenous digital subtraction angiography	350				250, 300, 350, 400
Peripheral venography	240, 300	270		200	250, 300, 350

Excretory urography	300, 350	270, 320	300	250, 300, 370	250, 300, 350, 400
*Approved uses for Iomeron (iomeprol) are from the U.K.					

Appendix 2. Iomeron (iomeprol injection) adult dosing recommendations per U.K. Summary of Product Characteristics.

Table of adult dosing recommendations for Iomeron 250 single dose (* Repeat as necessary)	
Venography	10 – 100 mL* maximum 250 mL 10 – 50 mL upper extremity 50 – 100 mL lower extremity
Cerebral arteriography	5 – 12 mL*
Digital subtraction angiography Intra arterial visceral peripheral Intravenous	 2 – 20 mL per artery* aorta 25-50 mL* both 250 mL maximum 5 – 10 mL per artery* maximum 250 mL 30 – 60 mL* maximum 250 mL
Computed tomography brain body	 50 – 150 mL 40 – 150 mL maximum 250 mL
Urography intravenous	50 – 150 mL

Table of adult dosing recommendations for Iomeron 300 single dose (* Repeat as necessary)	
Peripheral arteriography	10 – 90 mL*
Venography	10 – 100 mL* maximum 250 mL 10 – 50 mL upper extremity 50 – 100 mL lower extremity
Angiocardiography and left ventriculography	30 – 80 mL maximum 250 mL
Cerebral arteriography	5 – 12 mL*
Visceral arteriography	5 – 50 mL* or according to type of examination; maximum 250 mL
Digital subtraction angiography	

Intra arterial	
visceral	2 – 20 mL per artery* aorta 25-50 mL* both 250 mL maximum
peripheral	5 – 10 mL per artery* maximum 250 mL
Intravenous	30 – 60 mL* maximum 250 mL
Computed tomography	
brain	50 – 150 mL
body	40 – 150 mL maximum 250 mL
Urography intravenous	50 – 150 mL

Table of adult dosing recommendations for Iomeron 300 multidose (* Repeat as necessary)	
Computed tomography	
brain	50 – 150 mL
body	40 – 150 mL maximum 250 mL

Table of adult dosing recommendations for Iomeron 350 single dose (* Repeat as necessary)	
Peripheral arteriography	10 – 90 mL*
Venography	10 – 100 mL* maximum 250 mL 10 – 50 mL upper extremity 50 – 100 mL lower extremity
Aortography	50 – 80 mL
Angiocardiography and left ventriculography	30 – 80 mL maximum 250 mL
Coronary arteriography	4 – 10 mL per artery*
Visceral arteriography	5 – 50 mL* or according to type of examination; maximum 250 mL
Intravenous digital subtraction angiography	30 – 60 mL* maximum 250 mL
Computed tomography	
brain	50 – 150 mL
body	40 – 150 mL maximum 250 mL
Urography intravenous	50 – 150 mL

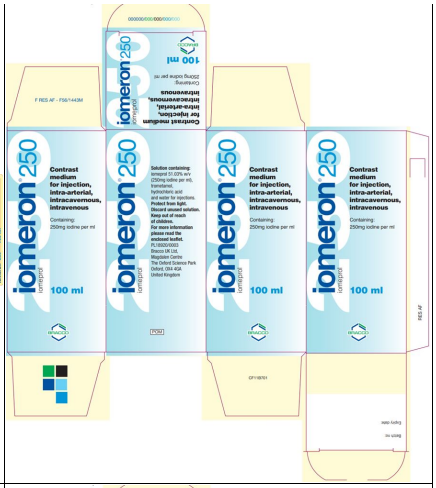
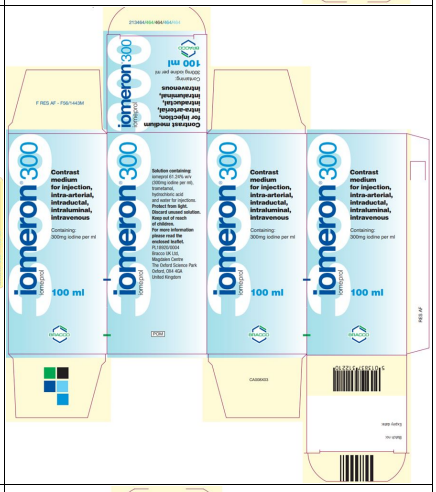
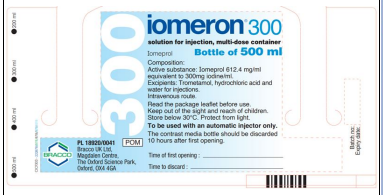
Table of adult dosing recommendations for Iomeron 350 multidose (* Repeat as necessary)	
Computed tomography brain body	 50 – 150 ml 40 – 150 ml maximum 250 mL

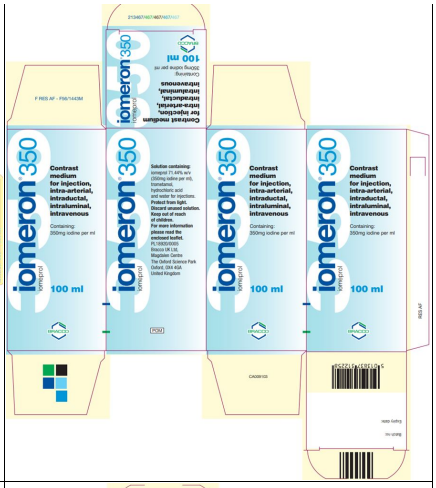
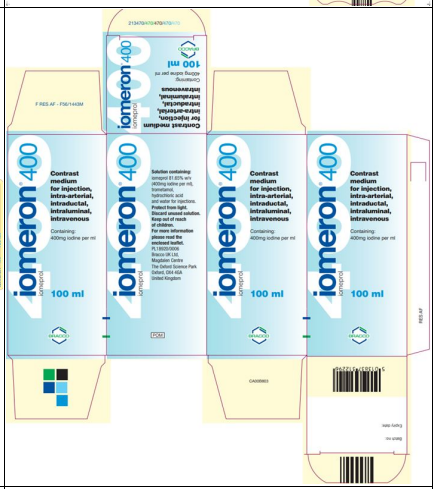
Table of adult dosing recommendations for Iomeron 400 single dose (* Repeat as necessary)	
Peripheral arteriography	10 – 90 mL*
Aortography	50 – 80 mL
Angiocardiography and left ventriculography	30 – 80 mL maximum 250 mL
Coronary arteriography	4 – 10 mL per artery*
Visceral arteriography	5 – 50 mL* or according to type of examination
Intravenous digital subtraction angiography	30 – 60 mL* maximum 250 mL
Computed tomography of the body	40 – 150 mL maximum 250 mL
Urography intravenous	50 – 150 mL

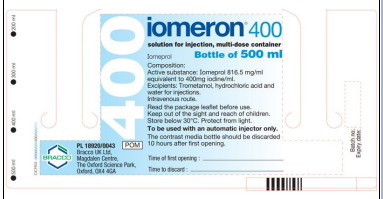
Table of adult dosing recommendations for Iomeron 400 multidose (* Repeat as necessary)	
Computed tomography of the body	40 – 150 mL maximum 250 mL

UK Iomeron Vial and Carton Labels

Product Description	Iodine Concentration (mg iodine/mL)	Fill Volume	Vial Label	Carton Label

Iomeron (iomeprol injection) 250	250	100 mL		
Iomeron (iomeprol injection) 300	300	100 mL		
Iomeron (iomeprol injection) 300	300	200 mL		
Iomeron (iomeprol injection) 300	300	500 mL		

Iomeron (iomeprol injection) 350	350	100 mL		
Iomeron (iomeprol injection) 350	350	200 mL		
Iomeron (iomeprol injection) 350	350	500 mL		
Iomeron (iomeprol injection) 400	400	100 mL		

Iomeron (iomeprol injection) 400	400	200 mL		
Iomeron (iomeprol injection) 400	400	500 mL		

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 250, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 51.03% w/v of iomeprol equivalent to 25% iodine or 250mg iodine/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for:

- venography
- cerebral arteriography
- digital subtraction angiography
- computed tomography enhancement
- urography
- cavernosography
- myelography

4.2 Posology and method of administration

venography	adults	10 - 100ml* max 250ml 10 - 50ml upper extremity 50 - 100 lower extremity
cerebral arteriography	adults	5 - 12ml*
	children	3 - 7ml or * *
digital subtraction angiography		
Intra arterial		
visceral	adults	2 - 20ml per artery* aorta 25-50ml* both 250ml max
peripheral	adults	5 - 10ml per artery* max 250ml
intravenous	adults	30 - 60ml* max 250ml
computed tomography		
brain	adults	50 - 150
	children	* *
body	adults	40 - 150ml max 250ml
	children	* *
urography intravenous	adults	50 - 150ml
	neonates	3 - 4.8ml/kg
	babies	2.5 - 4ml/kg
	children	1 - 2.5ml/kg or *
cavernosography	adults	40 - 250ml
myelography	adults	12 - 18ml by lumbar injection

* Repeat as necessary
* * According to body size and age

In elderly patients the lowest effective dose should be used.

Unless otherwise instructed by the doctor, a normal diet may be maintained on the day of the examination.

In myelography, lower doses may be used for lumbar or thoracic studies and higher doses for cervical or total columnar studies. Regardless of the nature of the myelographic study, Iomeron should be injected slowly over 1-2 minutes.

The X ray can be taken up to 60 minutes following injection. Post myelographic CT of the spinal column should be delayed for approximately four hours to allow dilution and clearance of excessive contrast.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.
Intrathecal concomitant administration of corticosteroids with contrast media is contraindicated.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

Hydration
Patients must be well hydrated, and any relevant abnormalities of fluid or electrolyte balance should be corrected prior to and following contrast media injection. Especially patients with diabetes mellitus, polyuria, oligouria, hyperuricaemia, infants, small children, and elderly patients, should not be exposed to dehydration. Also patients with severely compromised hepatic and renal impairment are more at risk. Caution should be exercised in hydrating patients with underlying conditions that may be worsened by fluid overload, including congestive heart failure.

Rehydration prior to use of iomeprol is recommended in patients with sickle cell disease.

Special population
Hypersensitivity to iodinated contrast media, allergic predisposition

A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatment**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing
In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighted against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases
Care should be taken in severe cardiac disease particularly heart failure and coronary artery disease. Reactions may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias. In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased. In these cases the risks associated with the catheterization procedure are increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders
Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease e.g. stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CNS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intra-arterial administration. Premedication with an alpha and beta receptor blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal impairment
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters before re-examining the patient with a contrast media. Preventive measures include:

- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;

avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;

A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus
Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children: Infants up to 1 year, especially the new-born, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.

Transient hypothyroidism may occur in neonates when the mother or the neonate has received an iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates 7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.

Elderly: There is special risk of reactions involving the circulatory system such that myocardial ischaemia, major arrhythmias and extrasystoles are more likely to occur. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Precautions for dedicated exams

Angiography
Non ionic contrast media have less antiocoagulant activity in vitro than ionic media. Meticulous attention should therefore be paid to angiographic technique. Non ionic media should not be allowed to remain in contact with blood in a syringe, and intravascular catheters should be flushed frequently to minimise the risk of clotting which, rarely, has led to serious thromboembolic complications.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

Myelography
Following intrathecal use, the patient should rest with the head and the chest elevated for 1 hour and be kept well hydrated. Thereafter, he/she may ambulate carefully, but bending down must be avoided. If remaining in bed, the head and chest should be kept

elevated for 6 hours. Patients, suspected of having a lower seizure threshold should be observed during this period.

Venography
Special care is required when venography is performed in patients with thrombosis, phlebitis, severe ischaemic disease, local infection or a totally obstructed artero-venous system.

4.5 Interaction with other medicinal products and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to iomeprol.

Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenotiazine derivatives should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure.

It has been reported that cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

Epidural and intrathecal corticosteroids should never be concurrently administered when iodinated contrast media are used, because corticosteroids may promote and affect the signs and symptoms of arachnoiditis (see section 4.3 - Contraindications).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy
Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative. Since, wherever possible, exposure to radiation should be

avoided during pregnancy, the benefits of any X ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk.

Breastfeeding
No human data exist concerning the excretion of iomeprol in breast milk. Animal studies have demonstrated that the excretion of iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.

Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

After intrathecal administration, it is recommended that the patient should wait 24 hours before driving or operating machinery.

4.8 Undesirable effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death. These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials among 4,903 adult patients and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class.

Within each frequency grouping, adverse reactions are presented in order of decreasing

seriousness.

4.8.1 Intravascular administration

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,515.

Adults

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 t o <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Frequency unknown*
Blood and lymphatic system disorders				Thrombocytopenia, Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack Paralysis Syncope Convulsion Loss of consciousness Dysarthria Paraesthesia Amnesia Somnolence Taste abnormality
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia Extrasystoles	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Palpitations Cyanosis

Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement
Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best

estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

Coronary artery thrombosis and coronary artery embolism have been reported as a complication of coronary catheterization procedures.

Vasospasm and consequent ischaemia have been observed during intra-arterial injections of contrast medium, in particular after coronary and cerebral angiography often procedurally related and possibly triggered by the tip of the catheter or excess catheter pressure.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

4.8.2 Intrathecal administration

Adults

Adults patients involved in clinical trials with intrathecal administration of Iomeprol were 388.

The most frequently reported adverse reactions following intrathecal administration of Iomeprol are headache, dizziness, nausea, vomiting and back pain. These reactions are usually mild to moderate and transient in nature. Rarely, headache may persist for days. Most side effects occur some hours (3 to 6 hours) after the procedure, due to the distribution of the contrast medium in the CSF circulation from the site of administration to the intravascular space (see section 5.2: Pharmacokinetic properties). Most reactions usually occur within 24 hours after injection.

System Organ Class	**Adverse Reactions**			
	Clinical Trials			**Post-marketing Surveillance**
	Very common (≥1/10)	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1000 to <1/100)**	**Frequency unknown***
Immune system disorders				Anaphylactoid reaction
Nervous system disorders	Headache	Dizziness	Hypoaesthesia	Epilepsy

			Paraesthesia Paraparesis Loss of consciousness Somnolence	
Vascular disorders		Hypertension	Hypotension Flushing	
Gastrointestinal disorders		Nausea Vomiting		
Skin and subcutaneous tissue disorders			Hyperhidrosis Pruritus	Rash
Musculoskeletal and connective tissue disorder		Back pain Pain in extremity	Musculoskeletal stiffness Neck pain	
General disorders and administration site conditions		Injection site reaction**	Feeling hot Pyrexia	

* Since the reactions were not observed during clinical trials with 388 patients, best estimate is that their relative occurrence is uncommon (≥ 1/1000 to <1/100.
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise application site pain, injection site discomfort, injection site pain and injection site warmth.

Paediatric patients

No adverse reactions were reported after intrathecal administration of Iomeprol both in clinical trials and in the post-marketing surveillance.

4.8.3 Administration to body cavities

After injection of an iodinated contrast media in body cavities, contrast media are slowly absorbed from the area of administration into the systemic circulation and subsequently cleared by renal elimination.

Blood amylase increased is common following ERCP. Very rare cases of pancreatitis have been described.

The reactions reported in cases of arthrography and fistulography usually represent irritative manifestations superimposed on pre-existing conditions of tissue inflammation.

Hypersensitivity reactions are rare, generally mild and in the form of skin reactions. However, the possibility of severe anaphylactoid reactions cannot be excluded.

As with other iodinated contrast media, pelvic pain and malaise may occur after hysterosalpingography.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary/ intrathecal contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

Following intrathecal administration to animals, iomeprol is completely cleared from the CSF and passes into the plasma compartment.

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Five years

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of containers

Colourless Type I or Type II glass bottles with rubber/aluminium cap.
Quantities of 20, 30, 50, 75, 100, 150, 200 or 250 ml of solution.

6.6 Special precautions for disposal and other handling

Bottles containing contrast media solution are not intended for the withdrawal of multiple doses. The rubber stopper should never be pierced more than once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.
Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present.

The contrast medium should not be drawn into the syringe until immediately before use. Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions with sterile syringes. Sterile techniques must be used with any spinal puncture or intravascular injection, and with catheters and guidewires. If non-disposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents.

It is desirable that solutions of contrast media for intravascular and intrathecal use should be at body temperature when injected.

Any residue of contrast medium in the syringe must be discarded. Solutions not used in one examination session or waste material, such as the connecting tubes, should be disposed in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

18920/0003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

11 December 1992 / 29 December 1998

10. DATE OF REVISION OF THE TEXT

19 January 2022

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 300, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 61.24% w/v of iomeprol equivalent to 30% iodine or 300mg iodine/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for:

- peripheral arteriography
- venography
- angiocardiography and left ventriculography
- cerebral arteriography
- visceral arteriography
- digital subtraction angiography
- computed tomography enhancement
- urography
- ERCP
- dacryocystography
- sialography
- fistulography
- galactography
- myelography

4.2 Posology and method of administration

peripheral arteriography	adults children	10 - 90ml * * *
venography	adults	10 - 100ml* max 250ml 10 - 50ml upper extremity 50 - 100 lower extremity
angiocardiography and left ventriculography	adults children	30 - 80ml max 250ml * *
cerebral arteriography	adults children	5 - 12ml* 3 - 7ml or * *
visceral arteriography	adults children	5 - 50ml* or according to type of examination; max 250ml * *
digital subtraction		

angiography		
Intra arterial		
visceral	adults	2 - 20ml per artery* aorta 25-50ml* both 250ml max
peripheral	adults	5 - 10ml per artery* max 250ml
intravenous	adults	30 - 60ml* max 250ml
computed tomography		
brain	adults	50 - 150ml
	children	* *
body	adults	40 - 150ml max 250ml
	children	* *
urography intravenous	adults	50 - 150ml
	neonates	3 - 4.8ml/kg
	babies	2.5 - 4ml
	children	1 - 2.5ml/kg or *
arthrography	adults	1 - 10ml
ERCP	adults	12 - 30ml
dacryocystography	adults	3 - 8ml
sialography	adults	1 - 3ml
fistulography	adults	1 - 50ml
galactography	adults	0.2 - 1.5ml
myelography	adults	10 - 15ml by lumbar injection

* Repeat as necessary
* * According to body size and age

In elderly patients the lowest effective dose should be used.

Unless otherwise instructed by the doctor, a normal diet may be maintained on the day of the examination.

In myelography, lower doses may be used for lumbar or thoracic studies and higher doses for cervical or total columnar studies. Regardless of the nature of the myelographic study, Iomeron should be injected slowly over 1-2 minutes.

The X ray can be taken up to 60 minutes following injection. Post myelographic CT of the spinal column should be delayed for approximately four hours to allow dilution and clearance of excessive contrast.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.
Intrathecal concomitant administration of corticosteroids with contrast media is contraindicated.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

Hydration
Patients must be well hydrated, and any relevant abnormalities of fluid or electrolyte balance should be corrected prior to and following contrast media injection. Especially patients with diabetes mellitus, polyuria, oligouria, hyperuricaemia, infants, small children, and elderly patients, should not be exposed to dehydration. Also patients with severely compromised hepatic and renal impairment are more at risk. Caution should be exercised in hydrating patients with underlying conditions that may be worsened by fluid overload, including congestive heart failure.

Rehydration prior to use of iomeprol is recommended in patients with sickle cell disease.

Special population
Hypersensitivity to iodinated contrast media, allergic predisposition
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatment**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing

In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighted against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases
Care should be taken in severe cardiac disease particularly heart failure and coronary artery disease. Reactions may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias.

In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased. In these cases the risks associated with the catheterization procedure are increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders
Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CMS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intra-arterial administration. Premedication with an alpha and beta receptor blocker is recommended in these patients.

Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal impairment
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters, in particular before re-examining the patient with a contrast media.

Preventive measures include:

- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;

avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;

A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus
Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children:
Infants up to 1 year, especially the new-born, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.

Transient hypothyroidism may occur in neonates when the mother or the neonate has received an iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates 7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.

Elderly:
There is special risk of reactions involving the circulatory system such that myocardial ischaemia, major arrhythmias and extrasystoles are more likely to occur. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Precautions for dedicated exams

Angiography
Non ionic contrast media have less antiocoagulant activity in vitro than ionic media. Meticulous attention should therefore be paid to angiographic technique. Non ionic media should not be allowed to remain in contact with blood in a syringe, and intravascular catheters should be flushed frequently to minimise the risk of clotting which, rarely, has led to serious thromboembolic complications.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

Myelography
Following intrathecal use, the patient should rest with the head and the chest elevated for 1 hour and be kept well hydrated. Thereafter, he/she may ambulate carefully, but bending down must be avoided. If remaining in bed, the head and chest should be kept elevated for 6 hours. Patients, suspected of having a lower seizure threshold should be

observed during this period.

Venography
Special care is required when venography is performed in patients with thrombosis, phlebitis, severe ischaemic disease, local infection or a totally obstructed artero-venous system.

4.5 Interaction with other medicaments and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to iomeprol.

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Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

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Epidural and intrathecal corticosteroids should never be concurrently administered when iodinated contrast media are used, because corticosteroids may promote and affect the signs and symptoms of arachnoiditis (see section 4.3 - Contraindications).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy
Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.
Since, wherever possible, exposure to radiation should be avoided during pregnancy,

the benefits of any X ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk.

Breastfeeding
No human data exist concerning the excretion of iomeprol in breast milk. Animal studies have demonstrated that the excretion of iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.

Stopping breastfeeding is unnecessary.

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There is no known effect on the ability to drive and operate machines.

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Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death.
These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

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Immune system disorders				Anaphylactoid reaction
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Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia Extrasystoles	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Palpitations Cyanosis
Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock

				Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement
Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its

symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

Coronary artery thrombosis and coronary artery embolism have been reported as a complication of coronary catheterization procedures.

Vasospasm and consequent ischaemia have been observed during intra-arterial injections of contrast medium, in particular after coronary and cerebral angiography often procedurally related and possibly triggered by the tip of the catheter or excess catheter pressure.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

4.8.2 Intrathecal administration

Adults

Adults patients involved in clinical trials with intrathecal administration of Iomeprol were 388.

The most frequently reported adverse reactions following intrathecal administration of Iomeprol are headache, dizziness, nausea, vomiting and back pain. These reactions are usually mild to moderate and transient in nature. Rarely, headache may persist for days. Most side effects occur some hours (3 to 6 hours) after the procedure, due to the distribution of the contrast medium in the CSF circulation from the site of administration to the intravascular space (see section 5.2: Pharmacokinetic properties). Most reactions usually occur within 24 hours after injection.

System Organ Class	**Adverse Reactions**			
	Clinical Trials			**Post-marketing Surveillance**
	Very common (≥1/10)	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1000 to <1/100)**	**Frequency unknown***
Immune system disorders				Anaphylactoid reaction
Nervous system disorders	Headache	Dizziness	Hypoaesthesia Paraesthesia Paraparesis	Epilepsy

			Loss of consciousness Somnolence	
Vascular disorders		Hypertension	Hypotension Flushing	
Gastrointestinal disorders		Nausea Vomiting		
Skin and subcutaneous tissue disorders			Hyperhidrosis Pruritus	Rash
Musculoskeletal and connective tissue disorder		Back pain Pain in extremity	Musculoskeletal stiffness Neck pain	
General disorders and administration site conditions		Injection site reaction**	Feeling hot Pyrexia	

* Since the reactions were not observed during clinical trials with 388 patients, best estimate is that their relative occurrence is uncommon (≥ 1/1000 to <1/100.
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise application site pain, injection site discomfort, injection site pain and injection site warmth.

Paediatric patients

No adverse reactions were reported after intrathecal administration of Iomeprol both in clinical trials and in the post-marketing surveillance.

4.8.3 Administration to body cavities

After injection of an iodinated contrast media in body cavities, contrast media are slowly absorbed from the area of administration into the systemic circulation and subsequently cleared by renal elimination.

Blood amylase increased is common following ERCP. Very rare cases of pancreatitis have been described.

The reactions reported in cases of arthrography and fistulography usually represent irritative manifestations superimposed on pre-existing conditions of tissue inflammation.

Hypersensitivity reactions are rare, generally mild and in the form of skin reactions. However, the possibility of severe anaphylactoid reactions cannot be excluded.

As with other iodinated contrast media, pelvic pain and malaise may occur after hysterosalpingography.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary/ intrathecal contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

Following intrathecal administration to animals, iomeprol is completely cleared from the CSF and passes into the plasma compartment.

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Five years

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of container

Colourless Type I or Type II glass bottles with rubber/aluminium cap.
Quantities of 20, 30, 50, 75, 100, 150, 200 or 250 ml of solution.

6.6 Special precautions for disposal and other handling

Bottles containing contrast media solution are not intended for the withdrawal of multiple doses. The rubber stopper should never be pierced more than once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present.

The contrast medium should not be drawn into the syringe until immediately before use. Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions with sterile syringes. Sterile techniques must be used with any spinal puncture or intravascular injection, and with catheters and guidewires. If non-disposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents.

It is desirable that solutions of contrast media for intravascular and intrathecal use should be at body temperature when injected.

Any residue of contrast medium in the syringe must be discarded. Solutions not used in one examination session or waste material, such as the connecting tubes, should be disposed in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

18920/0004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

11 December 1992 / 29 December 1998

10. DATE OF REVISION OF THE TEXT

19 January 2022

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 350, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 71.44% w/v of iomeprol equivalent to 35% iodine or 350mg iodine/ml.

For the full list of excipients, see section 6.1.For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for:

- peripheral arteriography
- venography
- aortography
- angiocardiography and left ventriculography
- coronary arteriography
- visceral arteriography
- digital subtraction angiography
- computed tomography enhancement
- urography
- dacryocystography
- sialography
- fistulography
- galactography

4.2 Posology and method of administration

peripheral arteriography	adults	10 - 90ml *
	children	* *
venography	adults	10 - 100ml* max 250ml 10 - 50ml upper extremity 50 - 100 lower extremity
aortography	adults	50 - 80ml
	children	* *
angiocardiography and left ventriculography	adults	30 - 80ml max 250ml
	children	* *
coronary arteriography	adults	4 - 10ml per artery *
visceral arteriography	adults	5 - 50ml* or according to type of examination; max 250ml
	children	* *

digital subtraction angiography

intravenous	adults	30 - 60ml* max 250ml

computed tomography

brain	adults	50 - 150ml
	children	* *
body	adults	40 - 150ml max 250ml
	children	* *

Urography

intravenous	adults	50 - 150ml
	neonates	3 - 4.8ml/kg
	babies	2.5 - 4ml
	children	1 - 2.5ml/kg or *
arthrography	adults	up to 10ml
dacryocystography	adults	3 - 8ml
sialography	adults	1 - 3ml
fistulography	adults	1 - 50ml
galactography	adults	0.2 - 1.5ml

* Repeat as necessary
* * According to body size and age

In elderly patients the lowest effective dose should be used.
Unless otherwise instructed by the doctor, a normal diet may be maintained on the day of the examination.

The X ray can be taken up to 60 minutes following injection.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

Hydration
Patients must be well hydrated, and any relevant abnormalities of fluid or electrolyte balance should be corrected prior to and following contrast media injection. Especially patients with diabetes mellitus, polyuria, oligouria, hyperuricaemia, infants, small children, and elderly patients, should not be exposed to dehydration. Also patients with severely compromised hepatic and renal impairment are more at risk. Caution should be exercised in hydrating patients with underlying conditions that may be worsened by fluid overload, including congestive heart failure.

Rehydration prior to use of iomeprol is recommended in patients with sickle cell disease.

Special population
Hypersensitivity to iodinated contrast media, allergic predisposition
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this

product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatment**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing
In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighted against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases
Care should be taken in severe cardiac disease particularly heart failure and coronary artery disease. Reactions may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias.
In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased. In these cases the risks associated with the catheterization procedure are increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders
Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of contrast medium into cerebral tissue possibly leading to CNS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intra-arterial administration. Premedication with an alpha and beta receptor blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal impairment
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters before re-examining the patient with a contrast media. Preventive measures include:

- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;

avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;

A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus
Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children: Infants up to 1 year, especially the new-born, are particularly susceptible to

electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.

Transient hypothyroidism may occur in neonates when the mother or the neonate has received an iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates 7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.

Elderly: There is special risk of reactions involving the circulatory system such that myocardial ischaemia, major arrhythmias and extrasystoles are more likely to occur. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Precautions for dedicated exams

Angiography

Non ionic contrast media have less antiocoagulant activity in vitro than ionic media. Meticulous attention should therefore be paid to angiographic technique. Non ionic media should not be allowed to remain in contact with blood in a syringe, and intravascular catheters should be flushed frequently to minimise the risk of clotting which, rarely, has led to serious thromboembolic complications.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

Venography

Special care is required when venography is performed in patients with thrombosis, phlebitis, severe ischaemic disease, local infection or a totally obstructed artero-venous system.

4.5 Interaction with other medicaments and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to iomeprol.

Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenotiazine derivatives should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure.

It has been reported that cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure

the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy
Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.

Breastfeeding
No human data exist concerning the excretion of iomeprol in breast milk. Animal studies have demonstrated that the excretion of iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.
Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

4.8 Undesirable effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with

pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death. These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials among 4,903 adult patients and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

4.8.1 Intravascular administration

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,515.

Adults

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 t o <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Frequency unknown*
Blood and lymphatic system disorders				Thrombocytopenia, Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack Paralysis Syncope Convulsion Loss of consciousness Dysarthria Paraesthesia Amnesia Somnolence Taste abnormality
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia

Cardiac disorders			Bradycardia Tachycardia Extrasystoles	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Palpitations Cyanosis
Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement
Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and	Feeling	Chest pain	Asthenia	Injection site

administration site conditions	hot	Injection site warmth and pain	Rigors Pyrexia	reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

Coronary artery thrombosis and coronary artery embolism have been reported as a complication of coronary catheterization procedures.

Vasospasm and consequent ischaemia have been observed during intra-arterial injections of contrast medium, in particular after coronary and cerebral angiography often procedurally related and possibly triggered by the tip of the catheter or excess catheter pressure.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

4.8.2 Administration to body cavities

After injection of an iodinated contrast media in body cavities, contrast media are slowly absorbed from the area of administration into the systemic circulation and subsequently cleared by renal elimination.

Blood amylase increased is common following ERCP. Very rare cases of pancreatitis have been described.

The reactions reported in cases of arthrography and fistulography usually represent irritative manifestations superimposed on pre-existing conditions of tissue inflammation.

Hypersensitivity reactions are rare, generally mild and in the form of skin reactions. However, the possibility of severe anaphylactoid reactions cannot be excluded.
As with other iodinated contrast media, pelvic pain and malaise may occur after

hysterosalpingography.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. No other drug should be mixed with the contrast medium.

6.3 Shelf Life

Five years

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of containers

Colourless Type I or Type II glass bottles with rubber/aluminium cap.
Quantities of 20, 30, 50, 75, 100, 150, 200 or 250 ml of solution.

6.6 Special precautions for disposal and other handling

Bottles containing contrast media solution are not intended for the withdrawal of multiple doses. The rubber stopper should never be pierced more than once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present.

The contrast medium should not be drawn into the syringe until immediately before use. Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions with sterile syringes. Sterile techniques must be used with any spinal puncture or intravascular injection, and with catheters and guidewires. If non-disposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents.

It is desirable that solutions of contrast media for intravascular and intrathecal use should be at body temperature when injected.

Any residue of contrast medium in the syringe must be discarded. Solutions not used in one examination session or waste material, such as the connecting tubes, should be disposed in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

18920/0005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

11 December 1992 / 29 December 1998

10. DATE OFREVISION OF THE TEXT

19 January 2022

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 400, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 81.65% w/v of iomeprol equivalent to 40% iodine or 400mg iodine/ml.

For the full list of excipients, see section 6.1.For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for:

- peripheral arteriography
- aortography
- angiocardiography and left ventriculography
- coronary arteriography
- visceral arteriography
- digital subtraction angiography
- computed tomography enhancement
- urography
- dacryocystography
- sialography
- fistulography
- galactography

4.2 Posology and method of administration

peripheral arteriography	adults	10 - 90ml *
	children	* *
aortography	adults	50 - 80ml
	children	* *
angiocardiography and left ventriculography	adults	30 - 80ml max 250ml
	children	* *

coronary arteriography	adults	4 - 10ml per artery *
visceral arteriography	adults	5 - 50ml* or according to type of examination;
	children	* *

digital subtraction angiography

intravenous	adults	30 - 60ml* max 250ml

computed tomography

body	adults	40 - 150ml max 250ml
	children	* *

urography

intravenous	adults	50 - 150ml
	neonates	3 - 4.8ml/kg
	babies	2.5 - 4ml
	children	1 - 2.5ml/kg or *
dacryocystography	adults	3 - 8ml
sialography	adults	1 - 3ml
fistulography	adults	1 - 50ml
galactography	adults	0.2 - 1.5ml

* Repeat as necessary
* * According to body size and age

In elderly patients the lowest effective dose should be used.
Unless otherwise instructed by the doctor, a normal diet may be maintained on the day of the examination.

The X ray can be taken up to 60 minutes following injection.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

Hydration
Patients must be well hydrated, and any relevant abnormalities of fluid or electrolyte balance should be corrected prior to and following contrast media injection. Especially patients with diabetes mellitus, polyuria, oligouria, hyperuricaemia, infants, small children, and elderly patients, should not be exposed to dehydration. Also patients with severely compromised hepatic and renal impairment are more at risk. Caution should be

exercised in hydrating patients with underlying conditions that may be worsened by fluid overload, including congestive heart failure.

Rehydration prior to use of iomeprol is recommended in patients with sickle cell disease.

Special population

Hypersensitivity to iodinated contrast media, allergic predisposition

A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatmen**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing

In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighted against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases

Care should be taken in severe cardiac disease particularly heart failure and coronary

artery disease. Reactions may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias.
In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased. In these cases the risks associated with the catheterization procedure are increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders
Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CMS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intra-arterial administration. Premedication with an alpha and beta receptor blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal impairment
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters before re-examining the patient with a contrast media. Preventive measures include:
- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;

avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;
A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus

Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children: Infants up to 1 year, especially the newborn, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.

Transient hypothyroidism may occur in neonates when the mother or the neonate has received an iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates 7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.

Elderly: There is special risk of reactions involving the circulatory system such that myocardial ischaemia, major arrhythmias and extrasystoles are more likely to occur. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Precautions for dedicated exams

Angiography
Non ionic contrast media have less antiocoagulant activity in vitro than ionic media. Meticulous attention should therefore be paid to angiographic technique. Non ionic media should not be allowed to remain in contact with blood in a syringe, and intravascular catheters should be flushed frequently to minimise the risk of clotting which, rarely, has led to serious thromboembolic complications.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

Venography
Special care is required when venography is performed in patients with thrombosis, phlebitis, severe ischaemic disease, local infection or a totally obstructed artero-venous system.

4.5 Interaction with other medicaments and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to iomeprol.

Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenotiazine derivatives should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure.

It has been reported that cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy
Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.
Since, wherever possible, exposure to radiation should be avoided during pregnancy, the benefits of any X ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk

Breastfeeding
No human data exist concerning the excretion of iomeprol in breast milk. Animal studies have demonstrated that the excretion of iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.

Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

4.8 Undesirable effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various

symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death.
These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials among 4,903 adult patients and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class.
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

4.8.1 Intravascular administration

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,515.

Adults

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 t o <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Frequency unknown*
Blood and lymphatic system disorders				Thrombocytopenia, Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack Paralysis Syncope

				Convulsion Loss of consciousness Dysarthria Paraesthesia Amnesia Somnolence Taste abnormality
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia Extrasystoles	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Palpitations Cyanosis
Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement

Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

Coronary artery thrombosis and coronary artery embolism have been reported as a complication of coronary catheterization procedures.

Vasospasm and consequent ischaemia have been observed during intra-arterial injections of contrast medium, in particular after coronary and cerebral angiography often procedurally related and possibly triggered by the tip of the catheter or excess catheter pressure.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

4.8.2 Administration to body cavities

After injection of an iodinated contrast media in body cavities, contrast media are slowly absorbed from the area of administration into the systemic circulation and subsequently cleared by renal elimination.

Blood amylase increased is common following ERCP. Very rare cases of pancreatitis have been described.

The reactions reported in cases of arthrography and fistulography usually represent irritative manifestations superimposed on pre-existing conditions of tissue inflammation.

Hypersensitivity reactions are rare, generally mild and in the form of skin reactions. However, the possibility of severe anaphylactoid reactions cannot be excluded.

As with other iodinated contrast media, pelvic pain and malaise may occur after hysterosalpingography.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. No other drug should be mixed with the contrast medium.

6.3 Shelf Life

Five years

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of containers

Colourless Type I or Type II glass bottles with rubber/aluminium cap.
Quantities of 20, 30, 50, 75, 100, 150, 200 or 250 ml of solution.

6.6 Special precautions for disposal and other handling

Bottles containing contrast media solution are not intended for the withdrawal of multiple doses. The rubber stopper should never be pierced more than once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present.

The contrast medium should not be drawn into the syringe until immediately before use. Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions with sterile syringes. Sterile techniques must be used with any spinal puncture or intravascular injection, and with catheters and guidewires. If non-disposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents.

It is desirable that solutions of contrast media for intravascular and intrathecal use should be at body temperature when injected.

Any residue of contrast medium in the syringe must be discarded. Solutions not used in one examination session or waste material, such as the connecting tubes, should be

disposed in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

18920/0006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

11 December 1992 / 29 December 1998

10. DATE OF REVISION OF THE TEXT

19 January 2022

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 300, solution for injection, multi-dose container

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 61.24% w/v of Iomeprol equivalent to 30% iodine or 300 mg iodine/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A clear colourless to pale yellow solution supplied in glass multi-dose container.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for computed tomography enhancement, including CTA (CT Angiography).

4.2 Posology and method of administration

brain	adults	50 - 150ml
	children	*
body	adults	40 - 150ml max 250ml
	children	*

* According to body size and age

In elderly patients the lowest effective dose should be used.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

A normal diet should be maintained until the patient refrains from eating 2 hours before the procedure.

Hydration
Any severe disorders of water and electrolyte balance must be corrected prior to administration. Adequate hydration must be ensured particularly in patients with diabetes mellitus, polyuria, oliguria and hyperuricaemia; also in babies, small children and the elderly. Rehydration prior to use of Iomeprol is recommended in patients with sickle cell disease.

Special population
Hypersensitivity to iodinated contrast media, allergic predisposition
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatment**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing
In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighed against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases
Care should be taken in patients with severe cardiac disease particularly heart failure and coronary artery disease. Cardiac manifestations may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias. In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders
Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CMS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intravascular administration. Premedication with an alpha and beta receptor-blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal failure
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters, in particular before re-examining the patient with a contrast media.
Preventive measures include:

- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;
- avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;

A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus
Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children:
Infants up to 1 year, especially the new-born, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.
Transient hypothyroidism may occur in neonates when the mother or the neonate has received an
iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates
7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.
Elderly:
The elderly are at special risk of reactions due to reduced physiological functions, especially when high dosage of contrast media is used. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

4.5 Interaction with other medicinal products and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to Iomeprol.

Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenothiazine derivatives should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure.

It has been reported that cardiac and/or hypertensive patients under treatment with

diuretics, ACE-inhibitors, and/or beta blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy
Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of Iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.
Since, wherever possible, exposure to radiation should be avoided during pregnancy, the benefits of any X ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk.

Breastfeeding
No human data exist concerning the excretion of Iomeprol in breast milk. Animal studies have demonstrated that the excretion of Iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.

Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

4.8 Undesirable effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions

sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death.
These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,515.

Adults

System Organ Class	**Adverse Reactions**			
	Clinical Trials			**Post-marketing Surveillance**
	Common (≥1/100 t o <1/10)	**Uncommon (≥1/1000 to <1/100)**	**Rare (≥1/10,000 to <1/1000)**	**Frequency unknown***
Blood and lymphatic system disorders				Thrombocytopenia, Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack

				Paralysis Syncope Convulsion Loss of consciousness Dysarthria Paraesthesia Amnesia Somnolence Taste abnormality
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Extrasystoles Palpitations Cyanosis
Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion

				Dysphagia Salivary gland enlargement
Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary/ intrathecal contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered Iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of Iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and Iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that Iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Five years
The maximum use time after a bottle stopper has been pierced is 10 hours.

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of container

Colourless type I or type II glass bottles with chlorobutyl or bromobutyl rubber stopper/aluminium cap containing 500 ml of solution.
Boxes of 1, 5 and 6 bottles.

6.6 Special precautions for disposal and other handling

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present. The stopper should be pierced only once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.
Multi-dose containers should be used only in conjunction with an automatic injector which has been approved for multipatient use.
After each patient, the connector between the injector and the patient should be replaced. All other devices should be replaced following the injector manufacturer's instructions. In any case, strictly follow the manufacturer's instructions.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 18920/0041

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

14/11/2018

10. DATE OF REVISION OF THE TEXT

12/11/2021

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 350, solution for injection, multi-dose container

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 71.44% w/v of Iomeprol equivalent to 35% iodine or 350 mg iodine/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A clear colourless to pale yellow solution supplied in glass multi-dose container.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for computed tomography enhancement, including CTA (CT Angiography).

4.2 Posology and method of administration

brain	adults	50 - 150ml
	children	*
body	adults	40 - 150ml max 250ml
	children	*

* According to body size and age

In elderly patients the lowest effective dose should be used.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

A normal diet should be maintained until the patient refrains from eating 2 hours before the procedure.

Hydration
Any severe disorders of water and electrolyte balance must be corrected prior to administration. Adequate hydration must be ensured particularly in patients with diabetes mellitus, polyuria, oliguria and hyperuricaemia; also in babies, small children and the elderly. Rehydration prior to use of Iomeprol is recommended in patients with sickle cell disease.

Special population
Hypersensitivity to iodinated contrast media, allergic predisposition
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly

outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	Major Symptoms	Primary Treatment
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing
In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighed against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases
Care should be taken in patients with severe cardiac disease particularly heart failure and coronary artery disease. Cardiac manifestations may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias. In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders

Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of contrast medium into cerebral tissue possibly leading to CNS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intravascular administration. Premedication with an alpha and beta receptor-blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal failure
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters, before re-examining the patient with a contrast media.
Preventive measures include:

- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;
- avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;

A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus
Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children: Infants up to 1 year, especially the new-born, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.
Transient hypothyroidism may occur in neonates when the mother or the neonate has

received an
iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates
7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.

Elderly:
The elderly are at special risk of reactions due to reduced physiological functions, especially when high dosage of contrast media is used. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

4.5 Interaction with other medicinal products and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to Iomeprol.

Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenothiazine derivatives should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure.

It has been reported that cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy

Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of Iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.
Since, wherever possible, exposure to radiation should be avoided during pregnancy, the benefits of any X ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk.

Breastfeeding
No human data exist concerning the excretion of Iomeprol in breast milk. Animal studies have demonstrated that the excretion of Iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.
Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

4.8 Undesirable effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death.
These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials among 4,903 adult patients and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,515.

Adults

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 t o <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Frequency unknown*
Blood and lymphatic system disorders				Thrombocytopenia, Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack Paralysis Syncope Convulsion Loss of consciousness Dysarthria Paraesthesia Amnesia Somnolence Taste abnormality
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Extrasystoles Palpitations Cyanosis

Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement
Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best

estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary/ intrathecal contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered Iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of Iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum

protein binding and Iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that Iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Five years
The maximum use time after a bottle stopper has been pierced is 10 hours.

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of containers

Colourless type I or type II glass bottles with chlorobutyl or bromobutyl rubber stopper/aluminium cap containing 500 ml of solution.
Boxes of 1, 5 and 6 bottles.

6.6 Special precautions for disposal and other handling

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present. The stopper should be pierced only once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.
Multi-dose containers should be used only in conjunction with an automatic injector which has been approved for multipatient use.
After each patient, the connector between the injector and the patient should be replaced. All other devices should be replaced following the injector manufacturer’s instructions. In any case, strictly follow the manufacturer’s instructions.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 18920/0042

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

14/11/2018

10. DATE OF REVISION OF THE TEXT

12/11/2021

1. NAME OF THE MEDICINAL PRODUCT

Iomeron 400, solution for injection, multi-dose container

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains 81.65% w/v of Iomeprol equivalent to 40% iodine or 400 mg iodine/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A clear colourless to pale yellow solution supplied in glass multi-dose container.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium used for computed tomography enhancement, including CTA (CT Angiography).

4.2 Posology and method of administration

computed tomography		
body	adults	40 - 150ml max 250ml
	children	*

* According to body size and age

In elderly patients the lowest effective dose should be used.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and special precautions for use

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Extreme caution during injection of contrast media is necessary to avoid extravasation.

A normal diet should be maintained until the patient refrains from eating 2 hours before the procedure.

Hydration
Any severe disorders of water and electrolyte balance must be corrected prior to administration. Adequate hydration must be ensured particularly in patients with diabetes mellitus, polyuria, oliguria and hyperuricaemia; also in babies, small children and the elderly. Rehydration prior to use of Iomeprol is recommended in patients with sickle cell disease.

Special population
Hypersensitivity to iodinated contrast media, allergic predisposition
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatment**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1-antihistamines H_2-antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen iv fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2-blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

Hypersensitivity testing
In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.

Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. The benefits of the use of a contrast-enhanced procedure should be carefully weighed against the possible risk. Adequate hydration and monitoring of renal function are recommended after CM administration.

Cardiovascular diseases
Care should be taken in patients with severe cardiac disease particularly heart failure and coronary artery disease. Cardiac manifestations may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias. In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased.

The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests.

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders
Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated.

There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection.

Anticonvulsant therapy should not be discontinued.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CMS disorders. There is a possibility of a reduced seizure threshold in alcoholics

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intravascular administration. Premedication with an alpha and beta receptor-blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal failure
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters, before re-examining the patient with a contrast media.

Preventive measures include:

- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys;
- avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;

A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary.

Diabetes mellitus
Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Children: Infants up to 1 year, especially the newborn, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used.
Transient hypothyroidism may occur in neonates when the mother or the neonate has received an
iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates
7-10 days and 1 month after exposure to Iomeron especially in preterm neonates.

Elderly:
The elderly are at special risk of reactions due to reduced physiological functions, especially when high dosage of contrast media is used. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people.

Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

4.5 Interaction with other medicinal products and other forms of interaction

Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to Iomeprol.
Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenothiazine derivatives should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure.

It has been reported that cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium and take precautions. Metformin should be stopped from time of contrast medium administration. After the procedure the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

Pregnancy
Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of Iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.
Since, wherever possible, exposure to radiation should be avoided during pregnancy, the benefits of any X ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk.

Breastfeeding
No human data exist concerning the excretion of Iomeprol in breast milk. Animal studies have demonstrated that the excretion of Iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.

Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

4.8 Undesirable effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to

15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death.
These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials among 4,903 adult patients and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class.
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,515.

Adults

System Organ Class	**Adverse Reactions**			
	Clinical Trials			**Post-marketing Surveillance**
	Common (≥1/100 t o <1/10)	**Uncommon (≥1/1000 to <1/100)**	**Rare (≥1/10,000 to <1/1000)**	**Frequency unknown***
Blood and lymphatic system disorders				Thrombocytopenia, Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack Paralysis Syncope Convulsion Loss of consciousness

				Dysarthria Paraesthesia Amnesia Somnolence Taste abnormality
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block Extrasystoles Palpitations Cyanosis
Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Hot flush Flushing Pallor
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Hyperventilation Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement
Skin and subcutaneous		Erythema	Rash	Acute generalized

tissue disorders		Urticaria Pruritus		exanthematous pustulosis Angioedema Cold sweat Sweating increased
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				Renal failure
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Fatigue Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4515 patients, best estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.
** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iomeprol injection.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 167 patients.

The Iomeprol safety profile is similar in children and adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary/ intrathecal contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered Iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of Iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and Iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

5.3 Preclinical Safety Data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that Iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

trometamol
hydrochloric acid
water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

Five years
The maximum use time after a bottle stopper has been pierced is 10 hours.

6.4 Special precautions for storage

Store below 30°C
Protect from light

6.5 Nature and contents of containers

Colourless type I or type II glass bottles with chlorobutyl or bromobutyl rubber stopper/aluminium cap containing 500 ml of solution.
Boxes of 1, 5 and 6 bottles.

6.6 Special precautions for disposal and other handling

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discolored or particulate matter is present. The stopper should be pierced only once. The use of proper withdrawal cannulas for piercing the stopper and drawing up the contrast medium is recommended.
Multi-dose containers should be used only in conjunction with an automatic injector which has been approved for multipatient use.
After each patient, the connector between the injector and the patient should be replaced. All other devices should be replaced following the injector manufacturer's instructions. In any case, strictly follow the manufacturer's instructions.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

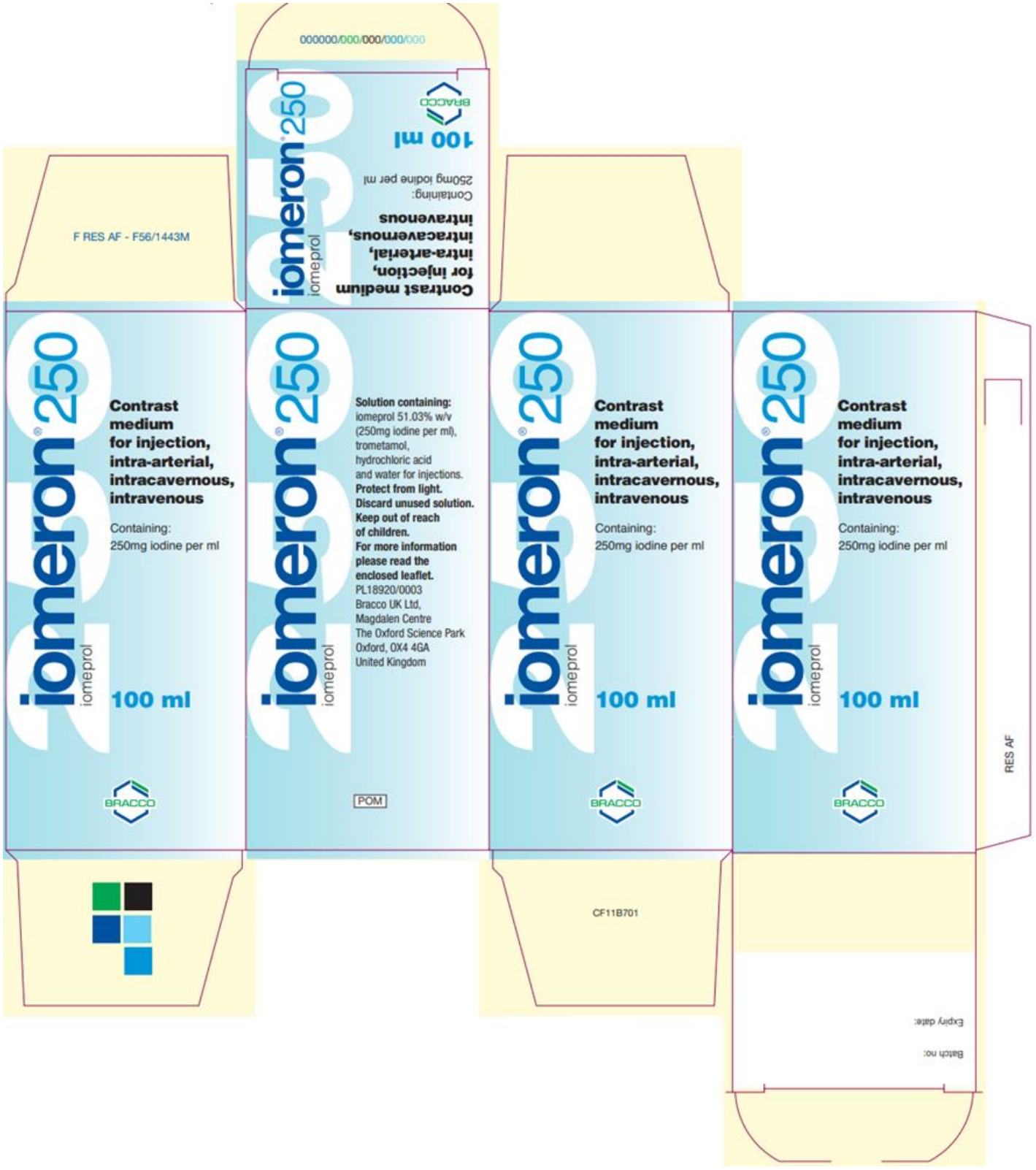
PL 18920/0043

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

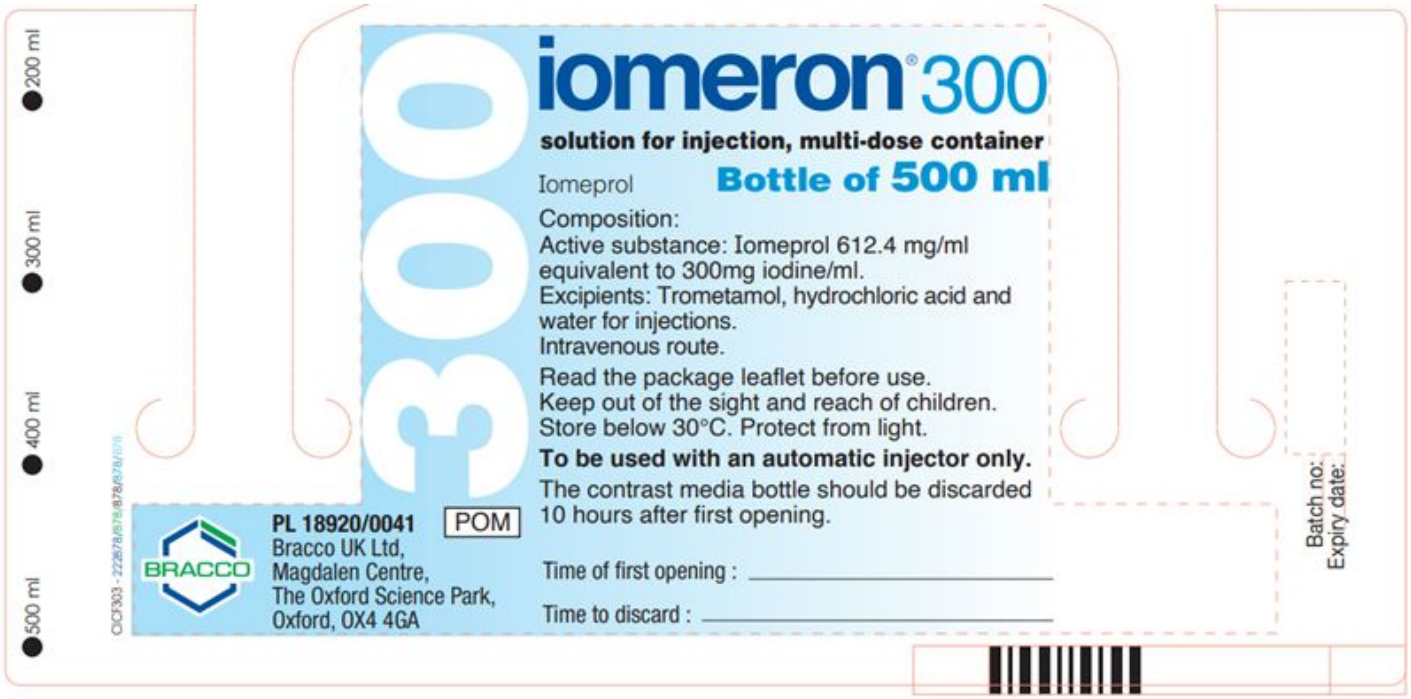
14/11/2018

10. DATE OF REVISION OF THE TEXT

12/11/2021


000000/000/000/000/000
F RES AF - F56/1443M
iomeron 250
iomeprol
Contrast medium for injection, intra-arterial, intracavernous, intravenous
Containing:
250mg iodine per ml
100 ml
BRACCO
Solution containing:
iomeprol 51.03% w/v
(250mg iodine per ml),
trometamol,
hydrochloric acid
and water for injections.
Protect from light.
Discard unused solution.
Keep out of reach
of children.
For more information
please read the
enclosed leaflet.
PL18920/0003
Bracco UK Ltd,
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom
POM
CF11B701
RES AF
Batch no:
Expiry date:


75
50
25
300
iomeron 300
iomeprol
POM
100 ml
iomeron 300
iomeprol
Solution for injection containing iomeprol 61.24% w/v (300mg I/ml), trometamol, hydrochloric acid and water for injections.
Protect from light. Discard unused solution.
Keep out of reach of children.
PL18920/0004
Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
BRACCO
Batch n:
Exp:
Batch n:
iomeron 300 100 ml
Batch n:
iomeron 300 100 ml
CE01OE03 - 222897/897/897/897/897


200 ml
300 ml
400 ml
500 ml
300
iomeron 300
solution for injection, multi-dose container
Iomeprol
Bottle of 500 ml
Composition:
Active substance: Iomeprol 612.4 mg/ml equivalent to 300mg iodine/ml.
Excipients: Trometamol, hydrochloric acid and water for injections.
Intravenous route.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Store below 30°C. Protect from light.
To be used with an automatic injector only.
The contrast media bottle should be discarded 10 hours after first opening.
Time of first opening : _____
Time to discard : _____
PL 18920/0041
POM
Bracco UK Ltd,
Magdalen Centre,
The Oxford Science Park,
Oxford, OX4 4GA
BRACCO
Batch no:
Expiry date:
CO303 - 222878/878/878/878/878


F RES AZ1 - F58/5848ZA
iomeron 350
iomeprol
Contrast medium for injection, intra-arterial, intraductal, intraluminal, intravenous
Containing:
350mg iodine per ml
200 ml
BRACCO
Solution containing:
iomeprol 71.44% w/v
(350mg iodine per ml),
trometamol, hydrochloric acid
and water for injections.
Protect from light.
Discard unused solution.
Keep out of reach of children.
For more information please
read the enclosed leaflet.
PL 18920/0005
Bracco UK Ltd,
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA
United Kingdom
POM
CA009203
Batch no:
Expiry date:

200 ml
300 ml
400 ml
500 ml

350

iomeron® 350

solution for injection, multi-dose container

Iomeprol

Bottle of 500 ml

Composition:
Active substance: Iomeprol 714.4 mg/ml equivalent to 350mg iodine/ml.
Excipients: Trometamol, hydrochloric acid and water for injections.
Intravenous route.

Read the package leaflet before use.
Keep out of the sight and reach of children.
Store below 30°C. Protect from light.

To be used with an automatic injector only.

The contrast media bottle should be discarded 10 hours after first opening.

Time of first opening : _____

Time to discard : _____

CIC3703 - 000000/000/000/000/000/000

BRACCO

PL 18920/0042
Bracco UK Ltd,
Magdalen Centre,
The Oxford Science Park,
Oxford, OX4 4GA

POM

Batch no:
Expiry date:

100
50

400

iomeron® 400

iomeprol

POM

200 ml

iomeprol
iomeron® 400

Solution for injection containing iomeprol 81.65% w/v (400mg I/ml), trometamol, hydrochloric acid and water for injections.

Protect from light. Discard unused solution.

Keep out of reach of children.

PL18920/0006

Bracco UK Ltd
Magdalen Centre
The Oxford Science Park
Oxford, OX4 4GA

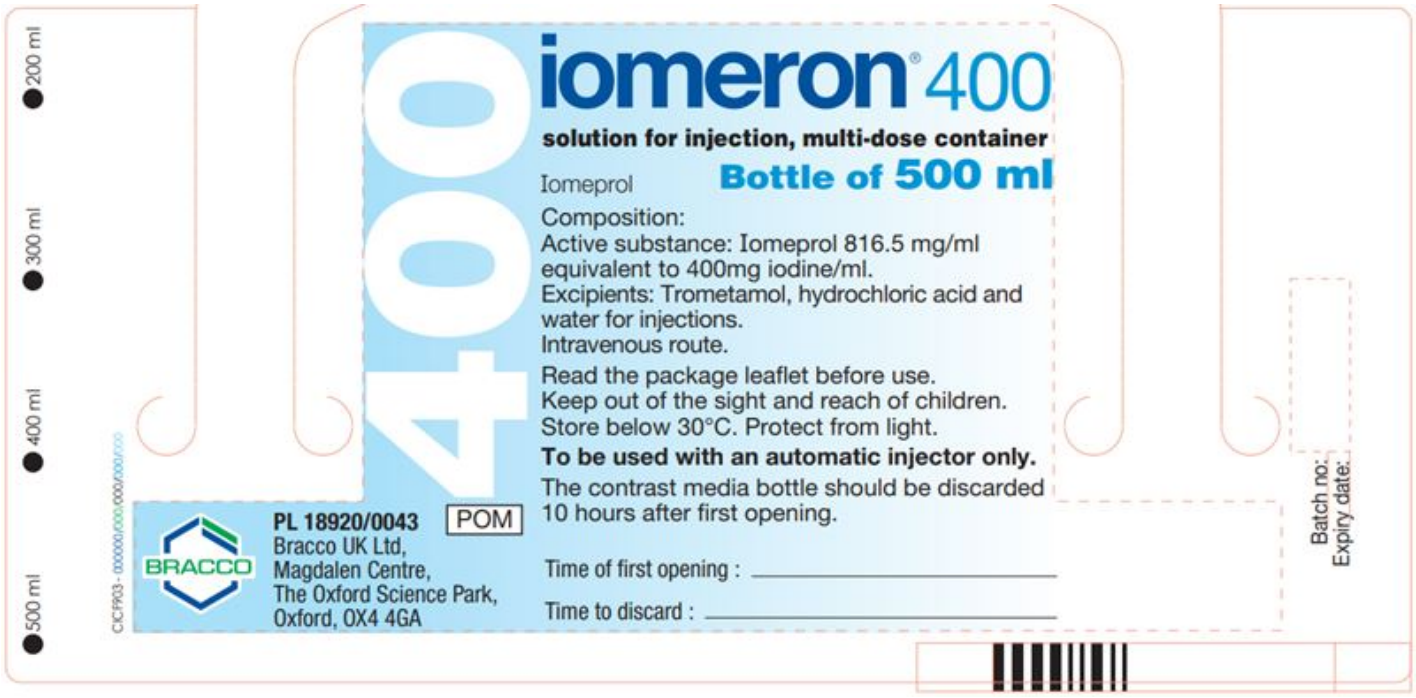
BRACCO

Batch n:
Exp.:

Batch n:
iomeron® 400 200 ml

Batch n:
iomeron® 400 200 ml

CE01OM03 - 222904/904/904/904/904



IOMERON

iomeprol injection injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-7250
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	510 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics			
Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-7250-10	56 in 1 BOX	07/01/2022	
1		100 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

IOMERON

iomeprol injection injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-7300
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	612 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-7300-10	56 in 1 BOX	07/01/2022	
1		100 mL in 1 BOTTLE, GLASS; Type 0: Not a		

1		Combination Product		
2	NDC:0270-7300-20	10 in 1 BOX	07/01/2022	
2		200 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

IOMERON

iomeprol injection injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-7350
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	714 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-7350-10	56 in 1 BOX	07/01/2022	
1		100 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
	NDC:0270			

2	NDC:0270-7350-15	30 in 1 BOX	07/01/2022	
2		150 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
3	NDC:0270-7350-20	10 in 1 BOX	07/01/2022	
3		200 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

IOMERON

iomeprol injection injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-7400
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	816 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-7400-10	10 in 1 BOX	07/01/2022	

1		100 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
2	NDC:0270-7400-13	56 in 1 BOX	07/01/2022	
2		100 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
3	NDC:0270-7400-16	100 in 1 BOX	07/01/2022	
3		100 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
4	NDC:0270-7400-20	30 in 1 BOX	07/01/2022	
4		200 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

IOMERON

iomeprol injection injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-9300
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	612 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-9300-06	6 in 1 BOX	07/01/2022	
1		500 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

IOMERON

iomeprol injection injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-9350
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	714 mg in 1 mL

Inactive Ingredients	
Ingredient Name	Strength
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics			
Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-9350-06	6 in 1 BOX	07/01/2022	

1		500 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
2	NDC:0270-9350-09	9 in 1 BOX	07/01/2022	
2		500 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

IOMERON

iomeprol injection injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0270-9400
Route of Administration	INTRAVASCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOMEPROL (UNII: 17E17JBP8L) (IOMEPROL - UNII:17E17JBP8L)	IOMEPROL	816 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
TROMETHAMINE (UNII: 023C2WHX2V)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0270-9400-01	9 in 1 BOX	07/01/2022	
1		500 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

2	NDC:0270-9400-03	9 in 1 BOX	07/01/2022	
2		500 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		
3	NDC:0270-9400-06	6 in 1 BOX	07/01/2022	
3		500 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Unapproved drug for use in drug shortage		07/01/2022	

Labeler - BRACCO DIAGNOSTICS INC (849234661)

Registrant - BRACCO DIAGNOSTICS INC (849234661)

Establishment

Name	Address	ID/FEI	Business Operations
BioChem Labor für biologishe und chemische Analytik GmbH		318354230	ANALYSIS(0270-7300, 0270-7350, 0270-7250, 0270-9400, 0270-9300, 0270-7400, 0270-9350)

Establishment

Name	Address	ID/FEI	Business Operations
SPIN S.p.A.		434967237	API MANUFACTURE(0270-9350, 0270-7250, 0270-7400, 0270-9400, 0270-7350, 0270-9300, 0270-7300)

Establishment

Name	Address	ID/FEI	Business Operations
Patheon Italia S.p.A		434078638	MANUFACTURE(0270-9300, 0270-9350, 0270-7350, 0270-9400, 0270-7250, 0270-7300, 0270-7400) , ANALYSIS(0270-7300, 0270-7350, 0270-7250, 0270-9400, 0270-9300, 0270-7400, 0270-9350)

Establishment

Name	Address	ID/FEI	Business Operations
BIPSO GmbH		342104149	MANUFACTURE(0270-9300, 0270-9350, 0270-7350, 0270-9400, 0270-7250, 0270-7300, 0270-7400) , ANALYSIS(0270-7350, 0270-7300, 0270-9400, 0270-7250, 0270-9300, 0270-7400, 0270-9350)