

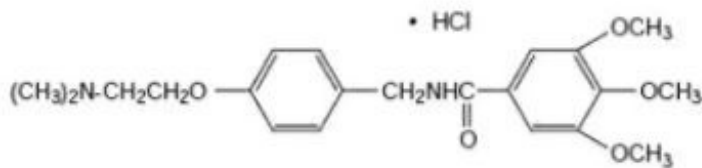
TIGAN- trimethobenzamide hydrochloride injection

General Injectables & Vaccines, Inc

Tigan 100 mg/mL Injection 2 mL Single Dose Vial

Description

Chemically, trimethobenzamide HCl is N-[p-[2-(dimethylamino)ethoxy]benzyl]-3,4,5-trimethoxybenzamide monohydrochloride. It has a molecular weight of 424.93 and the following structural formula:



Single-Dose Vials: Each 2-mL single-dose vial contains 200 mg trimethobenzamide hydrochloride compounded with 1 mg sodium

citrate and 0.4 mg citric acid as buffers and pH adjusted to approximately 5.0 with sodium hydroxide.

Multi-Dose Vials: Each mL contains 100 mg trimethobenzamide hydrochloride compounded with 0.45% phenol as preservative, 0.5 mg sodium citrate and 0.2 mg citric acid as buffers and pH adjusted to approximately 5.0 with sodium hydroxide.

Clinical Pharmacology

Mechanism of Action

The mechanism of action of Tigan® as determined in animals is obscure, but may involve the chemoreceptor trigger zone (CTZ), an area in the medulla oblongata through which emetic impulses are conveyed to the vomiting center; direct impulses to the vomiting center apparently are not similarly inhibited. In dogs pretreated with trimethobenzamide HCl, the emetic response to apomorphine is inhibited, while little or no protection is afforded against emesis induced by intragastric copper sulfate.

Pharmacokinetics

The pharmacokinetics of trimethobenzamide have been studied in healthy adult subjects. Following administration of 200 mg (100 mg/mL) Tigan I.M. injection, the time to reach maximum plasma concentration (T_{max}) was about half an hour, about 15 minutes longer for Tigan 300 mg oral capsule than an I.M. injection. A single dose of Tigan 300 mg oral capsule provided a plasma concentration profile of trimethobenzamide similar to Tigan 200 mg I.M. The relative bioavailability of the capsule formulation

compared to the solution is 100%. The mean elimination half-life of trimethobenzamide is 7 to 9 hours. Between 30 – 50% of a single dose in humans is excreted unchanged in the urine within 48 – 72 hours. The metabolic disposition of trimethobenzamide in humans is not known. Specifically, it is not known if active metabolites are generated in humans.

Special Populations

Age

The clearance of trimethobenzamide is not known in patients with renal impairment. However, it may be advisable to consider reduction in the dosing of trimethobenzamide in elderly patients with renal impairment considering that a substantial amount of excretion and elimination of trimethobenzamide occurs via the kidney and that elderly patients may have various degrees of renal impairment. (See **PRECAUTIONS: General and DOSAGE AND ADMINISTRATION**).

Gender

Systemic exposure to trimethobenzamide was similar between men (N=40) and women (N=28).

Race

Pharmacokinetics appeared to be similar for Caucasians (N=53) and African Americans (N=12).

Renal Impairment

The clearance of trimethobenzamide is not known in patients with renal impairment. However, it may be advisable to consider reduction in the dosing of trimethobenzamide in patients with renal impairment considering that a substantial amount of excretion and elimination of trimethobenzamide occurs via the kidney. (See **PRECAUTIONS: General and DOSAGE AND ADMINISTRATION**).

Indications

Tigan® is indicated for the treatment of postoperative nausea and vomiting and for nausea associated with gastroenteritis.

Contraindications

The injectable form of *Tigan*® is contraindicated in pediatric patients and in patients with known hypersensitivity to trimethobenzamide.

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Warnings

Tigan® may produce drowsiness. Patients should not operate motor vehicles or other dangerous machinery until their individual responses have been determined.

Usage in Pregnancy

Trimethobenzamide hydrochloride was studied in reproduction experiments in rats and rabbits and no teratogenicity was suggested.

The only effects observed were an increased percentage of embryonic resorptions or stillborn pups in rats administered 20 mg and 100 mg/kg and increased resorptions in rabbits receiving 100 mg/kg. In each study these adverse effects were attributed to one or two dams. The relevance to humans is not known. Since there is no adequate experience in pregnant or lactating women who have received this drug, safety in pregnancy or in nursing mothers has not been established.

Usage with Alcohol

Concomitant use of alcohol with *Tigan*® may result in an adverse drug interaction.

Precautions

During the course of acute febrile illness, encephalitides, gastroenteritis, dehydration and electrolyte imbalance, especially in children and the elderly or debilitated, CNS reactions such as opisthotonos, convulsions, coma and extrapyramidal symptoms have been reported with and without use of *Tigan*® (trimethobenzamide hydrochloride) or other antiemetic agents. In such disorders caution should be exercised in administering *Tigan*®, particularly to patients who have recently received other CNS-acting agents (phenothiazines, barbiturates, belladonna derivatives). Primary emphasis should be directed toward the restoration of body fluids and electrolyte balance, the relief of fever and relief of the causative disease process. Overhydration should be avoided since it may result in cerebral edema.

The antiemetic effects of *Tigan*® may render diagnosis more difficult in such conditions as appendicitis and obscure signs of toxicity due to overdosage of other drugs.

General

Adjustment of Dose in Renal Failure

A substantial route of elimination of unchanged trimethobenzamide is via the kidney. Dosage adjustment should be considered in patients with reduced renal function including some elderly patients. (See **CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION**).

Geriatric Use

Clinical studies of trimethobenzamide hydrochloride did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. Although there are studies

reported in the literature that included elderly patients greater than 65 years old with younger patients, it is not known if there are differences in efficacy or safety parameters for elderly and non-elderly patients treated with trimethobenzamide. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. (See **CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION**).

Adverse Reactions

There have been reports of hypersensitivity reactions and Parkinson-like symptoms. There have been instances of hypotension reported following parenteral administration to surgical patients. There have been reports of blood dyscrasias, blurring of vision, coma, convulsions, depression of mood, diarrhea, disorientation, dizziness, drowsiness, headache, jaundice, muscle cramps and opisthotonos. If these occur, the administration of the drug should be discontinued. Allergic-type skin reactions have been observed; therefore, the drug should be discontinued at the first sign of sensitization. While these symptoms will usually disappear spontaneously, symptomatic treatment may be indicated in some cases.

For medical advice about adverse reactions contact your medical professional. To report SUSPECTED ADVERSE REACTIONS, contact JHP at 1-866-923-2547 or MEDWATCH at 1-800-FDA-1088 (1-800-332-1088) or <http://www.fda.gov/medwatch/>.

Dosage and Administration

(See **WARNINGS** and **PRECAUTIONS**.)

Dosage should be adjusted according to the indication for therapy, severity of symptoms and the response of the patient.

Geriatric Patients

Dose adjustment such as reducing the total dose administered at each dosing or increasing the dosing interval should be considered in elderly patients with renal impairment (creatinine clearance ≤ 70 mL/min/1.73m²). Final dose adjustment should be based upon integration of clinical efficacy and safety considerations. (See **CLINICAL PHARMACOLOGY and PRECAUTIONS**).

Patients with Renal Impairment

In subjects with renal impairment (creatinine clearance ≤ 70 mL/min/1.73m²), dose

adjustment such as reducing the total dose administered at each dosing or increasing the dosing interval should be considered. (See **CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION**).

INJECTABLE, 100 mg/mL (Not for use in pediatric patients)

Usual Adult Dosage

2 mL (200 mg) t.i.d. or q.i.d. intramuscularly.

NOTE: The injectable form is intended for intramuscular administration only; it is not recommended for intravenous use.

Intramuscular administration may cause pain, stinging, burning, redness and swelling at the site of injection. Such effects may be minimized by deep injection into the upper outer quadrant of the gluteal region, and by avoiding the escape of solution along the route.

Storage

Store between 20° to 25°C (68° to 77°F).
(See USP Controlled Room Temperature.)

How Supplied

Tigan® (trimethobenzamide hydrochloride) is available as follows:

NDC 42023-119-25 100 mg/mL in 2 mL Single-Dose Vials, Pack of 25

NDC 42023-118-01 100 mg/mL in 20 mL Multi-Dose Vials, Pack of 1

Rx Only

Manufactured by:

Par Pharmaceutical

Chestnut Ridge, NY

R04/16

3000358F

OS118J-01-90-01

Sample Package Label

NDC # 52584 - 119 - 25
 ITEM# :2480294
 LOT # XXXXXXXXXX
 EXP : mm - yy

Packaged By
 General Injectables and Vaccines, Inc
 80 Summit View Lane
 Bastian, VA 24314

TIGAN (trimethobenzamide hydrochloride)
200MG/2ML
 100 MG/ML INJECTION
 2 ML SINGLE DOSE VIAL

SEE MANUFACTURER'S INSERT
 FOR COMPLETE PRODUCT AND
 PRESCRIBING INFORMATION

For Intramuscular (IM) Use Only (preferably by
 deep IM injection).
 NOT FOR USE IN CHILDREN.

Store between 20 to 25C (68 to 77F).
 (See USP Controlled Room Temperature.)

Keep out of children's reach.



MANUFACTURER INFORMATION
 Mfr: Par Pharmaceutical
 ORIG MFG LOT: XX - XXX - XX
 NDC: 42023 - 119 - 25

(10)XXXXXX
 (17)XXXXXXXX
 (01)XXXXXXXXXXXX
 (21)XXXXXXXXXXXX
 RX ONLY

TIGAN			
trimethobenzamide hydrochloride injection			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:52584-119(NDC:42023-119)
Route of Administration	INTRAMUSCULAR		
Active Ingredient/Active Moiety			
	Ingredient Name	Basis of Strength	Strength
	Trimethobenzamide Hydrochloride (UNII: WDQ5P1SX7Q) (Trimethobenzamide - UNII: W2X096QY97)	Trimethobenzamide Hydrochloride	100 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CITRATE (UNII: 1Q73Q2JULR)	0.5 mg in 1 mL
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	0.2 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:52584-119-25	1 in 1 BAG	08/01/2010	09/30/2024
1		2 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA017530	08/01/2010	09/30/2024

Labeler - General Injectables & Vaccines, Inc (108250663)

Revised: 12/2022

General Injectables & Vaccines, Inc