

ZANOSAR- streptozocin powder, for solution ESTEVE PHARMACEUTICALS, S.A.

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.

Zanosar (Streptozocin) powder, for injection (Esteve SAS)

Dear Health Care Provider Letter

DocuSign Envelope ID: 2664E376-5BB7-45CB-A51D-7538B8F9FA09



March 2023, 31st

Subject: Temporary importation of non-FDA approved Zanosar® (Streptozocin powder for concentrate for solution for infusion) to address shortage

Dear Healthcare Professional,

Due to a critical shortage of Zanosar® 1g (streptozocin sterile powder) in the United States, Esteve Pharmaceuticals S.A.S (Esteve), in coordination with the U.S. Food and Drug Administration (FDA) intends to temporarily import non-FDA-approved Zanosar® (Streptozocin powder for concentrate for solution for infusion, dosage of 1g for single-use per vial) for U.S. patient use. Imported non-FDA approved Zanosar® (Streptozocin powder for concentrate for solution for infusion) is labeled in English and currently marketed in the European Union and United Kingdom. **It is important to note that although both the FDA-approved product and Esteve product share the same brand name Zanosar®, they are different as noted in the below comparison table.**

Dosage schedules requirements for the imported, non-FDA-approved Zanosar® (Streptozocin powder for concentrate for solution for infusion), are the same as the FDA-approved Zanosar® (streptozocin sterile powder). **In this regard, please keep referring to the FDA-approved package insert for dosage information.**

Storage requirement for the imported, non-FDA-approved Zanosar® (Streptozocin powder for concentrate for solution for infusion) is 2°C to 8°C in a refrigerator.

Zanosar's® therapeutic indication is the same in the European and FDA-approved products (treatment of patients with advanced pancreatic carcinoma), however the wording is different.

Table of Important Differences Between FDA-approved Zanosar and unapproved imported product		
	U.S Product	Imported Product
Pharmaceutical form	Sterile powder	Powder for concentrate for solution for infusion
Marketing Authorization number	NDC 00703-4636-01	PL 40308/0001

Esteve Pharmaceuticals SAS

Immeuble Cap Sud 106, avenue Marx-Dormoy, 92120 Montrouge, France

T. + 33 (0)1 42 31 07 10 F. +33 (0)1 42 31 23 79

S.A.S au capital de 1 512 720 euros R.C.S. Nanterre 492 846 357

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Table of Important Differences Between FDA-approved Zanosar and unapproved imported product		
	U.S Product	Imported Product
Container label	<p> ■ Process Black (Top & Bar) ■ PMS 5/5 (Color Bar) ■ Pantone Green (Teva Color) </p>	
Shelf life	18 months	36 months
Indication	ZANOSAR is indicated in the treatment of metastatic islet cell carcinoma of the pancreas. Responses have been obtained with both functional and nonfunctional carcinomas. Because of its inherent renal toxicity, therapy with this drug should be limited to patients with symptomatic or progressive metastatic disease.	ZANOSAR is indicated for the systemic treatment of adult patients with inoperable, advanced or metastatic, progressive and/or symptomatic, well-differentiated, G1 or G2 neuroendocrine tumours of pancreatic origin, in combination with 5-Fluorouracil.
Administration	ZANOSAR sterile powder should be administered intravenously by rapid injection or short/prolonged infusion. It is not active orally. Although it has been administered intraarterially, this is not recommended pending further evaluation of the possibility that adverse renal effects may be evoked more rapidly by this route of administration.	ZANOSAR should be administered intravenously by infusion. The duration of infusion should be between 30 minutes and 4 hours. The administration of ZANOSAR requires hyperhydration. This medicinal product is vesicant in nature and as such should be administered with caution through a free-flowing line. In case of extravasation, administration should be stopped immediately. Healthcare professionals should take appropriate protection measures. The

	appropriate protection measures. The initial aim is to minimize the volume of extravasated product into the surrounding tissues and to aspirate as much as possible product from the canula with a syringe. Cold packs should be applied and appropriate medical monitoring should be performed.
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Table of Important Differences Between FDA-approved Zanosar and unapproved imported product		
	U.S Product	Imported Product
Instruction for reconstitution	Reconstitute ZANOSAR with 9.5 mL of dextrose injection, USP, or 0.9% sodium chloride injection, USP. The resulting pale-gold solution will contain 100 mg of streptozocin and 22 mg of citric acid per mL.	Each 20 mL vial of Zanosar must be reconstituted with 9.5 mL of sodium chloride 9 mg/ml (0.9%) solution for injection.
Reconstituted solution storage conditions	The total storage time for streptozocin after it has been placed in solution should not exceed 12 hours	The reconstituted solution should be immediately diluted. The chemical and physical in-use stability of the resulting solution has been demonstrated for 24 hours below 25°C in polyethylene Ecoflac® type bag containing a sodium chloride 9 mg/ml (0.9%) solution for injection.

Other Differences:

The barcode on the imported product label may not register accurately on U.S. scanning systems. Institutions should manually input the imported product information into their systems and confirm that the barcode, if scanned, provides correct information. Alternative procedures should be followed to assure that the correct drug product is being used and administered to individual patients.

In addition, the packaging of the imported product does not include serialization information. Esteve Zanosar® (Streptozocin powder for concentrate for solution for infusion) does not meet the Drug Supply Chain Security Act (DSCSA) requirements for the Interoperable Exchange of Information for Tracing of Human, Finished Prescription Drugs.

For your information, on the packaging (sticker, carton and leaflet), Keocyt is mentioned as the Marketing Authorization Holder instead of Esteve Pharmaceuticals S.A.S. Indeed, on January 17, 2022, the name change of the pharmaceutical company Keocyt has been amended to Esteve Pharmaceuticals S.A.S.

If you have any questions about the information contained in this letter, please contact us at:

ESTEVE medical inquiries department at contact-france@esteve.com.

Any quality problems or claims may be reported also by email to contact-france@esteve.com.

Any adverse events or any event related to safety associated with the use of non-FDA approved Zanosar® (Streptozocin powder for concentrate for solution for infusion) should be reported by email to pharmacovigilance@esteve.com.

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Adverse events or quality problems experienced with the use of this product may also 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 preaddressed form or submit by fax to 1-800-FDA-0178.

Yours faithfully,

Signature of authorized person:

DocuSigned by:

5A1C7835E2F7432...

Neus Gascón

Head of Drug Safety and Pharmacovigilance/ EUQPPV


31-03-2023

Esteve Pharmaceuticals SAS
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How supplied

NDC 68118-100-01: Each vial contains 1g Streptozocin Powder for concentrate for solution for infusion. Each carton contains 1 vial.

Vial Label



100, Rue Général de Gaulle
76520 FRANQUEVILLE SAINT PIERRE
Tél. : +33 (0)2 32 86 52 52
Fax : +33 (0)2 32 86 52 51

Description Produit n° 411382

Format (laize x développé) : 30 x 70

Client :
108650
VALDEPHARM SA

Ref client : 005P2180101
ETQ FL ZANOSAR 1g UNITED KINGDOM

APPROUVÉ
Par Neveu Sandrine , 11:37, 10/06/2021

APPROUVÉ
Par KOUBBI Eugénie , 11:47, 10/06/2021

10-Jun-21 - 08:24:33 MC-SN


Bon à Tirer n° 1

Signature client :
Date

ATTENTION PARTICULIÈRE :

- En signant ce BAT, vous validez : **TEXTES, CODES À BARRES (lisibilité et numéros), RÉFÉRENCES COULEURS.** Ce document n'est pas contractuel pour la colorimétrie.
- Si vos fichiers d'exécution n'étaient pas accompagnés d'éléments de contrôle, nous attirons votre attention sur la possibilité que ce BAT ne respecte pas vos souhaits initiaux.
- En signant la **FICHE DE DONNÉES TECHNIQUES**, vous validez les éléments techniques de l'étiquette.
- Afin de lancer votre dossier en production, merci de nous retourner impérativement le BAT et la fiche de données techniques signés.

Format 100.0%



DECOUPE HEX Magenta PrK

Carton Label



CLIENT : VALDEPHARM

PRODUIT : ZANOSAR 1g UK

N° code produit : 005S5135100

Adresse Cx : V 1485 04

DATE : 22/10/2018

**OPERATEUR :
Sylvie DELORME**

**VALIDE PAR :
Jacqueline CHAUVEAU**

Nelly THOUSEAU

EPREUVE N°1

BON A TIRER

Validation client :

CARTONEX

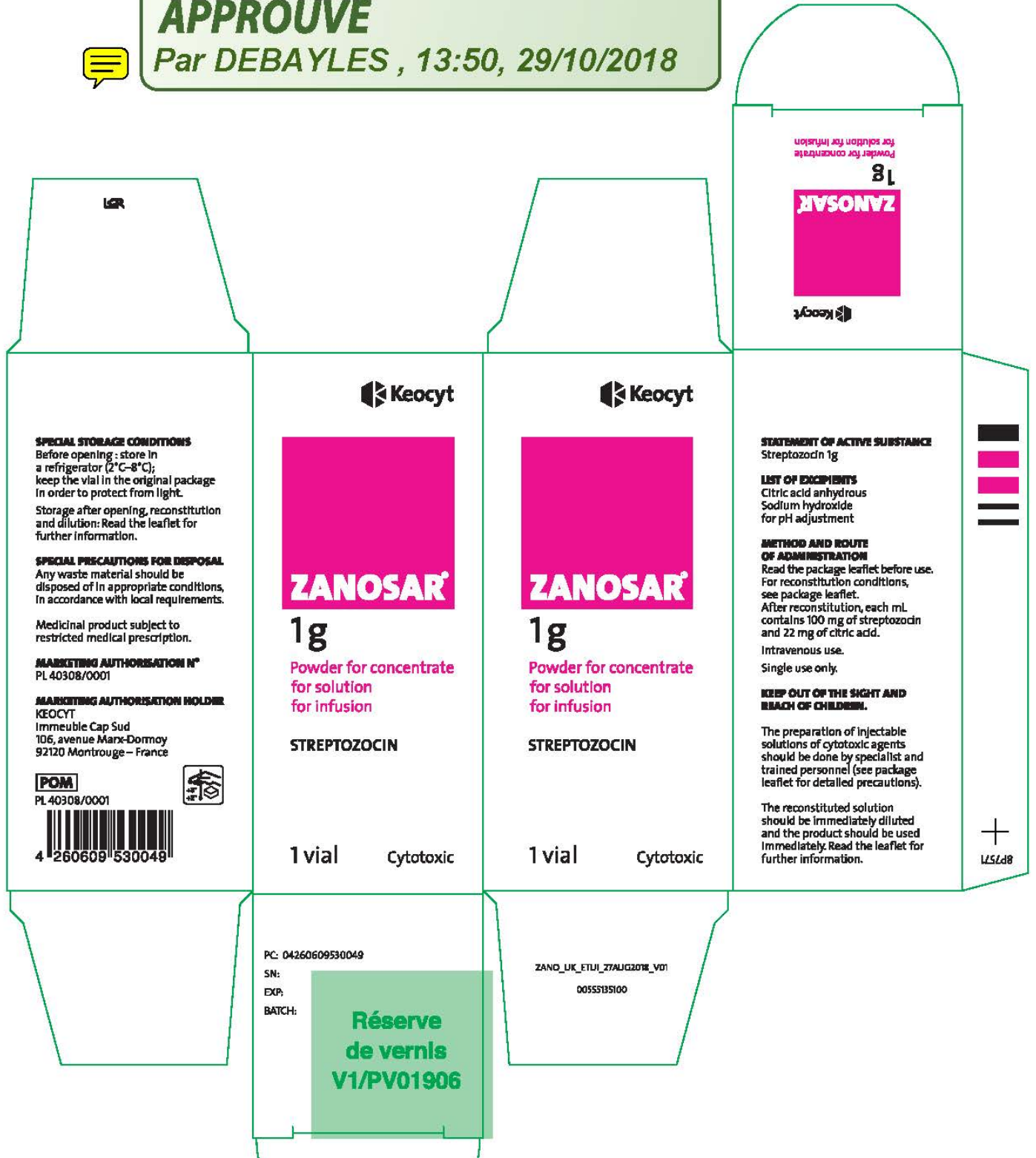
COULEURS : ● DECOUPE ● NOIR ● MAGENTA
+ Réserve de vernis V1/PV01906

CE DOCUMENT A VALEUR D'EPREUVE DE LECTURE DES TEXTES ET DE POSITIONNEMENT DES COULEURS. LES COULEURS DU TIRAGE SONT REFERENCIES SELON LES COULEURS PANTONE MENTIONNEES CI-DESSUS

Format étui : 35x38x82mm

APPROUVÉ

Par DEBAYLES , 13:50, 29/10/2018





ZANOSAR

streptozocin powder, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:68118-100
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
STREPTOZOCIN (UNII: 5W494URQ81) (STREPTOZOCIN - UNII:5W494URQ81)	STREPTOZOCIN	1 g in 10 mL

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68118-100-01	1 in 1 CARTON	02/01/2023	
1		10 mL in 1 VIAL, 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		02/01/2023	

Labeler - ESTEVE PHARMACEUTICALS, S.A. (460023922)

Revised: 4/2023

ESTEVE PHARMACEUTICALS, S.A.