

ERGOMAR SUBLINGUAL- ergotamine tartrate tablet
TerSera Therapeutics, LLC

Ergomar® Sublingual Tablets, 2 mg

(Ergotamine Tartrate Sublingual Tablets, USP)

Rx Only

WARNING

Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of ergotamine tartrate with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3A4 inhibition elevates the serum levels of ergotamine tartrate, the risk for vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased. Hence, concomitant use of these medications is contraindicated. (See also CONTRAINDICATIONS and WARNINGS section)

DESCRIPTION:

Ergomar® Sublingual Tablets

Ergotamine Tartrate Sublingual Tablets USP ... 2 mg

Inactive Ingredients: Microcrystalline Cellulose NF, Natural Peppermint Flavor Powder, Crospovidone NF, Saccharin Sodium USP Powder, D&C Yellow #10 Lake, Magnesium Stearate NF, FD&C Blue #1 Aluminum Lake.

CLINICAL PHARMACOLOGY:

Ergotamine is an alpha adrenergic blocking agent with a direct stimulating effect on the smooth muscle of peripheral and cranial blood vessels and produces depression of central vasomotor centers. The compound also has the properties of serotonin antagonism. In comparison to hydrogenated ergotamine, the adrenergic blocking actions are less pronounced and vasoconstrictive actions are greater.

Pharmacokinetics: Interactions

Pharmacokinetic interactions (increased blood levels of ergotamine) have been reported in patients treated orally with ergotamine and macrolide antibiotics (e.g., troleandomycin, clarithromycin, erythromycin), and in patients treated orally with ergotamine and protease inhibitors (e.g., ritonavir) presumably due to inhibition of cytochrome P450 3A metabolism of ergotamine (See **CONTRAINDICATIONS**). Ergotamine has also been shown to be an inhibitor of cytochrome P450 3A catalyzed reactions. No pharmacokinetic interactions involving other cytochrome P450 isoenzymes are known.

INDICATIONS AND USAGE

Ergomar[®] is indicated as therapy to abort or prevent vascular headache, e.g., migraine, migraine variants or so-called "histaminic cephalgia".

CONTRAINDICATIONS

Coadministration of ergotamine with potent CYP 3A4 inhibitors (ritonavir, nelfinavir, indinavir, erythromycin, clarithromycin and troleandomycin) has been associated with acute ergot toxicity (ergotism) characterized by vasospasm and ischemia of the extremities (See **PRECAUTIONS: Drug Interactions**), with some cases resulting in amputation. There have been rare reports of cerebral ischemia in patients on protease inhibitor therapy when ergotamine was coadministered, at least one resulting in death. Because of the increased risk for ergotism and other serious vasospastic adverse events, ergotamine use is contraindicated with these drugs and other potent inhibitors of CYP 3A4 (e.g., ketoconazole, itraconazole) (See **WARNINGS: CYP 3A4 Inhibitors**).

Ergomar[®] Sublingual Tablets may cause fetal harm when administered to pregnant women. Ergomar[®] Sublingual Tablets are contraindicated in women who are or may become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this product, the patient should be apprised of the potential hazard to the fetus. Peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function and sepsis.

Hypersensitivity to any of the components.

WARNINGS

CYP 3A4 Inhibitors (e.g., Macrolide Antibiotics and Protease Inhibitors)

Coadministration of ergotamine with potent CYP 3A4 inhibitors such as protease inhibitors or macrolide antibiotics has been associated with serious adverse events; for this reason, these drugs should not be given concomitantly with ergotamine (See **CONTRAINDICATIONS**). While these reactions have not been reported with less potent CYP 3A4 inhibitors, there is a potential risk for serious toxicity including vasospasm when these drugs are used with ergotamine. Examples of less potent CYP 3A4 inhibitors include: saquinavir, nefazodone, fluconazole, fluoxetine, grapefruit juice, fluvoxamine, zileuton, metronidazole, and clotrimazole. These lists are not exhaustive, and the prescriber should consider the effects on CYP 3A4 of other agents being considered for concomitant use with ergotamine.

Fibrotic Complications

There have been a few reports of patients on ergotamine tartrate and caffeine therapy developing retroperitoneal and/or pleuropulmonary fibrosis. There have also been rare reports of fibrotic thickening of the aortic, mitral, tricuspid, and/or pulmonary valves with long-term continuous use of ergotamine tartrate and caffeine. Ergomar[®] Sublingual Tablets should not be used for chronic daily administration (See **DOSAGE AND ADMINISTRATION**).

PRECAUTIONS

General

Although signs and symptoms of ergotism rarely develop even after long term intermittent use of the drug, care should be exercised to remain within the limits of recommended dosage. Ergotism is manifested by intense arterial vasoconstriction, producing signs and symptoms of peripheral vascular ischemia. Ergotamine induces vasoconstriction by a direct action on vascular smooth muscle. In chronic intoxication with ergot derivatives, headache, intermittent claudication, muscle pains, numbness, coldness and pallor of the digits may occur. If the condition is allowed to progress untreated, gangrene can result. While most cases of ergotism associated with ergotamine treatment result from frank overdosage, some cases have involved apparent hypersensitivity. There are few reports of ergotism among patients taking doses within the recommended limits or for brief periods of time. In rare instances, patients, particularly those who have used the medication indiscriminately over long periods of time, may display withdrawal symptoms consisting of rebound headache upon discontinuation of the drug.

Information for Patients

Patients should be advised that one Ergomar[®] Sublingual Tablet should be taken at the first sign of a migraine headache. No more than 2 tablets should be taken for any single migraine attack. No more than 5 tablets should be taken during any 7-day period. Administration of Ergomar[®] Sublingual Tablets should not exceed the dosing guidelines and should not be used for chronic daily administration (See **DOSAGE AND ADMINISTRATION**). Ergomar[®] Sublingual Tablets should be used only for migraine headaches. It is not effective for other types of headaches and it lacks analgesic properties. Patients should be advised to report to the physician immediately any of the following: numbness or tingling in the fingers and toes, muscle pain in the arms and legs, weakness in the legs, pain in the chest or temporary speeding or slowing of the heart rate, swelling or itching.

Drug Interactions

CYP 3A4 Inhibitors (e.g., Macrolide Antibiotics and Protease inhibitors)

See CONTRAINDICATIONS and WARNINGS.

Ergomar[®] Sublingual Tablets (Ergotamine Tartrate Sublingual Tablets USP) should not be administered with other vasoconstrictors. Use with sympathomimetics (pressor agents) may cause extreme elevation of blood pressure. The beta-blocker Inderal (propranolol) has been reported to potentiate the vasoconstrictive action of ergotamine by blocking the vasodilating property of epinephrine. Nicotine may provoke vasoconstriction in some patients, predisposing to a greater ischemic response to ergot therapy. The blood levels of ergotamine-containing drugs are reported to be elevated by the concomitant administration of macrolide antibiotics and vasospastic reactions have been reported with therapeutic doses of the ergotamine-containing drugs when coadministered with these antibiotics.

Pregnancy

Teratogenic Effects

Pregnancy Category X: There are no studies on the placental transfer or teratogenicity of Ergomar[®]. Ergotamine crosses the placenta in small amounts, although it does not appear to be embryotoxic in this quantity. However, prolonged vasoconstriction of the uterine vessels and/or increased myometrial tone leading to reduced myometrial and placental blood flow may have contributed to fetal growth retardation observed in animals. (See **CONTRAINDICATIONS**)

Nonteratogenic Effects

Ergomar[®] is contraindicated in pregnancy due to its oxytocic effects of ergotamine (See **CONTRAINDICATIONS**)

Labor and Delivery

Ergomar[®] is contraindicated in pregnancy due to its oxytocic effect which is maximal in the third trimester. (See **CONTRAINDICATIONS**)

Nursing Mothers

Ergot drugs are known to inhibit prolactin but there are no reports of decreased lactation with Ergomar[®]. Ergotamine is excreted in breast milk and may cause symptoms of vomiting, diarrhea, weak pulse and unstable blood pressure in nursing infants. Because of the potential for serious adverse reactions in nursing infants from Ergomar[®], a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Cardiovascular: Vasoconstrictive complications of a serious nature may occur at times. These include ischemia, cyanosis, absence of pulse, cold extremities, gangrene, precordial distress and pain, EKG changes and muscle pains. Although these effects occur most commonly with long-term therapy at relatively high doses, they have also been reported with short-term or normal doses. Other cardiovascular adverse effects include transient tachycardia or bradycardia and hypertension.

Gastrointestinal: Nausea and vomiting.

Neurological: paresthesias, numbness, weakness, and vertigo.

Allergic: Localized edema and itching.

Fibrotic Complications: (See **WARNINGS**).

DRUG ABUSE AND DEPENDENCE

There have been reports of drug abuse and psychological dependence in patients on ergotamine tartrate therapy. Due to the chronicity of vascular headaches, it is imperative

that patients be advised not to exceed recommended dosages with long-term use to avoid ergotism. (See **PRECAUTIONS**)

OVERDOSAGE

Symptoms include vomiting, numbness, tingling, pain and cyanosis of the extremities associated with diminished or absent peripheral pulses; hypertension or hypotension; drowsiness, stupor, coma, convulsions and shock. A case has been reported of reversible bilateral papillitis with ring scotomata in a patient who received five times the recommended daily adult dose over a period of 14 days. Treatment consists of removal of the offending drug. Maintenance of adequate pulmonary ventilation, correction of hypotension, and control of convulsions and blood pressure are important considerations. Treatment of peripheral vasospasm should consist of warmth, but not heat, and protection of the ischemic limbs. Vasodilators may be beneficial but caution must be exercised to avoid aggravating an already existent hypotension.

DOSAGE AND ADMINISTRATION

Procedure

For best results, dosage should start at the first sign of an attack. Early Administration Gives Maximum Effectiveness. At the first sign of an attack or to relieve symptoms after onset of an attack, one 2 mg tablet is placed under the tongue. Another tablet should be taken at half-hour intervals thereafter, if necessary, but dosage must not exceed three tablets in any 24 hour period. **Total weekly dosage should not exceed five tablets (10 mg) in any one week. Ergomar[®] Sublingual Tablets should not be used for chronic daily administration.**

HOW SUPPLIED

Ergomar[®] Sublingual Tablets, 2 mg

(Ergotamine Tartrate Sublingual Tablets USP)

Ergomar[®] Sublingual Tablets are round, green tablets each containing 2 mg of ergotamine tartrate. They are debossed with the product identification code "LB2" on one side, and are supplied in unit-dose cartons of 20 tablets (10 tablets x 2 cards), NDC 70720-120-20.

STORE AND DISPENSE

Store at 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature]; excursions permitted to 15° - 30°C (59° - 86°F). Protect from light and heat. Keep out of reach of children.

Manufactured for:
TerSera Therapeutics LLC
Deerfield, IL 60015, USA

By: Mikart, LLC
Atlanta, GA 30318

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PRINCIPAL DISPLAY PANEL - 2 mg Tablet Blister Pack Carton

20 Tablets

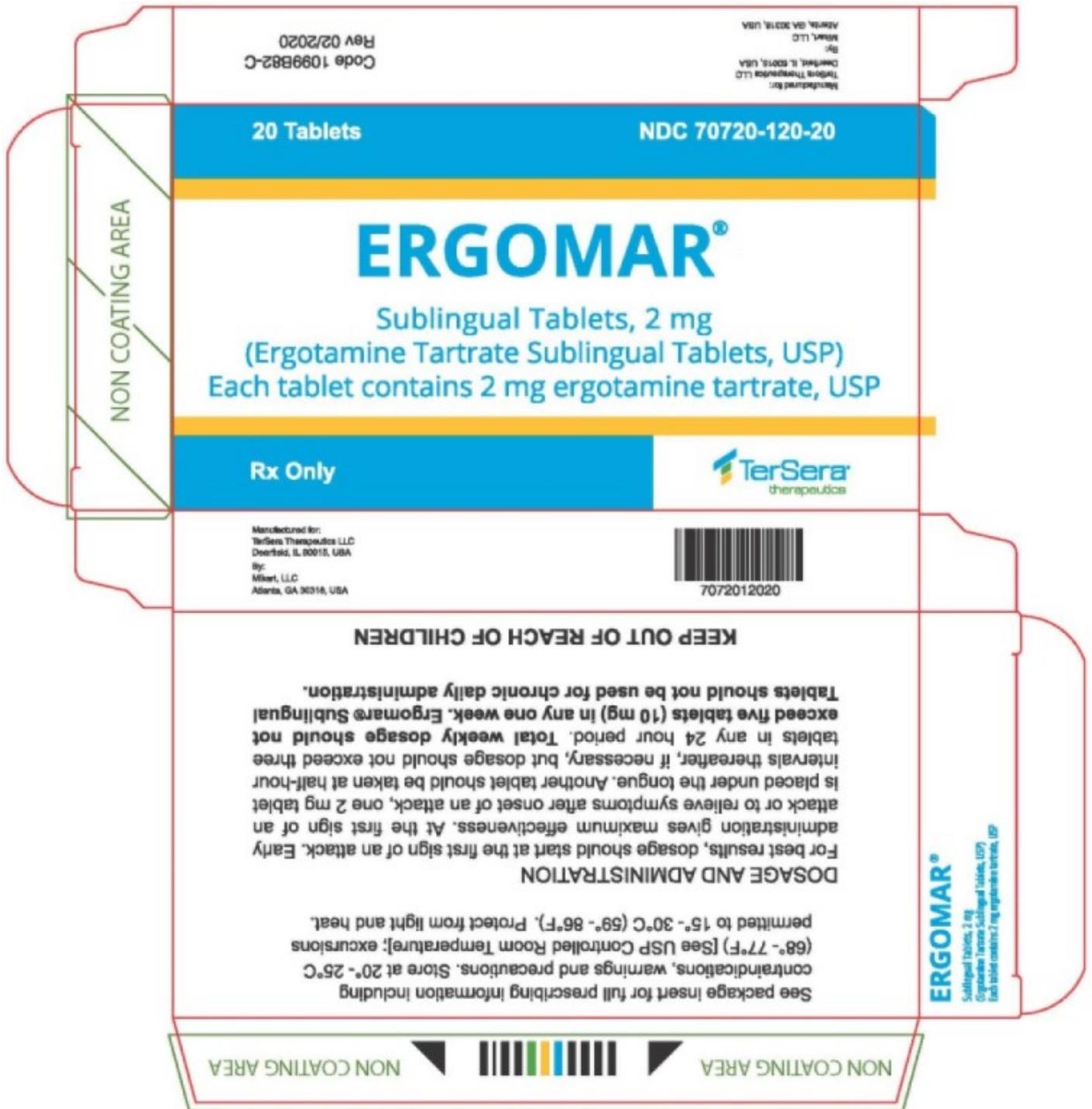
NDC 70720-120-20

ERGOMAR®

Sublingual Tablets, 2 mg
(Ergotamine Tartrate Sublingual Tablets, USP)
Each tablet contains 2 mg ergotamine tartrate, USP

Rx Only

TerSera®
therapeutics



ERGOMAR SUBLINGUAL

ergotamine tartrate tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:70720-120
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name		Basis of Strength	Strength	
Ergotamine Tartrate (UNII: MRU5XH3B48) (ERGOTAMINE - UNII:PR834Q503T)		Ergotamine Tartrate	2 mg	
Inactive Ingredients				
Ingredient Name			Strength	
Microcrystalline Cellulose (UNII: OP1R32D61U)				
Crospovidone (UNII: 2S7830E561)				
Saccharin Sodium (UNII: SB8ZUX40TY)				
Magnesium Stearate (UNII: 70097M6I30)				
FD&C Blue NO. 1 (UNII: H3R47K3TBD)				
Aluminum Oxide (UNII: LMI26O6933)				
D&C Yellow NO. 10 (UNII: 35SW5USQ3G)				
Product Characteristics				
Color	GREEN	Score	no score	
Shape	ROUND	Size	6mm	
Flavor	PEPPERMINT	Imprint Code	LB2	
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70720-120-20	2 in 1 CARTON	09/20/2016	
1		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
2	NDC:70720-120-03	1 in 1 CARTON	09/20/2016	
2		3 in 1 BLISTER PACK; Type 0: Not a Combination Product		
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
ANDA	ANDA087693	09/20/2016		

Labeler - TerSera Therapeutics, LLC (080226115)

Establishment

Name	Address	ID/FEI	Business Operations
Mikart, LLC		030034847	LABEL(70720-120) , PACK(70720-120) , MANUFACTURE(70720-120)