FAES FARMA

SUMMARY OF PRODUCT CHARACTERISTICS FOR PHARMACEUTICAL PRODUCTS

1 NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

VENOSMIL 200 MG CAPSULES

1.1 Strength

Hidrosmin 200 mg per capsule

1.2 Pharmaceutical form

Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 *Qualitative declaration*

Hidrosmin
Magnesium stearate

2.2 *Quantitative declaration*

Hidrosmin	200 mg
Magnesium stearate	2 mg

3 PHARMACEUTICAL FORM

Capsules.
Hard, orange gelatine capsules containing a fine yellow powder

4 CLINICAL PARTICULARS

4.1.*Therapeutic indications*

VENOSMIL is a medicinal product indicated for:

- Treatment of the symptoms related to slight venous insufficiency in adults.

4.2.*Posology and method of administration*

Oral way.
Once removed from the blister, the capsule must be taken immediately. It can be taken with water or another drink to aid swallowing.

Posology

Adults
One 200 mg capsule three times a day.

Paediatric population
The use of Venosmil is not recommended in children.

If symptoms do not improve in two weeks the clinical situation should be reevaluated.

Avenida Autonomía, 10
48940 Leioa (Bizkaia) España
T. +34 94 481 83 00
F. +34 94 481 83 34
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In case of necessity the treatment can be continued with the same daily dose until 2-3 months.

4.3.*Method of administration*
Oral way.

4.4.*Contraindications*
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.5.*Special warnings and precautions for use*
Patients must be advised that they must not use the medicinal product for long periods without medical supervision.

Paediatric population
The use of Venosmil is not recommended in children.

4.6. *Interaction with other medicinal products and others forms of interaction*
No specific studies have been made of possible pharmacokinetic and/or pharmacodynamic interactions between hidrosmin and other medications or foods.

4.7. *Additional information on special populations*
No additional information is provided.

4.8. *Fertility, pregnancy and lactation*
Pregnancy
No clinical data are available for Venosmil capsules and gel as regards the use of hidrosmin in pregnant women.

Animal studies have shown no direct or indirect hazardous effects on pregnancy, foetal development, delivery or postnatal development.
However, as a precautionary measure, the use of Venosmil is not recommended during pregnancy unless, in the physician's opinion, the potential benefits of its administration outweigh the possible risks.

Lactation
No clinical data are available on hidrosmin use in breastfeeding women. It is not known whether hidrosmin is excreted in human breast milk, therefore its use during breastfeeding is not recommended.

Fertility
No data are available in humans.

4.9.*Effects on ability to drive and use machines*
The influence of VENOSMIL on the ability to drive and use machines is non-existent or negligible.

FAES FARMA S.A.
Dir. Téc. Farmacéutico

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4.10. *Undesirable effects*

During the period of marketing of hidrosmin, the following undesirable effects have been reported, though their frequency has not been clearly established.

The most commonly observed undesirable effects are:

Immune system disorders: hypersensitivity (allergic) reactions to the active substance or to one of the excipients.

Nervous system disorders: headache, dizziness.

Gastrointestinal disorders: epigastric pain, nausea.

Skin and subcutaneous tissue disorders: rash, pruritus.

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 National Pharmacovigilance System for Medicinal Products for Human Use.

4.11. Overdose

No cases of overdose have been described. The good tolerance of Venosmil means that, in practice, the possibility of intoxication is non-existent, even in cases of accidental overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Capillary stabilising agents. Bioflavonoids C05CA05.

Actions

The only active substance in Venosmil is a drug known as hidrosmin which, as a result of its chemical composition, belongs to the flavonoid group. This drug is a standard mixture mainly comprising 5'- and 3'-mono-*O*-(β-hydroxyethyl)-diosmin and 5,3'-di-*O*-(β-hydroxyethyl)-diosmin.

5.1.1. Mechanism of action

Although the mechanism of action of hidrosmin has not been fully elucidated, it could be related to inhibition of the degradation of catecholamines, specifically inhibition of catechol-O-methyltransferase.

5.1.2. Pharmacodynamics effects

Although the exact mechanism of action is unknown, hidrosmin has four main pharmacological actions:

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a) It reduces the capillary permeability induced by various agents such as histamine, bradykinin, etc. and reduces the capillary fragility induced by a deficiency diet.
b) It increases the deformability of red blood cells and the viscosity of the blood.
c) It induces the contraction of smooth muscle in the vein wall in a gradual and sustained manner.
d) It produces dilation of the lymphatic collectors and increases the rate of lymphatic conduction, thereby improving lymphatic flow.

5.1.3. Clinical efficacy and safety

The efficacy of VENOSMIL was evaluated in two clinical trials in a total of 70 patients with acute and chronic venous disease, who were treated with 200 mg hidrosmin orally three times per day and/or 2 g hidrosmin topically (gel) two or three times per day for one and two months Hidrosmin was effective at reducing oedema, ulcers and varicose eczema. Venosmil therefore possesses intrinsic activity against the consequences of venous stasis secondary to varicose dilation of the veins in the lower limbs, producing an improvement in the clinical symptoms of peripheral venous insufficiency (pain, heaviness, oedema, etc.) that is significantly different to that produced by placebo.

5.2. Pharmacokinetic properties

After oral administration of single doses of hidrosmin in healthy volunteers, a biphasic curve of plasma concentrations of the product with respect to time was observed. An initial peak was observed at 15 minutes post-administration, subsequently decreasing slowly. A new increase in plasma levels was observed at 4 hours post-administration, with a stabilisation phase being achieved at between 5 and 8 hours post-administration. Plasma levels subsequently decreased, being practically undetectable at 24 hours post-administration.

Elimination of hidrosmin is relatively fast, with 90% of the dose being excreted in 48 hours. It is mainly excreted in faeces, with approximately 80% of the dose administered being eliminated via this pathway. Only 16-18% is excreted via the urine.

5.3. Preclinical safety data

After oral, intraperitoneal and intravenous administration in rat and mouse, the acute LD50 for hidrosmin is very high (>5000 mg/kg) with respect to the clinical dose (10 mg/kg/day).

In sub-acute toxicity studies (1 month), oral doses of 70, 700 and 7000 mg/kg/day in rat and oral doses of 50, 250 and 750 mg/kg/day in dog did not produce significant alterations in the various biological and anatomical/histological parameters studied that could be related to the drug.

Chronic toxicity studies with hidrosmin (6 months) did not show that the product produced any significant alteration in rat or dog administered oral doses of 50, 500, 2500 mg/kg/day and 25, 125 mg/kg/day, respectively.

No signs of teratogenicity or embryotoxicity were observed in teratogenicity studies in rabbit, rat and mouse at doses of 3-150, 6-600 and 50-200 times the clinically recommended therapeutic range, respectively.

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6 PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Magnesium stearate

The gelatine capsule comprises gelatine, erythrosine (E-127), quinoline yellow (E-104), titanium dioxide (E-171) and water.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

5 years.

6.4. Special precautions for storage

Store below 30ºC

6.5. Nature and contents of container

Aluminium/PVC blister packs containing 60 or 90 capsules.

6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

FAES FARMA, S.A.
Máximo Aguirre, 14
48940 Leioa, (Vizcaya)
SPAIN

8 MARKETING AUTHORISATION NUMBER

56.707

9 DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

Date of first authorization: 5 December 1985
Date of latest renewal: 1 December 2010

10 DATE OF REVISION OF THE TEXT

July 2016

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