

SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE PRODUCT

Diosper

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Diosmin/Hesperidin (450/50) mg/tablet

1. Diosmin $C_{28}H_{32}O_{15}$
4H-1-benzopyran-4-one,7-{6-0(6-deoxy-a-L-mannopyranosyl-b-Dylycopyranosyl]wxy}-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl).
2. Hesperidin $C_{28}H_{34}O_{15}$
7-Rhamnoglucose-3-5-dihydro-4-methoxy flavone

3. PHARMACEUTICAL FORM

Film coated tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Diosper can be administered as supplementary therapy for chronic venous insufficiency complications in the lower limbs.

4.2. Posology and method of administration

Administration

It is administered orally with water during meals.

Dosage

The daily recommended dose is 2 tablets, administered 1 at lunch and 1 at dinner.

4.3. Contraindications

Diosper is contra-indicated in patients, who have shown hypersensitivity to any of the substances present in the drug.

4.4. Special warnings and special precautions for use

No special precautions are associated with the use of the product.

4.5. Interactions with other products and other forms of interaction

No interactions have been reported upon co-administration of Diosper with other medicines. Furthermore, no interaction was observed upon administration of Diosper with anticoagulants of warfarin.

4.6. Administration during Pregnancy and Lactation

Pregnancy:

There were no teratogenic observations in human studies.

It is, however, recommended that Diosper should not be administered during the first three months of pregnancy.

Lactation:

In the absence of data concerning the diffusion of the drug substance in the breast milk, breast feeding is not recommended during treatment.

4.7. Effects on ability to drive and operate machines

Diosper does not interfere with the ability to drive or operate machines.

4.8 Side effects

Possible side-effects to be observed: cutaneous allergies, gastrointestinal disorders, headaches and flushes.

4.9 Overdose

No overdose symptoms have been observed. Therefore no special treatment is recommended.

5. PHARMACOLOGICAL DATA

5.1. Pharmacodynamic properties

Diosper is a venotonic and vascular protecting product.

As derived from pharmacological studies, the product acts on the venous system by reducing the venous dilatation and venous stasis. It improves the micro-circulation by normalizing the capillary permeability and reinforcing the capillary resistance.

Clinical pharmacology studies have been used for the evaluation and quantitation of haemodynamic effect on venous system. The results confirmed the pharmacological efficacy in humans.

In dose/effect related studies, the effect of administered dose on venous plethysmography parameters such as capacity, dilatation and discharge time, was found to be statistically significant. Thus the optimum therapeutic effect is achieved by administering 2 tablets per day.

Relevant studies have shown that the drug increases the venous tone; the plethysmography of venous obliteration detected with a Hg-pressure measurement, revealed a reduction in venous discharge time.

In double blind clinical studies, the pharmacological activity of the product was compared with that of the placebo. The results demonstrated a statistically significant difference. In patients with symptoms of capillary friability, it increases capillary resistance as measured by vasostereometry.

In other clinical studies, the therapeutic efficacy of the drug has been demonstrated in phlebology during the chronic treatment of both functional and organic venous insufficiency. It also ameliorates the symptoms of haemorrhoids.

5.2. Pharmacokinetic properties

In human studies, the drug is primarily excreted in the faeces after oral administration of the product containing ¹⁴C- labelled diosmin. 14% of the administered dose is excreted via the urine.

The plasma half-life of the drug is 11 hours. The drug undergoes extensive metabolism, as indicated by the presence of various phenol acids in the urine.

5.3. Toxicity data

The drug is well tolerated, as long as it is taken according to physician instructions.

No toxicity data have been reported.

6. PHARMACEUTICAL DATA

6.1. Excipients

Sodium starch glycolate, Cellulose microcrystalline, Gelatin, Magnesium stearate, Talc.

Coating: White beeswax, Glycerol, Hypromellose 2910, Macrogol 6000, Sodium lauryl sulfate, Iron oxide yellow E 172, Iron oxide red E 172, Titanium dioxide E 171, Magnesium stearate.

6.2. Incompatibilities

None known.

6.3. Shelf life

48 months.

6.4. Special precautions for storage

Diosper should be stored at ambient conditions ($\leq 25^{\circ}\text{C}$).
Keep out of the reach of children.

6.5. Presentation - Packaging

Salmon-pink oblong tablets in PVC/aluminium blister printed with the product's characteristics.
Each blister contains 10 tablets. Box of 30 tablets along with a patient information leaflet.

6.6. Instructions for use and handling

No special instructions are required for use.

7. MARKETING AUTHORISATION HOLDER

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Representative of the Marketing Authorisation Holder:

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8. MARKETING AUTHORISATION NUMBER(S)

122/00501

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

{To be advised later}

10. DATE OF REVISION OF THE TEXT

March 2003