HEMORIF / HEMORIF DS FILM-COATED TABLET

1. NAME OF THE MEDICINAL PRODUCT

Hemorif (Diosmin 450mg + Hesperidin 50mg) Film-coated Tablet
Hemorif DS (Diosmin 900mg + Hesperidin 100mg) Film-coated Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Hemorif Film-coatedTablet:

Diosmin (Micronized) 450.000 mg
Hesperidine 50.000 mg

Hemorif DS Film-coated Tablet:

Diosmin (Micronized) 900.000 mg
Hesperidine 100.000 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hemorif Film-coated Tablet:

A brown to light pink colored oval shaped, film coated tablet engraved 'SQUARE' on one side.

Hemorif DS Film-coated Tablet:

A yellowish brown to brown colored, caplet shaped, biconvex film coated tablets plain on both sides.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Treatment of symptoms related to venolymphatic insufficiency (heavy legs, pain, early morning restless legs).
- Treatment of functional symptoms related to acute hemorrhoidal attack.

4.2. Posology and method of administration

Posology
Hemorif:
- Venolymphatic insufficiency: 2 tablets daily in two divided doses, midday and evening at meal times.
- Acute hemorrhoidal attack: 6 tablets daily (in 3 divided doses) for the first 4 days, then 4 tablets per day (in 2 divided doses) for the next 3 days.

Hemorif DS:
- Venolymphatic insufficiency: 1 tablet daily, in the morning at breakfast.
- Acute hemorrhoidal attack: 3 tablets daily (in 3 divided doses) for the first 4 days, then 2 tablets per day (in 2 divided doses) for the next 3 days.

Paediatric population

The safety and efficacy of HEMORIF and HEMORIF DS in children and adolescents under 18 years of age have not been established.

Method of administration

Oral route.

4.3. Contraindications

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

4.4. Special warnings and precautions for use

Hemorrhoidal attack

The administration of this product does not preclude treatment for other anal conditions. The treatment must be short-term. If symptoms do not subside promptly, a proctological examination should be performed and the treatment should be reviewed.

4.5. Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. No clinically relevant drug interaction has been reported to date from post marketing experience on the product.

4.6. Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of micronised purified flavonoid fraction in pregnant women.

Animal studies do not indicate reproductive toxicity.

As a precautionary measure, it is preferable to avoid the use of HEMORIF and HEMORIF DS during pregnancy.

Breast-feeding
It is unknown whether the active substance/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from HEMORIF and HEMORIF DS therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
Reproductive toxicity studies showed no effect on fertility in male and female rats.

4.7. Effects on ability to drive and use machines

No specific studies on the effects of flavonoid fraction on the ability to drive and use machines have been performed. However, on the basis of the overall safety profile of flavonoid fraction, HEMORIF and HEMORIF DS have no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

The following undesirable effects have been reported and are ranked using the following frequency:

Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1000, <1/100); rare (≥1/10000, <1/1000); very rare (<1/10000), and not known (cannot be estimated from the available data).

Nervous system disorders
Rare: dizziness, headaches, malaise.

Gastrointestinal disorders
Common: diarrhoea, dyspepsia, nausea, vomiting.
Uncommon: colitis.
Frequency not known: abdominal pain

Skin and subcutaneous tissue disorders
Rare: rash, pruritus, urticaria.
Frequency not known: Isolated face, eyelid and lip oedema. Exceptionally, Quincke's oedema.

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 reporting system.

4.9. Overdose

Symptoms

There is limited experience with HEMORIF, HEMORIF DS overdose. The most frequently reported adverse events in overdose cases were gastrointestinal events (such as diarrhoea, nausea, abdominal pain) and skin events (such as pruritus, rash).

Management

Management of overdose should consist in treatment of clinical symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: VASOPROTECTIVES/ CAPILLARY STABILIZING AGENTS/ BIOFLAVONOIDS (C05CA53: Cardiovascular system)

Pharmacodynamic effects
In pharmacology:
HEMORIF, HEMORIF DS exerts a dual action on the venous return system:

- at vein and venule level, it increases parietal tone and exerts an anti-stasis action,
- at the microcirculatory level, it reinforces capillary resistance and normalises capillary permeability.

In clinical pharmacology:
Controlled, double-blind studies using methods that allow demonstrating and quantifying the activity on venous haemodynamics have confirmed the pharmacological properties of this medicinal product in humans.

- Dose/effect relationship:

Statistically-significant dose-effect relationships have been demonstrated for the following venous plethysmography parameters: capacitance, distensibility and emptying time. The best dose/effect ratio is obtained with 2 HEMORIF tablets/ 1 HEMORIF DS tablet.

- Venotonic activity:

It increases venous tone: venous occlusion plethysmography with a mercury strain gauge revealed a reduction in venous emptying time.

- Microcirculatory activity:

Controlled, double-blind studies have demonstrated a statistically-significant difference between this medicinal product and placebo. In patients with signs of capillary fragility, it increases capillary resistance as measured by angiosterrometry,

Efficacy and clinical safety

- In clinical practice:

Controlled double-blind clinical studies versus placebo demonstrated the therapeutic activity of the medicinal product in phlebology, in the treatment of chronic venous insufficiency (functional and organic) of the lower limbs.

5.2. Pharmacokinetic properties

In humans, following oral administration of the medicinal product with carbon 14-labelled diosmin:

- Excretion is essentially faecal and urinary excretion is on average 14% of the administered quantity,
- The elimination half-life is 11 hours,
- The product is highly metabolised, this metabolism is revealed by the presence of different phenol acids in the urine.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Microcrystalline Cellulose (PH 101), Povidone, Sodium Starch Glycolate (Type A), Colloidal Silicon Dioxide, Magnesium Stearate

Film-coating:

- Opadry-31K-56501 (Brown): HPMC 2910/Hypromellose, Titanium Dioxide, Lactose Monohydrate, Triacetin, Iron Oxide Yellow, Iron oxide Red, Iron Oxide Black
- Opadry-03B54802 (Pink): HPMC 2910/Hypromellose 6 CP, Titanium Dioxide, Macrogol/PEG 400, Iron Oxide Yellow, Iron Oxide Red, iron Oxide Black

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

Please refer to expiry date on the blister strip or outer carton.

6.4. Special precautions for storage

Store below 30°C.

6.5. Nature and contents of container

30 film coated tablets in blister packs.

6.6. Special instructions for disposal and other handling

No special requirements.

7. MANUFACTURER

SQUARE LIFESCIENCES LTD.

Patikabari, Hemayetpur, Pabna 6602, Bangladesh

8. DATE OF REVISION OF THE TEXT

10 January 2025