1. NAME OF THE MEDICINAL PRODUCT

DAFLON 1000 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Micronized purified flavonoid fraction ..... 1000 mg

Corresponding to:

Diosmin: 90 percent ..... 900 mg

Flavonoids expressed as hesperidin: 10 percent ..... 100 mg

Mean moisture……..... 40 mg

For one film-coated tablet

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Salmon coloured, oblong shaped film-coated tablet, scored on both faces.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

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

- 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 Daflon 1000mg 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 (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of DAFLON 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 DAFLON 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 (see section 5.3).

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, DAFLON 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 DAFLON 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:
  DAFLON 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 1 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

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium starch glycolate, microcrystalline cellulose, gelatine, magnesium stearate, talc

Film-coating: titanium dioxide (E 171), glycerol, sodium lauryl sulphate, macrogol 6000, hypromellose, yellow iron oxide (E 172), red iron oxide (E 172), magnesium stearate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

4 years

6.4. Special precautions for storage

Store below 30°C.

6.5. Nature and contents of container

10 or 30 film coated tablets in blister packs (PVC-Aluminium).

Not all pack sizes may be marketed.

6.6. Special instructions for disposal and other handling

No special requirements.

7. MANUFACTURER

Les Laboratoires Servier Industrie
905, route de Saran
45520 Gidy
France

8. PRODUCT REGISTRATION HOLDER

Servier Malaysia Sdn Bhd
Unit No.25-02, Level 25, Imazium
No.8, Jalan SS21/37, Damansara Uptown
47400 Petaling Jaya, Selangor Darul Ehsan

9. DATE OF REVISION OF THE TEXT

17.05.2022