SUMMARY OF PRODUCT CHARACTERISTICS

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 humidity ..... 40 mg

For one film-coated tablet

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

The score line is only used to make it easier to take the tablet, it does not divide it into equal doses.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

4.2. Posology and method of administration

Oral use

Usual dosage: 1 tablet daily at meal times.

Haemorrhoidal attack: 3 tablets per day for the first 4 days, then 2 tablets per day for 3 days.

4.3. Contraindications

Hypersensitivity to the micronised purified flavonoid fraction or to any of the excipients (see section 6.1).

4.4. Special warnings and precautions for use

The administration of this product does not preclude specific treatment for other anal conditions. The treatment must be short-term. If symptoms do not subside rapidly, 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. However, 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.
Experimental studies performed in animals have not revealed a teratogenic effect (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
Toxicity studies on reproduction have not shown any 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 the flavonoid fraction on the ability to drive and use machines have been performed. However, in view of the overall safety profile of the flavonoid fraction, DAFLON does not modify, or to a negligible extent, the ability to drive or use machines.

4.8. Undesirable effects

The following undesirable effects have been reported and are classified as a function of their 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.
Unknown frequency: abdominal pain.

Skin and subcutaneous tissue disorders
Rare: rash, pruritus, urticaria.
Unknown frequency: isolated oedema of the face, eyelids and lips. Exceptionally, angioneurotic 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)

- In pharmacology:

Daflon exerts a dual action on the vascular 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 plethysmographic parameters: capacitance, distensibility and emptying time. The best dose/effect ratio is obtained with 2 tablets.
  - 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.

- In clinical practice:

Controlled double-blind clinical studies versus placebo have 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 from conventional studies on repeated administration toxicology, genotoxicity and reproductive function toxicity have not revealed any specific risk for humans.

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

No special storage conditions.

6.5. Nature and contents of container

18, 30, 36 or 40 film-coated tablets in blister packs (PVC/Aluminium).
Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

LES LABORATOIRES SERVIER
50 RUE CARNOT
92284 SURESNES CEDEX
FRANCE

8. DATE OF REVISION OF THE TEXT

01/2019