SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAFLON 500 mg, film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Micronised purified flavonoid fraction ..... 500.000 mg
Corresponding to:
Diosmin: 90 per cent ..... 450.000 mg
Flavonoids expressed as hesperidin: 10 per cent ..... 50.000 mg
Mean humidity ..... 20.000 mg

For one film-coated tablet

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

4.2. Posology and method of administration

Posology

Usual dose: 2 tablets daily, i.e. 1 tablet at midday and 1 tablet in the evening, at meal times.

Haemorrhoidal attack: 6 tablets per day for the first 4 days, then 4 tablets per day for 3 days.

Paediatric population

The safety and efficacy of Daflon 500 mg 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

Haemorrhoidal attack:

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.
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 have shown no effects on female and male 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 the 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 classified as a function of their frequency.

Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), and not known (cannot be estimated from the available data).

<u>Nervous system disorders</u>

Rare: dizziness, headaches, malaise.

<u>Gastrointestinal disorders</u>

Common: diarrhoea, dyspepsia, nausea, vomiting.

Uncommon: colitis.

Unknown frequency: abdominal pain.

<u>Skin and subcutaneous tissue disorders</u>

Rare: rash, pruritus, urticaria.

Unknown frequency: isolated face, eyelid and lips oedema. Exceptionally, Quincke's oedema.

<u>Reporting of suspected adverse reactions</u>

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 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.

Efficacy and clinical safety

- 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 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

3 years.

6.4. Special precautions for storage

Store below 30°C. Store in the original carton.

6.5. Nature and contents of container

15, 20, 30, 36, 60, 100 or 120 film-coated tablets in blisters (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

January 2019