1. NAME OF THE MEDICINAL PRODUCT
DAFLON 500 mg, micronized purified flavonoid fraction

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Micronized purified flavonoid fraction (MPFF), corresponding to a ratio of 90% of diosmin (450 mg) and 10% of active combined flavonoids expressed as hesperidin, isorhoifolin, linarin, and diosmetin (50 mg)
Excipients: see section 6.1

3. PHARMACEUTICAL FORM
Salmon-colored tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
- Treatment of the symptoms and signs of organic and idiopathic, functional, chronic venous insufficiency of the lower limbs, such as heavy legs, pain, heat sensation, edema, functional impairment, nocturnal cramps and in conjunction with conventional treatment in venous leg ulcers.
- Treatment of the symptoms of acute hemorrhoidal attacks, and chronic hemorrhoidal disease.

4.2 Posology and method of administration
Venous insufficiency and chronic hemorrhoidal disease: 2 tablets daily, with meals.
Acute hemorrhoidal attacks:
6 tablets daily (in 2 divided doses) the first 4 days, then 4 tablets daily the following 3 days.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings and precautions for use
The administration of this product for the symptomatic treatment of acute haemorrhoids does not preclude treatment for other anal conditions.
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. However and taking into consideration the huge post marketing experience on the product, no drug interaction has been reported to date.

4.6 Fertility, pregnancy and breastfeeding
Pregnancy: no teratogenic effects have been shown in several studies and no adverse effects have been reported in humans.
Breast-feeding: in the absence of data on excretion in milk, treatment should be avoided during breastfeeding.
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 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 500 mg has nor or negligible influence on these abilities.

4.8 Undesirable effects
The following adverse effects or events have been reported and are ranked using the following frequency:
very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Nervous system disorders:
• Rare effects: dizziness, headache, malaise
Gastrointestinal disorders:
• Common effects: diarrhoea, dyspepsia, nausea, vomiting.
• Uncommon effects: colitis
Skin and subcutaneous tissue disorders:
• Rare effects: rash, pruritus, urticaria.
• Not known: isolated face, lip, eyelid oedema.
Exceptionally Quincke’s oedema
using venous plethysmographic evaluation. The optimal dose/effect relationship is obtained with 2 tablets daily of Daflon 500 mg.

**Clinical efficacy**

Double-blind, placebo-controlled studies have demonstrated Daflon 500 mg's efficacy on chronic venous insufficiency. Daflon 500 mg significantly improves disabling symptoms of venous insufficiency which affect everyday active life: heavy legs, pain, heat sensation, edema, functional impairment, nocturnal cramps. In addition to conventional compression therapy, Daflon 500 mg has also been demonstrated to cure 3 times as many venous leg ulcers as placebo, to increase by 32% the chance of healing an ulcer at 6 months, and to accelerate their complete healing of a mean of 5 weeks.

Daflon 500 mg is highly effective in the treatment of chronic hemorrhoidal disease. It significantly improves symptoms and signs such as: anal discomfort, pain, redness, anal discharge, proctitis, tenesmus, pruritus, erythema, and bleeding. Daflon 500 mg also significantly reduces the frequency, severity, and duration of acute hemorrhoidal attacks and relapses.

**5.2 Pharmacokinetic properties**

In man, oral administration of Daflon 500 mg containing 14C-labeled diosmin has shown the following characteristics:

- excretion is mainly urinary, accounting for a mean of 57.9% of the dose administered;
- elimination half-life of 11 hours;
- extensive metabolism, evidenced by the presence of various phenolic derivatives in the urine.

**Note:** The diosmin contained in Daflon 500 mg tablets has been subjected to a high-tech process called micronization, to enhance the bioavailability of the product. Micronization allows a decrease in the size of the particles of Daflon 500 mg to less than 2 µm. This process has been demonstrated to significantly increase intestinal absorption and therapeutic efficacy of Daflon 500 mg as compared to nonmicronized diosmin.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Sodium starch glycolate, microcrystalline cellulose,
gelatin, magnesium stearate, talc, glycerol, sodium lauryl sulfate, methylhydroxypropylcellulose, macrogol 6000, titanium dioxide (E 171), yellow iron oxide (E 172), and red iron oxide (E 172).

6.2 Incompatibilities
Not applicable

6.3 Shelf life
4 years

6.4 Special precautions for storage
Store below 30°C.

6.5 Pack sizes
10, 30, 60, 90 and 100 coated tablets.
Not all pack-sizes are necessarily marketed in all countries.

6.6 Special precautions for disposal
No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER
Les Laboratoires Servier
50, rue Carnot
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France

For any updates please refer to www.servier.com. As the SmPC may vary from country to country please also refer to SERVIER’s local agents and/or distributors.