SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAFLON 500 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

For a film-coated tablet:
Micronized purified flavonoid fraction ........................................... 500 mg
Corresponding to:
  . Diosmin (90 %) ................................................................. 450 mg
  . Flavonoids expressed as hesperidin (10 %) ......................... 50 mg

For a 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, early morning restless legs).
    - Treatment of functional symptoms related to acute hemorrhoidal attack.

4.2. Posology and method of administration
    - Usual dosage: 2 tablets daily in two divided doses, midday and evening at meal times.
    - Acute hemorrhoidal attack: 6 tablets per day for the first 4 days, then 4 tablets per day for 3 days.

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

4.4. Special warnings and special precautions for use
    The administration of this product for the symptomatic treatment of acute hemorrhoids 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 lactation

**Pregnancy:**
No teratogenic effects have been shown in several studies and no adverse effect have been reported in human.

**Breast-feeding:**
In the absence of data on excretion in milk, treatment should be avoided during breast-feeding.

**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 no or negligible influence on these abilities.

4.8. Undesirable effects

**Summary of the safety profile**

Side effects reported with Daflon in clinical trials are of mild intensity. They consist mainly in gastro intestinal events (diarrhoea, dyspepsia, nausea, vomiting).

**Tabulated list of adverse reactions**
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).

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Rare</td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malaise</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Common</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dyspepsia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Colitis</td>
</tr>
<tr>
<td></td>
<td>Not known*</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Rare</td>
<td>Pruritus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urticaria</td>
</tr>
<tr>
<td></td>
<td>Not known*</td>
<td>Isolated face, lip, eyelid oedema. Exceptionally Quincke's oedema</td>
</tr>
</tbody>
</table>

* Post-marketing experience
Reporting of suspected adverse reactions

Reporting of 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 ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal.

4.9. Overdose

No case of overdose with DAFLON® 500 mg has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Venotonic and vascular protector.
ATC code: C05CA53.

- Pharmacology
  It is active upon the return vascular system in the following way:
  - it reduces venous distensibility and stasis,
  - in the microcirculation, it normalises capillary permeability and increases capillary resistance.

- Clinical pharmacology
  Double blind controlled studies using methods by which the effects of the product on venous haemodynamics could be demonstrated and quantified have confirmed the above pharmacological properties in man.
  - Dose-effect relationship: a statistically significant dose-effect relationship was established with respect to venous plethysmographic parameters: capacitance, distensibility and rate of emptying. The optimum dose-effect ratio was obtained with 2 tablets.
  - Venous tonic activity: DAFLON® 500 mg increases venous tone: venous occlusion plethysmography with a mercury stress gauge demonstrated a decrease in the rate of emptying.
  - Microcirculatory activity: double-blind controlled studies showed a statistically significant difference between placebo and the drug. In patients presenting with signs of capillary fragility, DAFLON® 500 mg increases capillary resistance, as measured by angiostereometry.

- Clinical trials
  Double-blind placebo-controlled trials have demonstrated the activity of the drug in phlebology, in the treatment of chronic venous insufficiency of the lower limbs (both functional and organic).

5.2. Pharmacokinetic properties

In man, following oral administration of the substance containing 14C Diosmin:
- Excretion is mainly faecal, a mean of 14% of the dose administered is excreted in the urine.
- The elimination half-life is 11 hours.
- The drug is extensively metabolised as evidenced by the presence of various phenol acids in the urine.
5.3. Preclinical safety data
   In animals, experimental studies did not show any teratogenic effect.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

   Tablet core: gelatin, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, talc.
   Film-coating: glycerol, macrogol 6000, magnesium stearate, methylhydroxypropylcellulose, red iron oxide (E172), sodium lauryl sulfate, titanium dioxide, yellow iron oxide (E172).

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

   30 tablets in heat-sealed blister packs (PVC/aluminium).

6.6. Instructions for use and handling

   No special requirements.

7. MARKETING AUTHORISATION HOLDER

   Les Laboratoires Servier
   50, rue Carnot
   92284 Suresnes cedex
   France

8. MARKETING AUTHORISATION NUMBER

   MA 066/00501

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

   26th October 2005 / 4th February 2013
10. DATE OF REVISION OF THE TEXT

4th February 2016