ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAFLON 500 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Micronised purified flavonoic 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 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, restless leg at bedtime).
- Treatment of functional symptoms related to acute hemorrhoidal attack.

4.2 Posology and method of administration

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

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 micronised purified flavonoic fraction or to any of the excipients (see 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

The data available to date do not suggest the existence of clinically significant interactions.

4.6 Pregnancy and lactation

Pregnancy
Experimental studies performed in animals have not revealed a teratogenic effect. Moreover, no harmful effects have been reported to date in humans.

Breastfeeding
In the absence of data concerning excretion into breast milk, breastfeeding is not recommended during treatment.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Some cases of common gastrointestinal disorders and neurovegetative disorders have been described, which never require cessation of treatment.

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: French national agency for the safety of medicines and health products (Ansm) and the network of Regional Pharmacovigilance Centres – Website: www.ansm.sante.fr

4.9 Overdose

No cases of overdose have been reported. However, overdose risks exacerbating the undesirable effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Medicinal product acting on the capillaries
C. Cardiovascular system

- In pharmacology:

Daflon exerts an action on the vascular return system:
  - at the venous level, it reduces venous distensibility and reduces venous stasis;
  - at the microcirculatory level, it normalises capillary permeability and reinforces capillary resistance.

- 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 physiopathology 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 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 of 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

Not given.

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

15, 20, 30, 60, 100 or 120 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. MARKETING AUTHORISATION HOLDER

LES LABORATOIRES SERVIER
50, RUE CARNOT
92284 SURESNES CEDEX
FRANCE

8. MARKETING AUTHORISATION NUMBER(S)

- 328 658-6 or 34009 328 658 6 4: 15 film-coated tablets in blister packs (PVC/aluminium)
- 328 659-2 or 34009 328 659 2 5: 20 film-coated tablets in blister packs (PVC/aluminium)
- 328 660-0 or 34009 328 660 0 7: 30 film-coated tablets in blister packs (PVC/aluminium)
- 383 418-3 or 34009 383 418 3 6: 60 film-coated tablets in blister packs (PVC/aluminium)

- 558 335-4 or 34009 558 335 4 3: 100 film-coated tablets in blister packs (PVC/aluminium)
- 276 281-4 or 34009 276 281 4 6: 120 film-coated tablets in blister packs (PVC/aluminium)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[to be completed by the Marketing Authorisation Holder]

10. DATE OF REVISION OF THE TEXT

[to be completed by the Marketing Authorisation Holder]

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

PRESCRIBING AND DISPENSING CONDITIONS

Medicinal product not subject to medical prescription.