ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PHLEBODIA 600 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Diosmin (expressed in anhydrous and pure diosmin) ..... 600 mg

For one film-coated tablet.

Excipient with known effect: cochineal red A.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Improvement of symptoms associated with venolymphatic insufficiency: heavy legs, pain, primo-decubitus restlessness,
- Supportive treatment for capillary fragility functional disorders,
- Treatment of functional signs associated with haemorrhoidal crisis.

4.2. Posology and method of administration

Posology

- For venous insufficiency: 1 tablet per day, in the morning before breakfast.
- For haemorrhoidal crisis: 2 to 3 tablets per day during meals.

Method of administration

Oral route.

4.3. Contraindications

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

This drug is generally not recommended during breast-feeding (cf. section 4.6).

4.4. Special warnings and precautions for use

Haemorrhoidal crisis: the administration of this product does not dispense patients from following specific treatments for other anal diseases.

The treatment must be short-term only.

If symptoms do not show signs of improvement rapidly, a proctological examination should be performed and the treatment should be revised.

This medicinal product contains an azo dye (cochineal red A) and may cause allergic reactions.

4.5. Interactions with other medicinal products and other forms of interaction

Not applicable.

4.6. Fertility, pregnancy and lactation

Pregnancy

Animal studies have not shown any teratogenic effect. As no teratogenic effect was observed in animals, a malformative effect in humans is not expected. Indeed, to date, substances responsible for malformations in humans have been revealed teratogens in animals during well-conducted studies carried out on two species.

To date, no malformative or fetotoxic effects have been observed in clinical trials. However, monitoring data on pregnancies in patients exposed to diosmin are insufficient in terms of excluding all risks.

Therefore, this medicinal product should not be used during pregnancy unless necessary.

Breast-feeding

As there are no data on whether this medicinal product passes into breast milk, the treatment is not recommended during lactation.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

A few cases of gastrointestinal disorders, rarely leading to discontinuation 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 of your country.

4.9. Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: VASOPROTECTIVES/CAPILLARY STABILIZING AGENTS, ATC code: C05CA03 (cardiovascular system).

Venotonic and vasoprotective agent inducing venous constriction, increasing vascular resistance and reducing vascular permeability.

Various studies have been carried out in both animals and humans to illustrate these properties:

In animals

Venotonic properties

Increase in venous pressure in anaesthetised dogs following IV administration.

Vasoprotective properties

- Action on capillary permeability, anti-oedematous action and anti-inflammatory action in rats.
- Action on erythrocyte deformability measured by erythrocyte filtration time.
- Increase of capillary resistance in vitamin P factor-deficient rats and guinea-pigs.
- Reduction of bleeding time in vitamin P factor-deficient guinea-pigs.
- Reduction of capillary permeability, induced by chloroform, histamine or hyaluronidase.

In humans

Venotonic properties demonstrated in clinical pharmacology

- Increase of the vasoconstrictive action of adrenaline, noradrenaline and serotonin on superficial veins of the hand or on an isolated saphenous vein.
- Increase of venous tonus, demonstrated by measurement of venous capacitance using strain gauge plethysmography; reduction of the venous stasis.

- The venoconstrictive effect is dose-related.
- Reduction of mean venous pressure (in superficial system as well as in deep vein system), illustrated by a double-blind, placebo-controlled trial under Doppler monitoring.
- Increase of systolic and diastolic blood pressure in post-operative orthostatic hypotension.
- Activity after saphenectomy.

Vasculoprotective properties

- Increase of the capillary resistance which is dose-related.

5.2. Pharmacokinetic properties

The pharmacokinetic study on diosmin marked with carbon-14 in animals showed:

- Rapid absorption from the 2nd hour after administration, with maximum concentration being achieved after 5 hours;
- Distribution of low intensity with the exception of the kidneys, the liver, the lungs and especially the vena cava and saphenous veins, where radioactivity levels measures were always higher than in the other examined tissues.
  This preferential binding of diosmin and/or its metabolites at a vascular level increases until the 9th hour and persists for the next 96 hours.
- Elimination was mostly urinary (79%) but also faecal (11%) and biliary (2.4%), with evidence of an enterohepatic cycle.
  These results show that the diosmin is properly absorbed following oral administration.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Talc, anhydrous colloidal hydrophobic silica, micronised stearic acid, microcrystalline cellulose.

Film-coating: film-former agent(Sepifilm 002)*, colouring agent (Sepisperse AP 5523)**, opaglos 6000***.

* Composition of film-former agent (Sepifilm 002): hypromellose, microcrystalline cellulose, macrogol stearate 400.

** Composition of the colouring agent (Sepisperse AP 5523): propylene glycol, hypromellose, titanium dioxide, cochineal red A aluminium lake, black iron oxide, red iron oxide.

*** Composition of Opaglos 6000: carnauba wax, beeswax, shellac, ethanol 95°.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

5 years

6.4. Special precautions for storage

No special storage conditions.

6.5. Nature and contents of container

PVC/Aluminium blister of 15 or 30 tablets.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

LABORATOIRES INNOTHERA
22 AVENUE ARISTIDE BRIAND
94110 ARCUEIL

8. MARKETING AUTHORISATION NUMBER(S)

[to be completed later by the holder]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[to be completed later by the holder]

10. DATE OF REVISION OF THE TEXT

[to be completed later by the holder]

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.