# SUMMARY OF PRODUCT CHARACTERISTICS

# ANNEXE I

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## 1. NAME OF MEDICINAL PRODUCT

PHLEBODIA 600 mg, film-coated tablets

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Diosmin (expressed in anhydrous and pure diosmin) .....600.000 mg

For a film-coated tablet

Excipient: Cochineal Red A
For full list of excipients see section 6.1.

## 3. PHARMACEUTICAL FORM

Film-coated tablet.

## 4. CLINICAL PARTICULARS

### 4.1. - Therapeutic indications

- Improvement of the symptoms of venolymphatic insufficiency: heavy legs, pain, primo-decubitus restlessness,
- Complement treatment of capillary fragility.
- Treatment of functional signs related to acute haemorrhoids,

### 4.2. Posology and method of administration

Oral use :
- Venous insufficiency: 1 tablet per day, in the morning before breakfast.
- Acute haemorrhoids: 2 to 3 tablets per day during meals.

## 4.3. Contraindications

This drug is generally not recommended during lactation (see Section 4.6.).

## 4.4. Special warning and precautions for use

Acute haemorrhoids: the administration of this product does not substitute the specific treatment of other anal diseases.

Treatment should be of short duration.

If the symptoms are not resolved quickly, a proctological examination should be performed and the treatment should be revised.

This medicinal product contains an azoic agent, the cochineal red A (E 124), and could induce allergic reactions.

## 4.5. Interactions with other medicinal products and other forms of interactions

Not applicable

## 4.6. Pregnancy and lactation

**- Pregnancy:**
Animal studies did not reveal any teratogenic effect. Because no teratogenic effect has been reported in animals, malformations in humans are not expected. Indeed, up to date, substances causing malformations in humans have been found to be teratogenic in animals during well-conducted studies in 2 species.
Up to date, in clinical setting this medicinal product did not reveal any malformative or fetotoxical effect. Nevertheless, data on pregnancies exposed to diosmin use is not sufficient to exclude a risk.
Consequently, this medicinal product should not be used during pregnancy unless clearly necessary.

**- Lactation:**
In the absence of data about the passage of the medicinal product 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

Occasional cases of gastrointestinal disorders rarely leading to discontinuation of treatment.

### 4.9. Overdose

Not applicable.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

**VASCULOPROTECTIVE / DRUG ACTING ON CAPILLARIES**
**(C05CA03: cardiovascular system)**

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

Studies were conducted in animals and in humans to show these properties:

**Animal studies**

*Venotonic properties:*

- Increase of venous pressure in anaesthetised dogs following IV administration.

*Vasculoprotective properties:*

- Effect on capillary permeability, anti-oedematous action and anti-inflammatory action in rats.
- Effect 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 the capillary permeability, induced by chloroform, histamine or hyaluronidase.

**Clinical studies**

*Venotonic properties demonstrated in clinical pharmacology:*

- Increase of the vasoconstrictive action of adrenaline, noradrenaline and serotonin on superficial veins in the hand or the isolated human saphenous vein.
- Increase of the 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) demonstrated by a double blind study vs. Placebo controled under Doppler control;
- Increase of systolic and diastolic blood pressure in post-surgical orthostatic hypotension.
- Activity after saphenectomy.

*Vasculoprotective properties:*

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

### 5.2. Pharmacokinetic properties

The following was demonstrated in the pharmacokinetic study in animals using $C^{14}$ labelled diosmin:

- Rapid absorption since the 2nd hour after administration. The maximum concentration was reached after 5 hours;
- Distribution of low intensity with the exception of kidneys, liver, lungs and especially the vena cava and saphenous veins, in which the levels of detected radioactivity were always higher than in other tissues.
  This preferential binding of diosmin and/or its metabolites to venous tissue increases until the 9th hour and after persists during the following 96 hours.
- Elimination is mostly urinary (79%), also faecal (11%) and biliary (2.4%) excretion, with an enterohepatic cycle.
  These results therefore indicate that diosmin is well absorbed following oral administration.

### 5.3. Preclinical safety data

Not applicable

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Uncoated tablet:
Talc, hydrophobic colloidal anydrous silica, micronized stearic acid, microcrystalline cellulose.

Coating: film-former (Sepifilm ™ 002)*, colouring agent (Sepisperse ™ AP 5523)**, Opaglos® 6000***.

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

Do not store above 30°C.

### 6.5. Nature and contents of container

PVC/aluminium blister of 15 or 30 tablets.

### 6.6. Special precautions for disposal

No special requirements.

## 7. MARKETING AUTHORISATION HOLDER

Laboratoires INNOTHERA
22 Avenue Aristide Briand
94110 ARCUEIL
FRANCE

## 8. MARKETING AUTHORISATION NUMBER

337 268.2 : 15 tablets in blister (PVC/Aluminium)
337 269.9 : 30 tablets in blister (PVC/Aluminium)

## 9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

22 June 1994/22 June 2009

## 10. DATE OF REVISION OF THE TEXT

13 November 2013

## 11. DOSIMETRY

Not applicable.

## 12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

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**CONDITIONS OF PRESCRIPTION AND DELIVERY**

Without prescription