SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PHLEBODIA 600 mg, film-coated tablets

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

- Venous insufficiency: 1 tablet per day during a meal.
- Haemorrhoidal crisis: 2 to 3 tablets per day during meals.

Pediatric population

The safety and efficacy of PHLEBODIA in children and adolescents aged less than 18 years have not yet been established.

Method of administration

Oral route.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

This medicinal product contains an azo colouring agent (cochineal Red A) and may cause

allergic reactions.

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.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically relevant drug interaction has been reported to date with diosmin.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of diosmin in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of PHLEBODIA during pregnancy.

Breast-feeding

It is unknown whether diosmin or its metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from PHLEBODIA therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

Reproductive toxicity studies did not show effects on fertility in male and female rats (see section 5.3).

4.7 Effects on ability to drive and use machines

No specific studies on the effects of diosmin on the ability to drive or use machines have been performed. Nevertheless, according to the global safety profile of diosmin, PHLEBODIA has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The undesirable effects are listed according to the MedDRA classification of system organ classes and according to the frequency of occurrence as follows: 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) and not known (cannot be determined from the available data).

System organ class	Common	Uncommon	Rare
Gastrointestinal disorders*	Gastralgia	Bloating, diarrhea, dyspepsia, nausea	Vomiting
Skin and subcutaneous tissue disorders		Allergic reactions such as rash, pruritus, urticaria, angioedema	

*Gastrointestinal disorders rarely lead to treatment discontinuation.

To reports any side effect(s):

Saudi Arabia:

- The National Pharmacovigilance Centre (NPC):

– SFDA Call Center: 19999
– E-mail: npc.drug@sfda.gov.sa
– Website: https://ade.sfda.gov.sa/

Other GCC States:

– Please contact the relevant competent authority.

4.9 Overdose

No cases of overdose associated with adverse reactions were reported with PHLEBODIA administered alone.

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 pharmacodynamic studies have been carried out to illustrate these properties.

In humans

Venotonic properties

- 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), demonstrated by a double-blind study vs. placebo-controlled under Doppler control.

- Increase of systolic and diastolic blood pressure in post-operative orthostatic hypotension.
- Activity after saphenectomy.

Vasculoprotective properties

- Increase of the capillary resistance which is related to the oral dose administered.

5.2 Pharmacokinetic properties

Absorption

After oral administration of PHLEBODIA, diosmin is metabolized to diosmetin by intestinal bacteria. Diosmetin is then absorbed and is found in the blood compartment as glucuroconjugates and sulfoconjugates. Diosmetin-3-O-glucuronide was shown to be a major diosmin's metabolite.

The plasmatic concentration peak is reached between 12 and 15 hours after PHLEBODIA intake.

Distribution

In animals, the pharmacokinetic study on diosmin marked with carbon-14 showed a preferential radioactivity distribution in the vena cava and saphenous veins.

Elimination

In animals, the elimination is urinary (79%), faecal (11%) and biliary (2.4%), with evidence of an enterohepatic cycle.

In humans, diosmetin-3-O-glucuronide is found in the urine.

5.3 Preclinical safety data

Non-clinical data from repeated toxicity, genotoxicity and reproductive toxicity studies did not reveal any particular risk for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Talc, 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 8 stearate type I.

** Composition of the colouring agent (Sepisperse AP 5523): propylene glycol,

hypromellose, titanium dioxide, cochineal red A, black iron oxide, red iron oxide.

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

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.

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
FRANCE

8. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 November 2016

9. DATE OF REVISION OF THE TEXT

13 January 2020

10. DOSIMETRY

Not applicable.

11. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.