

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAFLON 1000 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Micronized purified flavonoid fraction	1000 mg
Corresponding to:	
Diosmin: 90 percent	900 mg
Flavonoids expressed as hesperidin: 10 percent	100 mg
Mean moisture	40mg

For one film-coated tablet

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- ~~Treatment of symptoms related to venolymphatic insufficiency (heavy legs, pain, restless leg syndrome).~~
- ~~Treatment of symptoms related to venolymphatic insufficiency (heavy legs, pain, restless legs syndrome at bedtime).~~
- Treatment of functional symptoms related to acute haemorrhoidal attack.

Commented [DCRE_CB1]: Indication Philippines: Daflon 500 mg is recommended for treating venous circulation disorders (swollen legs, pain, nocturnal cramps)

4.2. Posology and method of administration

Posology

~~Usual dosage~~In venous disease: 1 tablet daily in the morning, at meal time.

In acute h~~Ha~~emorrhoidal attacks: 3 tablets per day for the first 4 days, then 2 tablets per day for the next 3 days.

Pediatric population

The safety and efficacy of Daflon in children and adolescents under 18 years of age have not been established.

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Commented [DCRE_CB2]: ok

Method of administration

Oral route.

Commented [DCRE_CB3]: ok

4.3. Contraindications

Hypersensitivity to the ~~micronised purified flavonoid fraction~~active substance or to any of the excipients ~~(see section listed in section 6.1.)~~

4.4. Special warnings and precautions for use

The administration of this product for the symptomatic treatment of acute haemorrhoids does not preclude treatment for other anal conditions. ~~The treatment must be short-term. The treatment must be of short duration.~~

Commented [DCRE_CB4]: ok

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. No clinically relevant drug interaction has been reported to date from post marketing experience on the product.~~

~~No interaction studies have been performed. However, no cases of drug interaction have been reported since the marketing of the product.~~

4.6. Fertility, pregnancy and lactation

Pregnancy

~~There are no or limited amount of data from the use of Micronised Purified Flavonoid Fraction in pregnant women.~~

~~Animal studies do not indicate reproductive toxicity (see section 5.3).~~

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

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

Breastfeeding

~~It is unknown whether the active substance/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 DAFLON therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.~~

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

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 specific 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 has nor or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

The following undesirable effects have been reported and are classified as a function of their frequency. Very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon ($\geq 1/1,000$, $< 1/100$); rare ($\geq 1/10,000$, $< 1/1,000$); very rare ($< 1/10,000$), and not known (cannot be estimated from the available data).

Nervous system disorders

Rare: dizziness, headaches, malaise.

Gastrointestinal disorders

Common: diarrhoea, dyspepsia, nausea, vomiting.

Uncommon: colitis.

Unknown frequency: abdominal pain.

Skin and subcutaneous tissue disorders

Rare: rash, pruritus, urticaria.

Unknown frequency: isolated face, eyelid and lips oedema.

Exceptionally, Quincke's oedema.

~~The following undesirable effects have been reported and are ranked using the following frequency:~~

~~Very common ($\geq 1/10$); common ($\geq 1/100, < 1/10$); uncommon ($\geq 1/1000, < 1/100$); rare ($\geq 1/10000, < 1/1000$); very rare ($< 1/10000$), not known (cannot be estimated from the available data).~~

Nervous system disorders

~~Rare: dizziness, headaches, malaise.~~

Gastrointestinal disorders

~~Common: diarrhoea, dyspepsia, nausea, vomiting.~~

~~Uncommon: colitis.~~

~~Frequency not known: abdominal pain~~

Skin and subcutaneous tissue disorders

~~Rare: rash, pruritus, urticaria.~~

~~Frequency not known: isolated face, eyelid and lip oedema. Exceptionally, Quincke's oedema.~~

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.

4.9. Overdose

Symptoms

There is limited experience with DAFLON overdose. The most frequently reported adverse events in overdose cases were gastrointestinal events (such as diarrhoea, nausea, abdominal pain) and skin events (such as pruritus, rash).

Management

Management of overdose should consist in treatment of clinical symptoms.

No case of overdose with DAFLON has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotheapeutic class: Vasculoprotectives/ Capillary stabilizing agents/ Bioflavonoids, ATC code: (C05CA53: Cardiovascular system)

Pharmacodynamic effects

Daflon exerts a dual action on the vascular return system:

o at vein and venule level, it increases parietal tone and exerts an anti-stasis action;

o at the microcirculatory level, it reinforces capillary resistance and normalises capillary permeability.

Pharmacology

DAFLON exerts a dual action on the venous return system:

at vein and venule level, it increases parietal tone and exerts an anti-stasis action,

at the microcirculatory level, it reinforces capillary resistance and normalises capillary permeability.

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 11 hours.
- the product is highly metabolised, this metabolism is revealed by the presence of different phenol acids in the urine.

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.

—o Dose/effect relationship:

Statistically significant dose-effect relationships have been demonstrated for the following venous plethysmography parameters: capacitance, distensibility and emptying time. The best dose/effect ratio is obtained when 1000mg tablets daily are taken.

—o Venotonic activity:

It increases venous tone: venous occlusion plethysmography with a mercury strain gauge revealed a reduction in venous emptying time.

—o 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 angiostrometry.

Clinical practice:-

Double-blind placebo-controlled trials have demonstrated the therapeutic effect 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 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 11 hours.
- the product is highly metabolised, this metabolism is revealed by the presence of different phenol acids in the urine.

In man, following oral administration of the substance containing 14C-Diosmin:

- Excretion is mainly faecal and 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

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity and toxicity to reproduction.

Preclinical data from conventional toxicology studies of repeated dose toxicity, genotoxicity and reproductive function did not reveal any particular risk to humans.

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 stéarate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

4 years

6.4. Special precautions for storage

Below 30°C.

Commented [DCRE_CB5]: In fact for ASEAN zone, we usually mention the storage condition "below 30°C".

6.5. Nature and contents of container

18, 30, 36 or 40 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

Commented [DCRE_CB6]: Servier Philippines

8. DATE OF REVISION OF THE TEXT

~~October 2016~~

January 2019.

DAFLON 1000 mg, film-coated tablet
Micronised purified flavonoid fraction

Read all of this leaflet carefully before you start taking this medicine. It contains important information for your treatment, you.

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.
- You must talk to a doctor if you do not feel better or if you feel worse.

In this leaflet:

1. WHAT DAFLON 1000mg, film-coated tablet IS AND WHAT IT IS USED FOR
2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE DAFLON 1000 mg, film-coated tablet
3. HOW TO TAKE DAFLON 1000 mg, film-coated tablet
4. POSSIBLE SIDE EFFECTS
5. HOW TO STORE DAFLON 1000 mg, film-coated tablet
6. CONTENTS OF THE PACK AND OTHER INFORMATION

1. WHAT DAFLON 1000 mg, film-coated tablet IS AND WHAT IT IS USED FOR?

Pharmacotherapeutic group: **VASOPROTECTIVES Vasculoprotectives/ CAPILLARY STABILIZING AGENTS/ BIOFLAVONOIDS, (C05CA53: Cardiovascular system), ATC code: C05CA53**

This medicine is a venotonic (it increases venous tone) and a vasculoprotector (it increases resistance in small blood vessels).

It is recommended for treating:

- venous circulation disorders (swollen legs, pain, restless legs),
- and functional symptoms due related to acute haemorrhoidal attack.

If the hemorrhoid symptoms do not disappear within 15 days, talk to your doctor.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE DAFLON 1000 mg, film-coated tablet?

Do not take DAFLON

- if you are allergic (hypersensitive) to micronized purified flavonoid fraction or any of the ingredients of this medicine (listed in section 6).

If you have any further questions on the use of this product, ask your doctor or pharmacist.

Warnings and precautions

Do not hesitate to ask your doctor or your pharmacist for advice before taking DAFLON 1000 mg, film-coated tablets.

Haemorrhoidal attack: If the haemorrhoid disorder persists for more than 15 days, it is essential that you consult your doctor.

If you have an acute attack of haemorrhoids, you can take DAFLON for a short period of time. Please ask your doctor if symptoms persist.

Children and adolescents

DAFLON is not intended for use in children and adolescents below 18 years of age.

Other medicines and DAFLON

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicine, including medicines obtained without prescription.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

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

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Breast feeding

In the absence of data in breast-feeding women, it is preferable to avoid breast-feeding while taking this treatment.

3. HOW TO TAKE DAFLON 1000 mg, film-coated tablet ?

Posology

Always take DAFLON exactly as your doctor has told you.
If you are not sure, check with your doctor or pharmacist

The usual dose is 1 tablet daily in the morning at mealtime.

In the case of haemorrhoidal attack: the usual recommended dose is 3 tablets daily for 4 days, then 2 tablets daily for the next 3 days at mealtimes.

Method and route of administration

Swallow the tablet with adequate amount of water.

Duration of treatment

Your doctor will tell you how long the treatment will last. Do not stop the treatment without prior consultation to your doctor.

If you take more DAFLON 1000 mg, film-coated tablets than you should

Contact your doctor or pharmacist immediately.
The experience of overdoses with DAFLON is limited but reported symptoms include diarrhoea, nausea, abdominal pain, pruritus and rash.

If you take more DAFLON 1000mg, film-coated tablets than you should, contact your doctor immediately.

— If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

— If you forget to take DAFLON 1000mg, film-coated tablets

Do not take a double dose to make up for a forgotten dose.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. ~~___~~—POSSIBLE SIDE EFFECTS

Like all medicines, ~~DAFLON 1000 mg, film-coated tablet, this medicine~~ can cause side effects, although not everybody gets them.

The frequency of the possible side effects listed below is defined using the following system:

These can include:

- very common (affects more than 1 in 10 users)
- common (affects between 1 and 10 in 100 users)
- uncommon (affects between 1 and 10 in 1,000 users)
- rare (affects between 1 and 10 in 10,000 users)
- very rare (affects fewer than 1 in 10,000 users)
- not known (cannot be estimated from the available data)

They may include:

Common

Diarrhoea, dyspepsia (difficult digestion), nausea, vomiting.

Uncommon

Colitis (inflammation of the large intestine).

Rare -Dizziness, headache, discomfort, itching, rash, -urticaria.

Not known (cannot be estimated from the available data) :

Abdominal pain, isolated oedema (swelling) of the face, eyelids and lips.

Exceptionally

Quincke's oedema (swelling of the face, lips, mouth, tongue or throat which could cause breathing difficulties).

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system.

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE DAFLON 1000 mg, film-coated tablet?

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the box. The expiry date refers to the last day of that month.

Do not throw away medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

~~Store below 30°C.~~

~~Store in the original outer packaging.~~

~~— Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.~~

6. CONTENT OF THE PACK AND OTHER INFORMATION

What DAFLON 1000 mg, film-coated tablet, film-coated tablet contains?

The active substances are is:

Micronised purified flavonoid fraction	1000.000 mg
<u>Corresponding to:</u>	
Diosmin: 90 per cent	900.000
mg	
Flavonoids expressed as hesperidin: 10 per cent	100.000
mg	
Mean humidity	40.000
mg	

For one film-coated tablet

The other ingredients are:

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.

What DAFLON 1000 mg, film-coated tablets looks like is DAFLON 1000 mg, film-coated tablet and contents of the pack

Film-coated tablets. Boxes of 18, 30, 36 or 40 film-coated tablets.

18, 30, 36, 40 film-coated tablets in blister (PVC-Aluminium)

Not all pack size may be marketed.

Marketing Authorisation Holder and manufacturer

Marketing Authorisation Holder

LES LABORATOIRES SERVIER
50, RUE CARNOT
92284 SURESNES CEDEX
FRANCE

Manufacturer

LES LABORATOIRES SERVIER INDUSTRIE
905, route de Saran
45520 Gidy
FRANCE

This leaflet was last approved in January 2019.

Commented [DCRE_CB7]: Please adapt locally.

HEALTH EDUCATION ADVICE:

- Drink 1.5 to 2 litres of water per day, eat foods that are high in fibre to avoid constipation (fruit, green vegetables, whole grains).
- Avoid fats, coffee, alcohol and spicy foods.

• Take regular exercise to stimulate the blood flow.

Avoid carrying objects that are too heavy.