Annex III

Summary of product characteristics, labelling and package leaflet

Note:

This Summary of Product Characteristics, labelling and package leaflet is the outcome of the referral procedure to which this Commission decision relates.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the Reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Plendil and associated names (see Annex I) 2.5 mg prolonged-release tablets
Plendil and associated names (see Annex I) 5 mg prolonged-release tablets
Plendil and associated names (see Annex I) 10 mg prolonged-release tablets

[See Annex I – to be completed nationally]

5. 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2.5 mg felodipine.

Excipients with known effect:
Each tablet contains 28 mg lactose and 2.5 mg polyoxyl 40 hydrogenated castor oil.

Each tablet contains 5 mg felodipine.

Excipients with known effect:
Each tablet contains 28 mg lactose and 5 mg polyoxyl 40 hydrogenated castor oil.

Each tablet contains 10 mg felodipine.

Excipients with known effect:
Each tablet contains 28 mg lactose and 10 mg polyoxyl 40 hydrogenated castor oil.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release tablet
The tablet is yellow, circular, biconvex, engraved A/FL on one side and 2.5 on the other side, with a diameter of 8.5 mm.

The tablet is pink, circular, biconvex, engraved A/Fm on one side and 5 on the other side, with a diameter of 9 mm.

The tablet is reddish-brown, circular, biconvex, engraved A/FE on one side and 10 on the other side, with a diameter of 9 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hypertension

Stable angina pectoris

4.2 Posology and method of administration

Posology

Hypertension
The dose should be adjusted individually. Treatment can be started with 5 mg once daily. Depending on the patient's response, the dosage can, where applicable, be decreased to 2.5 mg or increased to 10 mg daily. If necessary another antihypertensive agent may be added. The standard maintenance dose is 5 mg once daily.

Angina pectoris
The dose should be adjusted individually. Treatment should be initiated with 5 mg once daily and, if needed, increased to 10 mg once daily.

Elderly population
Initial treatment with lowest available dose should be considered.

Renal impairment
Dose adjustment is not needed in patients with impaired renal function.

Hepatic impairment
Patients with impaired hepatic function may have elevated plasma concentrations of felodipine and may respond to lower doses (see section 4.4).

Paediatric population
There is limited clinical trial experience of the use of felodipine in hypertensive paediatric patients (see sections 5.1 and 5.2).

Method of administration

The tablets should be taken in the morning and be swallowed with water. In order to keep the prolonged-release properties, the tablets must not be divided, crushed or chewed. The tablets can be administered without food or following a light meal not rich in fat or carbohydrate.

4.3 Contraindications

- Pregnancy
- Hypersensitivity to felodipine or any of the excipients listed in section 6.1
- Decompensated heart failure
- Acute myocardial infarction
- Unstable angina pectoris
- Haemodynamically significant cardiac valvular obstruction
- Dynamic cardiac outflow obstruction

4.4 Special warnings and precautions for use

The efficacy and safety of felodipine in the treatment of hypertensive emergencies has not been studied.

Felodipine may cause significant hypotension with subsequent tachycardia. This may lead to myocardial ischaemia in susceptible patients.

Felodipine is cleared by the liver. Consequently higher therapeutic concentrations and response can be expected in patients with clearly reduced liver function (see section 4.2).

Concomitant administration of drugs that strongly induce or inhibit CYP3 A4 enzymes result in extensively decreased or increased plasma levels of felodipine, respectively. Therefore such combinations should be avoided. (see section 4.5).

Plendil contains lactose. Patients with rare hereditary problems of galactose intolerance or glucose-galactose malabsorption should not take this medicinal product.

Plendil contains castor oil, which may cause stomach upset and diarrhoea.

Mild gingival enlargement has been reported in patients with pronounced gingivitis/peridontitis. The enlargement can be avoided or reversed by careful oral hygiene.

4.5 Interaction with other medicinal products and other forms of interaction

Felodipine is metabolised in the liver by cytochrome P450 3A4 (CYP3A4). Concomitant administration of substances which interfere with CYP3A4 enzyme system may affect plasma concentrations of felodipine.

Enzyme interactions

Enzyme inhibiting and enzyme inducing substances of cytochrome P450 isoenzyme 3A4 may exert an influence on the plasma level of felodipine.

Interactions leading to increased plasma concentration of felodipine
CYP3A4 enzyme inhibitors have been shown to cause an increase in felodipine plasma concentrations. Felodipine C_{max} and AUC increased 8-fold and 6-fold, respectively, when felodipine was coadministered with the strong CYP3A4 inhibitor itraconazole. When felodipine and erythromycin were coadministered, the C_{max} and AUC of felodipine were increased by about 2.5-fold. Cimetidine increased the felodipine C_{max} and AUC by approximately 55%. The combination with strong CYP3A4 inhibitors should be avoided.

In case of clinically significant adverse events due to elevated felodipine exposure when combined with strong CYP3A4 inhibitors, adjustment of felodipine dose and/or discontinuation of the CYP3A4 inhibitor should be considered.

Examples:
- Cimetidine
- Erythromycin
- Itraconazole
- Ketoconazole
- Anti HIV/protease inhibitors (e.g. ritonavir)
- Certain flavonoids present in grapefruit juice

Felodipine tablets should not be taken together with grapefruit juice.

Interactions leading to decreased plasma concentration of felodipine
Enzyme inducers of the cytochrome P450 3A4 system have been shown to cause a decrease in plasma concentrations of felodipine. When felodipine was coadministered with carbamazepine, phenytoin or phenobarbital, the C_{max} and AUC of felodipine were decreased by 82% and 96% respectively. The combination with strong CYP3A4 inducers should be avoided.

In case of lack of efficacy due to decreased felodipine exposure when combined with potent inducers of CYP3A4, adjustment of felodipine dose and/or discontinuation of the CYP3A4 inducer should be considered.

Examples:
- Phenytoin
- Carbamazepine
- Rifampicin
- Barbiturates
- Efavirenz
- Nevirapine
- Hypericum perforatum (Saint John's wort)

Additional interactions

Tacrolimus: Felodipine may increase the concentration of tacrolimus. When used together, the tacrolimus serum concentration should be followed and the tacrolimus dose may need to be adjusted.

Cyclosporin: Felodipine does not affect plasma concentrations of cyclosporin.

4.6 Fertility, pregnancy and lactation

Pregnancy

Felodipine should not be given during pregnancy. In non-clinical reproductive toxicity studies there were foetal developmental effects, which are considered to be due to the pharmacological action of felodipine.

Breastfeeding

Felodipine has been detected in breast milk, and due to insufficient data on potential effect on the infant, treatment is not recommended during breastfeeding.

Fertility

There are no data on the effects of felodipine on patient fertility. In a nonclinical reproductive study in the rat (see section 5.3), there were effects on fetal development but no effect on fertility at doses approximating to therapeutic.

4.7 Effects on ability to drive and use machines

Felodipine has minor or moderate influence on the ability to drive and use machines. If patients taking felodipine suffer from headache, nausea, dizziness or fatigue and ability to react may be impaired. Caution is recommended especially at the start of treatment.

4.8 Undesirable effects

Summary of the safety profile

Felodipine can cause flushing, headache, palpitations, dizziness and fatigue. Most of these adverse reactions are dose-dependent and appear at the start of treatment or after a dose increase. Should such adverse reactions occur, they are usually transient and diminish with time.

Dose-dependent ankle swelling can occur in patients treated with felodipine. This results from precapillary vasodilatation and is not related to any generalised fluid retention.

Mild gingival enlargement has been reported in patients with pronounced gingivitis/periodontitis. The enlargement can be avoided or reversed by careful oral hygiene.

Tabulated list of adverse reactions

The adverse reactions listed below have been identified from clinical trials and from post marketing surveillance.

The following definitions of frequencies are used:
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

6. Table 1 Undesirable effects

System organ class	**Frequency**	**Adverse reaction**
Nervous system disorders	Common Uncommon	Headache Dizziness, paraesthesia
Cardiac disorders	Uncommon	Tachycardia, palpitations
Vascular disorders	Common Uncommon Rare	Flush Hypotension Syncope
Gastrointestinal disorders	Uncommon Rare Very rare	Nausea, abdominal pain Vomiting Gingival hyperplasia, gingivitis
Hepatobiliary disorders	Very rare	Increased liver enzymes
Skin and subcutaneous tissue disorders	Uncommon Rare Very rare	Rash, pruritus Urticaria Photosensitivity reactions, leucocytoclastic vasculitis
Musculoskeletal and connective tissue disorders	Rare	Arthralgia, myalgia
Renal and urinary disorders	Very rare	Pollakisuria
Reproductive system and breast disorders	Rare	Impotence/sexual dysfunction
General disorders and administration site conditions	Very common Uncommon Very rare	Peripheral oedema Fatigue Hypersensitivity reactions, e.g. angio-oedema, fever

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 listed in Appendix V.

4.9 Overdose

Symptoms
Overdosage may cause excessive peripheral vasodilatation with marked hypotension and sometimes bradycardia.

Management
If justified: activated charcoal, gastric lavage if performed within one hour after ingestion.

If severe hypotension occurs, symptomatic treatment should be instituted.

The patient should be placed supine with the legs elevated. In case of accompanying bradycardia, atropine 0.5-1 mg should be administered intravenously. If this is not sufficient, plasma volume should be increased by infusion of e.g., glucose, saline, or dextran. Sympathomimetic medicinal products with predominant effect on the α1-adrenoceptor may be given if the above-mentioned measures are insufficient.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: calcium channel blockers, dihydropyridine derivatives; ATC code: C08CA02

Mechanism of action

Felodipine is a vascular selective calcium antagonist, which lowers arterial blood pressure by decreasing systemic vascular resistance. Due to the high degree of selectivity for smooth muscle in the arterioles, felodipine in therapeutic doses has no direct effect on cardiac contractility or conduction. Because there is no effect on venous smooth muscle or adrenergic vasomotor control, felodipine is not associated with orthostatic hypotension.

Felodipine possesses a mild natriuretic/diuretic effect and fluid retention does not occur.

Pharmacodynamic effects

Felodipine is effective in all grades of hypertension. It can be used as monotherapy or in combination with other antihypertensive medicinal products, eg, ß-adrenoceptor blockers, diuretics or ACE-inhibitors, in order to achieve an increased antihypertensive effect. Felodipine reduces both systolic and diastolic blood pressure and can be used in isolated systolic hypertension.

Felodipine has anti-anginal and anti-ischaemic effects due to improved myocardial oxygen supply/demand balance. Coronary vascular resistance is decreased and coronary blood flow and myocardial oxygen supply are increased by felodipine due to dilatation of both epicardial arteries and arterioles. The reduction in systemic blood pressure caused by felodipine leads to decreased left ventricular afterload and myocardial oxygen demand.

Felodipine improves exercise tolerance and reduces anginal attacks in patients with stable effort-induced angina pectoris. Felodipine can be used as monotherapy or in combination with ß-adrenoceptor blockers in patients with stable angina pectoris.

Haemodynamic effects
The primary haemodynamic effect of felodipine is a reduction of total peripheral vascular resistance, which leads to a decrease in blood pressure. These effects are dose-dependent. Generally, a reduction in blood pressure is evident two hours after the first oral dose and lasts for at least 24 hours and the trough/peak ratio is usually well above 50%.

Plasma concentrations of felodipine are positively correlated to the decrease in total peripheral resistance and blood pressure.

Cardiac effects
Felodipine in therapeutic doses has no effect on cardiac contractility or atrioventricular conduction or refractoriness.

Antihypertensive treatment with felodipine is associated with significant regression of pre-existing left ventricular hypertrophy.

Renal effects
Felodipine has a natriuretic and diuretic effect due to reduced tubular reabsorption of filtered sodium. Felodipine does not affect daily potassium excretion. The renal vascular resistance is decreased by felodipine. Felodipine does not influence urinary albumin excretion.

In cyclosporin-treated renal transplant recipients, felodipine reduces blood pressure and improves both the renal blood flow and the glomerular filtration rate. Felodipine may also improve early renal graft function.

Clinical efficacy

In the HOT (Hypertension Optimal Treatment) study, the effect on major cardiovascular events (ie, acute myocardial infarction, stroke and cardiovascular death) was studied in relation to diastolic blood pressure targets $\leq$ 90 mmHg, $\leq$ 85 mmHg and $\leq$ 80 mmHg and achieved blood pressure, with felodipine as baseline therapy.

A total of 18,790 hypertensive patients (DBP 100-115 mmHg), aged 50-80 years were followed for a mean period of 3.8 years (range 3.3-4.9). Felodipine was given as monotherapy or in combination with a betablocker, and/or an ACE-inhibitor and/or a diuretic. The study showed benefits of lowering SBP and DBP down to 139 and 83 mmHg, respectively.

According to the STOP-2 (Swedish Trial in Old Patients with Hypertension-2 study), performed in 6614 patients, aged 70-84 years, dihydropyridine calcium antagonists (felodipine and isradipine) have shown the same preventive effect on cardiovascular mortality and morbidity as other commonly used classes of antihypertensive medicinal products – ACE inhibitors, beta-blockers and diuretics.

7. Paediatric population

There is limited clinical trial experience of the use of felodipine in hypertensive paediatric patients. In a randomised, double-blind, 3-week, parallel group study in children aged 6-16 years with primary hypertension, the antihypertensive effects of once daily felodipine 2.5 mg (n=33), 5 mg (n=33) and 10 mg (n=31) were compared with placebo (n=35). The study failed to demonstrate the efficacy of felodipine in lowering blood pressure in children aged 6-16 years (see section 4.2)

The long-term effects of felodipine on growth, puberty and general development have not been studied. The long-term efficacy of antihypertensive therapy as therapy in childhood to reduce cardiovascular morbidity and mortality in adulthood has also not been established.

5.2 Pharmacokinetic properties

Absorption

Felodipine is administered as extended-release tablets, from which it is completely absorbed in the gastrointestinal tract. The systemic availability of felodipine is approximately 15% and is independent of dose in the therapeutic dose range. The extended-release tablets produce a prolonged absorption phase of felodipine. This results in even felodipine plasma concentrations within the therapeutic range for 24 hours. Maximum blood plasma levels (t_{max}) are achieved with the prolonged-release form after 3 to 5 hours. The rate but not the extent of absorption of felodipine is **increased** when taken simultaneously with food with a high fat content.

Distribution

The plasma protein binding of felodipine is approximately 99%. It is bound pre-dominantly to the albumin fraction. Volume of distribution at steady state is 10 L/kg.

Biotransformation

Felodipine is extensively metabolised in the liver by cytochrome P450 3A4 (CYP3A4) and all identified metabolites are inactive. Felodipine is a high clearance medicinal product with an average blood clearance of 1200 ml/min. There is no significant accumulation during long-term treatment.

Elderly patients and patients with reduced liver function have on average higher plasma concentrations of felodipine than younger patients. The pharmacokinetics of felodipine is not changed in patients with renal impairment, including those treated with haemodialysis.

Elimination

The half-life of felodipine in the elimination phase is approximately 25 hours and steady state is reached after 5 days. There is no risk of accumulation during long-term treatment. About 70% of a given dose is excreted as metabolites in the urine; the remaining fraction is excreted in the faeces. Less than 0.5% of a dose is recovered unchanged in urine.

Linearity/non-linearity

Plasma concentrations are directly proportional to dose within the therapeutic dose range 2.5 – 10 mg.

Paediatric population

In a single dose (felodipine prolonged-release 5 mg) pharmacokinetic study with a limited number of *children aged between 6 and 16* years (n=12) *there was no apparent relationship between the age and AUC, C_{max} or half-life of felodipine.*

5.3 Preclinical safety data

Reproduction toxicity
In a study on fertility and general reproductive performance in rats treated with felodipine, a prolongation of parturition resulting in difficult labour/increased foetal deaths and early postnatal deaths was observed in the medium and high dose groups. These effects were attributed to the inhibitory effect of felodipine in high doses on uterine contractility. No disturbances of fertility were observed when doses within the therapeutic range were given to rats.

Reproduction studies in rabbits have shown a dose-related reversible enlargement of the mammary glands of the parent animals and dose-related digital anomalies in the foetuse. The anomalies in the foetuses were induced when felodipine was administered during early foetal development (before day 15 of pregnancy). In a reproduction study in monkeys, an abnormal position of the distal phalange(s) was noticed.

There were no other pre clinical findings considered to be of concern and the reproductive findings are considered to be related to the pharmacological action of felodipine, when given to normotensive animals. The relevance of these findings for patients receiving felopidine is unknown. However, there have been no reported clinical incidences of phalangeal changes in foetus/neonate exposed to felodipine in-utero, from the information maintained within the internal patient safety databases.

8.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Hydroxypropylcellulose
Hypromellose 50 mPa·s
Hypromellose 10000 mPa·s
Lactose anhydrous
Microcrystalline cellulose
Polyoxyl 40 hydrogenated castor oil
Propyl gallate
Sodium aluminium silicate
Sodium stearyl fumarate

Coating

Carnauba wax
Iron oxide yellow (E172)
Hypromellose 6 mPa·s
Macrogol 6000
Titanium dioxide (E 171)

[Plendil 5 mg and 10 mg]
Carnauba wax
Iron oxide reddish-brown (E172)
Iron oxide yellow (E172)
Hypromellose 6 mPa·s
Macrogol 6000
Titanium dioxide (E 171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

[To be completed nationally]

6.4 Special precautions for storage

[To be completed nationally]

6.5 Nature and contents of container

High-density polyethylene bottle with a cap of polypropylene
PVC/PVDC blister and Aluminum blister

Pack Size	**Carton (pack) contents**
20 tablets	2 blisters of 10 tablets
28 tablets	4 blisters of 7 tablets
30 tablets	3 blisters of 10 tablets 1 bottle of 30 tablets
98 tablets	7 blisters of 14 tablets

100 tablets	10 blisters of 10 tablets
14 tablets	1 blister of 14 tablets
20 tablets	2 blisters of 10 tablets
28 tablets	1 blister of 28 tablets
	2 blisters of 14 tablets
	4 blisters of 7 tablets
30 tablets	3 blisters of 10 tablets
	1 bottle of 30 tablets
90 tablets	3 blisters of 30 tablets
98 tablets	7 blisters of 14 tablets
100 tablets	1 bottle of 100 tablets
	10 blisters of 10 tablets
14 tablets	1 blister of 14 tablets
20 tablets	2 blisters of 10 tablets
28 tablets	1 blister of 28 tablets
	2 blisters of 14 tablets
	4 blisters of 7 tablets
30 tablets	1 bottle of 30 tablets
	3 blisters of 10 tablets
98 tablets	7 blisters of 14 tablets
100 tablets	1 bottle of 100 tablets
	10 blisters of 10 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

[To be completed nationally]

Detailed information on this medicinal product is available on the website of {name of MS/Agency}

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Plendil and associated names (see Annex I) 2.5 mg prolonged-release tablets
Plendil and associated names (see Annex I) 5 mg prolonged-release tablets
Plendil and associated names (see Annex I) 10 mg prolonged-release tablets

[See Annex I - To be completed nationally]

felodipine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 2.5 mg (or 5 mg, or 10 mg) felodipine

3. LIST OF EXCIPIENTS

Contains lactose and polyoxyl 40 hydrogenated castor oil. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

9.	2.5 mg tablet	20 tablets 28 tablets 30 tablets 98 tablets 100 tablets
10.	5 mg tablet	14 tablets 20 tablets 28 tablets 30 tablets 90 tablets 98 tablets 100 tablets
11.	10 mg tablet	14 tablets 20 tablets 28 tablets 30 tablets 98 tablets 100 tablets

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

{Name and Address}
{tel}
{fax}
{e-mail}

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

<Justification for not including Braille accepted>

[To be completed nationally]

12.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Plendil and associated names (see Annex I) 2.5 mg prolonged-release tablets
Plendil and associated names (see Annex I) 5 mg prolonged-release tablets
Plendil and associated names (see Annex I) 10 mg prolonged-release tablets

[See Annex I - To be completed nationally]

felodipine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

{Name}

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PACKAGE LEAFLET

Package leaflet: Information for the patient

Plendil and associated names (see Annex I) **2.5 mg [5 mg or, 10 mg] prolonged-release tablets**
[See Annex I - To be completed nationally]
felodipine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness 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.

What is in this leaflet

1. What Plendil is and what it is used for

Plendil contains the active substance felodipine. This belongs to a group of medicinces called calcium antagonists. It lowers blood pressure by dilating small blood vessels. It does not negatively affect the heart function.

Plendil is used in the treatment of high blood pressure (hypertension) and heart and chest pain brought on by for example exercise or stress (angina pectoris).

2. What you need to know before you take Plendil

Do not take Plendil
- if you are pregnant. You should tell your doctor as soon as possible if you become pregnant while using this medicine.
- if you are allergic to felodipine or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from uncompensated heart failure.
- if you have acute myocardial infarction (heart attack).
- if you have chest pain of recent onset, or angina pectoris that is lasting for more than 15 minutes or longer or is more severe than usual.
- if you have disease of a heart valve or heart muscle, until you have talked to your doctor.

Warnings and precautions
Plendil, like other blood-pressure lowering medicinal products, may in rare cases lead to pronounced low blood pressure which in some patients may result in an inadequate supply of blood to the heart. Symptoms of excessive low blood pressure and inadequate blood supply to the heart itself, frequently include dizziness and chest pain. If you experience these symptoms, seek emergency care immediately.

Talk to your doctor before taking Plendil, especially if you have problems with your liver.

Taking Plendil may cause your gums to become swollen. Practice good oral hygiene to help avoid your gums from swelling (see section 4).

Children
The use of Plendil is not recommended in children.

Other medicines and Plendil
Tell your doctor if you are taking, have recently taken or might take any other medicines. Some medicines/herbal remedies can affect treatment with Plendil.
Examples are:
- cimetidine (medicine to treat gastric ulcers)
- erythromycin (medicine to treat infections)
- itraconazole (medicine to treat fungi)
- ketoconazole (medicine to treat fungi)
- medicines to treat HIV protease inhibitors (such as ritonavir)
- medicines to treat HIV infection (such as efavirenz, nevirapine)
- phenytoin (medicine to treat epilepsy)
- carbamazepine (medicine to treat epilepsy)
- rifampicin (medicine to treat infections)
- barbiturates (medicine to treat anxiety, sleeping problems and epilepsy)
- tacrolimus (medicine used in organ transplantations)

Medicines containing St John's wort (*Hypericum perforatum*) (herbal product used to treat depression) may reduce the effect of Plendil and should therefore be avoided.

14. Plendil with food and drink

Do not drink grapefruit juice if you are treated with Plendil, as this may increase the effect of Plendil and the risk of side effects.

Pregnancy and breast-feeding
Pregnancy
Do not use Plendil if you are pregnant.

15. Breast-feeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. Plendil is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed.

Driving and using machines
Plendil can have minor or moderate influence on your ability to drive and use machines. If you experience headache, nausea, dizziness or fatigue your ability to react may be impaired. Caution is recommended especially at the start of treatment.

Plendil contains lactose and castor oil
Plendil contains lactose that is a type of sugar. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

Plendil contains castor oil, which may cause stomach upset and diarrhoea.

3. How to take Plendil

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Plendil extended release tablets should be taken in the morning and be swallowed with water. The tablet must not be divided, crushed or chewed. This medicine can be taken without food or following a light meal not high in fat or carbohydrates.

16. Hypertension
Treatment should be started with 5 mg once a day. If necessary, your doctor may increase the dose or add another blood-pressure lowering medicine. The usual dose when treating this disease for a long time is 5-10 mg once a day. In elderly patients, a starting dose of 2.5 mg daily may be considered.

17. Stable angina pectoris
Treatment should be started with 5 mg once a day and if needed, your doctor may increase the dose to 10 mg once a day.

18. If you have liver problems
The level of felodipine in your blood may be increased. Your doctor may lower the dose.

19. Elderly people
Your doctor may initiate treatment with the lowest available dose.

If you take more Plendil than you should
If you take more than the recommended number of doses of Plendil, you may suffer from very low blood pressure and sometimes palpitations, high or, rarely, slow heart rate. Therefore, it is very important that you take the number of doses prescribed by your doctor. If you experience symptoms such as feeling faint, light-headedness or dizziness, contact your doctor immediately.

If you forget to take Plendil
If you forget to take a tablet, leave out that dose completely. Take your next dose at the right time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Plendil
If you stop taking this medicine your condition may return. Please consult your doctor and seek advice before you stop taking Plendil. Your doctor will advise you how long to take your medicine.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following happen to you, stop taking Plendil and tell a doctor straight away:
- Hypersensitivity and allergic reactions: The signs may include raised lumps on your skin (weals) or swelling of your face, lips, mouth, tongue or throat.

The following undesirable effects have been identified. Most of these reactions appear at start of treatment or after a dose increase. Should such reactions occur, they are usually brief and diminish in intensity with time. If you experience any of the following symptoms and they persist, please tell your doctor.

Mild enlargement of the gums has been reported in patients with an inflammation in the mouth (gingivitis/periodontitis). The enlargement can be avoided or reversed by careful oral hygiene.

Very common: may affect more than 1 in 10 people
- Ankle swelling

Common: may affect up to 1 in 10 people
- Headache
- Flushing

Uncommon: may affect up to 1 in 100 people
- Abnormally rapid heart rate
- Palpitations
- Too low blood pressure (hypotension)
- Nausea
- Abdominal pain
- Burning/prickling/numbness
- Rash or itching
- Fatigue
- Dizziness

Rare: may affect up to 1 in 1,000 people
- Fainting
- Vomiting
- Nettle rash
- Pain in joints
- Muscular pain
- Impotence/sexual dysfunction

Very rare: may affect up to 1 in 10,000 people
- Gingivitis (swollen gums)
- Increased liver enzymes
- Skin reactions due to increased sensitivity to sunlight
- Inflammation of small blood vessels of the skin
- A need to pass water frequently
- Hypersensitivity reactions such as fever or swelling of the lips and tongue

Other undesirable effects may occur. If you have any bothersome or unusual reaction while taking Plendil, check with your doctor right away.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Plendil

[To be completed nationally]

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 carton, blister and bottle after 'EXP'. The expiry date refers to the last day of that month.

Do not use this medicine if you notice the packaging is torn or damaged.

Do not throw away any 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.

6. Contents of the pack and other information

What Plendil contains

- The active substance felodipine. Each tablet contains 2.5 mg 5 mg or 10 mg of felodipine.

- The other ingredients are:
  Tablet core:
  Hydroxypropylcellulose
  Hypromellose 50 mPa·s
  Hypromellose 10000 mPa·s
  Lactose anhydrous
  Microcrystalline cellulose
  Polyoxyl 40 hydrogenated castor oil
  Propyl gallate
  Sodium aluminium silicate
  Sodium stearyl fumarate

  Tablet coating:
  Carnauba wax
  Iron oxide reddish-brown (E172) (Only used for Plendil 5 mg and 10 mg)
  Iron oxide yellow (E172)
  Hypromellose 6 mPa·s
  Macrogol 6000
  Titanium dioxide (E 171)

What Plendil looks like and contents of the pack

Plendil 2.5 mg prolonged-release tablet is yellow, circular, biconvex, engraved A/FL on one side and 2.5 on the other side, with a diameter of 8.5 mm.

Plendil 5 mg prolonged-release tablet is pink, circular, biconvex, engraved A/Fm on one side and 5 on the other side, with a diameter of 9 mm.

Plendil 10 mg prolonged-release tablet is reddish-brown, circular, biconvex, engraved A/FE on one side and 10 on the other side, with a diameter of 9.

Pack sizes of 20, 28, 30, 98 and 100 tablets

Pack sizes of 14, 20, 28, 30, 90, 98 and 100 tablets

Pack sizes of 14, 20, 28, 30, 98 and 100 tablets

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]
[See Annex I - To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, United Kingdom: Plendil

France: Flodil
Germany: Modip
Italy: Feloday, Prevex
Portugal: Preslow
Sweden: Felodipin AstraZeneca

[See Annex I - To be completed nationally]

This leaflet was last revised in {MM/YYYY} {month YYYY}

[To be completed nationally]

Detailed information on this medicine is available on the website of {MS/Agency}