Directions for Use **Please Read Carefully!**

Felocor ® 5mg / 10 mg Modified-release Tablets

Content
Each **Felocor® 5 mg** and **Felocor® 10 mg** modified release tablet contains felodipine 5 mg and 10mg respectively.

Description
Felocor® 5 mg: Round, biconvex film-coated tablets; pale red to grey-red tablets with embossment F 5 on one side.
Felocor® 10 mg: Round, biconvex film-coated tablets; pale red to grey-red tablets with embossment F 10 on one side.

Pharmacodynamics
Felodipine is a vasoselective calcium antagonist. It has a stronger effect on the vascular smooth muscle than on the myocardial muscle. Felodipine selectively dilates arterioles with no effect on venous vessels.
Felodipine leads to dose-related lowering of the blood pressure via vasodilation and consequently a reduction of peripheral vascular resistance. It reduces both systolic and diastolic blood pressure. The hemodynamic effect of felodipine is accompanied by reflex (baroreceptor-mediated) tachycardia. Reflex tachycardia is uncommon in this modified-released product, in particular during chronic use.
At therapeutic doses, felodipine has no direct effect in either cardiac contractility or cardiac conduction. Felodipine reduces renal vascular resistance. The glomerular filtration rate remains unchanged.
Felodipine has weak natriuretic/diuretic effect and does not provoke fluid retention. Felodipine can either be used as monotherapy or concomitantly with beta-blockers, diuretics or ACE-inhibitors.

Pharmacokinetics
Absorption
Felodipine is completely absorbed following oral administration. With the extended release tablets, the absorption phase is prolonged. This results in even felodipine plasma concentrations within the therapeutic range over 24 hours. Peak plasma levels are reached after 3 – 5 hours. Steady-state is reached approximately 3 days after starting treatment. Due to an excessive first-pass effect, only approximately 15% of the administered dose is systematically available.
Distribution
The plasma protein binding of felodipine is more than 99%. The volume of distribution is approximately 10 L/kg at steady state, indicating large tissue distribution. There is no significant accumulation during long-term treatment.
Metabolism
Felodipine is extensively metabolised in the liver by CYP3A4. All identified metabolites are inactive.
Elimination
No unchanged parent substance is detectable in the urine. The average half-life of felodipine in the terminal phase is 25 hours. The inactive hydrophilic metabolites formed by hepatic biotransformation are mainly eliminated renally (to approximately 70%), and the remainder is excreted in the faeces. The mean plasma clearance is 1100 mL/L and is dependent on the hepatic blood flow.
Elderly
Increased plasma concentrations have been measured in elderly patients.
Impaired hepatic function
Increased plasma concentrations of up to 100% have been measured in patients with impaired hepatic function.
Impaired renal function
Renal impairment does not affect the pharmacokinetics of felodipine, although accumulation of inactive metabolites occurs in renal failure.
Effect on food
According to studies performed with felodipine tablets, a high-fat meal may have an impact on pharmacokinetics parameters.

Indications
Felocor® 5mg / Felocor® 10mg is used in the treatment of hypertension and stable angina pectoris.

Side effects
Like other arteriolar dilators, felodipine can cause flushing, headache, palpitations, dizziness and fatigue. Most of these reactions are dose-dependent and appear at the start of treatment or after a dose increase. Should such reactions occur, they are usually transient and diminish with time.
As with other dihydropyridines, dose-dependent ankle swelling can occur in patients treated with felodipine. This results from precapillary vasodilatation and is not related to any generalized fluid retention.
As with other calcium antagonists, mild gingival enlargement has been reported in patients with pronounced gingivitis/periodontitis.
The enlargement can be avoided or reversed by careful dental hygiene.
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).)
Nervous system disorders
Common: Headache
Uncommon: Dizziness, paraesthesia
Cardiac disorders
Uncommon: Tachycardia, palpitations
Vascular disorders
Common: Flush
Uncommon: Hypotension
Rare: Syncope
Gastrointestinal disorders
Uncommon: Nausea, abdominal pain
Rare: Vomiting
Very rare: Gingival hyperplasia, gingivitis
Hepatobilliary disorders
Very rare: Increased liver enzymes
Skin and subcutaneous system disorders
Uncommon: Rash, pruritus
Rare: Urticaria
Very rare: 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: Peripheral oedema
Uncommon: Fatigue
Very rare: Hypersensitivity reactions e.g. angio-oedema, fever

Precautions
Felodipine may cause significant hypotension with subsequent tachycardia. This may lead to myocardial ischaemia in susceptible patients.
Felodipine must be used with caution in patients with a propensity for tachycardia.
Felodipine is cleared by the liver. Consequently, can higher therapeutic concentrations and response be expected in patients with clearly reduced liver function (see Recommended Dosage).
Excipients with known effect
The tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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.

Contraindications

Felodipine is contraindicated in patients:

- With hypersensitivity to felodipine (or other dihydropyridines) or to any of the excipients
- With cardiogenic shock (as with other calcium channel blockers, treatment should be discontinued in patients who develop cardiogenic shock)
- Hemodynamically significant cardiac valvular obstruction
- Dynamic cardiac outflow obstruction
- With unstable angina pectoris
- Who have had an acute myocardial infarction (within 4-8 weeks of a myocardial infarction)
- With decompensated heart failure
- During pregnancy

Drug Interactions

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

Enzyme inhibitors have been shown to cause an increase in felodipine plasma concentrations. Examples are:

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

Interactions leading to decreased plasma concentration of felodipine

Enzyme inducers may cause a decrease in plasma concentrations of felodipine. Examples are:

- Phenytoin
- Carbamazepine
- Rifampicin
- Barbiturates
- Efavirenz
- Nevirapine
- Hypericum perforatum (St 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.

Other extensively bound drugs: The high degree of plasma protein binding of felodipine does not appear to affect the unbound fraction of other extensively bound drugs such as warfarin.

Pregnancy

Felodipine should not be given during pregnancy

Lactation

Felodipine is detected in breast milk. When taken in therapeutic doses by the nursing mother it is, however, not likely to affect the infant.

Recommended dosage

Tablets should be taken in the morning, be swallowed with water and 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.

Hypertension

The dose should be adjusted individually. Treatment should be started with 5 mg once daily. If necessary the dose may be further increased or another antihypertensive agent added. The usual maintenance doses are 5 mg to 10 mg once daily. In elderly patients initial treatment with 2.5 mg daily should be considered. For dose of 2.5 mg a medicinal product with an appropriate strength should be used

Angina pectoris

The dose should be adjusted individually. Treatment should be started with 5 mg once daily, increasing to 10 mg once daily if needed.

Elderly

The recommended initial dose should be adjusted in the elderly. Subsequent dose increases should be undertaken with particular caution. For dose of 2.5 mg a medicinal product with an appropriate strength should be used

Impaired renal function

The pharmacokinetics are not significantly affected in patients with mild to moderate impaired renal function. Caution should be taken in patients with severe renal impairment.

Hepatic impairment

Patients with impaired hepatic function may have elevated plasma concentrations of felodipine and may response to lower doses.

Paediatric population

There is limited experience of felodipine treatment in children. Felodipine should not be used in children.

Method and duration of administration

The modified-release tablets should be taken orally in the morning with a sufficient amount of fluid (e.g. a glass of water, but it should NOT be taken with grapefruit juice!) (See *Drug Interaction*). The modified-release tablet should be swallowed whole and not chewed or crushed. The tablets may be taken on empty stomach or with a light meal, however a high-fat meal should be avoided (see *Pharmacokinetics*).

Symptoms and Treatment of Overdosage and Antidote

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

Management

Activated charcoal, if necessary gastric lavage. 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 drugs with predominant effect on the α1-adrenoceptor may be given if the above-mentioned measures are insufficient

Presentation:

Box of 30, 50 and 100 modified-release tablets.

Store in a cool dry place, not above 30°C

Keep out of reach of children

Jauhi daripada kanak-kanak.

Shelf life: Please refer to the outer box label.

Keep medicines out of reach of children

Manufactured for:
Hexal AG
Holzkirchen, Germany.
By:
Salutas Pharma GmbH
(A wholly owned subsidiary of Hexal AG)
Date of revision: Aug 2017