Core Safety Profile

Active substance: Lacidipine
Pharmaceutical form(s)/strength: Tablets containing 2,4 or 6 mg lacidipine
P - RMS: EE/H/PSUR/0002/001
Date of FAR: 09.11.2009
4.1 Therapeutic indications

As a treatment of hypertension either alone or in combination with other antihypertensive agents eg. beta-blockers, diuretics and ACE inhibitors.

4.2 Posology and method of administration

The initial dosage is 2 mg once daily. It should be taken at the same time each day, preferably in the morning, with or without food.

The treatment of hypertension should be adapted to the severity of the condition, and according to individual response.

The dose may be increased to 4 mg and if necessary to 6 mg, after adequate time has been allowed for the full pharmacological effect to occur. In practice this should not be less than three to four weeks, unless the clinical condition requires a more rapid upward titration.

Populations

• Hepatic impairment
  No dose modification is required in patients with hepatic impairment.

• Renal impairment
  As lacidipine is not excreted by the kidneys the dose does not require modification in patients with renal impairment.

• Children
  No experience has been gained with lacidipine in children.

• Elderly
  No dose modification is required.
  Treatment may be continued indefinitely.

4.3 Contraindications

• Hypersensitivity to any component of the preparation.
• As with other dihydropyridines, lacidipine is contraindicated in patients with severe aortic stenosis.

4.4 Special warnings and precautions for use

In specialised studies lacidipine has been shown not to affect the spontaneous function of the SA node or to cause prolonged conduction within the AV node. However the theoretical potential for a calcium antagonist to affect the activity of the SA and AV nodes should be noted, and therefore lacidipine should be used with caution in patients with pre-existing abnormalities in the activity of the SA and AV nodes.

As has been reported with other dihydropyridine calcium channel antagonists, lacidipine should be used with caution in patients with congenital or documented acquired QT prolongation. Lacidipine should also be used with caution in patients treated concomitantly with medications known to prolong the QT interval such as, class I and III antiarrhythmics, tricyclic antidepressants, some antipsychotics, antibiotics (e.g. erythromycin) and some antihistamines (e.g. terfenadine).

As with other calcium antagonists, lacidipine should be used with caution in patients with poor cardiac reserve.

As with other dihydropyridine calcium antagonists lacidipine should be used with care in patients with previously diagnosed unstable angina pectoris as well as inpatients who develop unstable angina during treatment.
Lacidipine should be used with caution in patients after recent myocardial infarction. There is no evidence that lacidipine is useful for secondary prevention of myocardial infarction.

The efficacy and safety of lacidipine in the treatment of malignant hypertension has not been established.

Lacidipine should be used with caution in patients with impaired liver function because antihypertensive effect may be increased.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interactions with other medicinal products and other forms of interaction

Co-administration of lacidipine with other agents recognised to have a hypotensive effect, including anti-hypertensive agents, (e.g. diuretics, beta-blockers, or ACE inhibitors), may have an additive hypotensive effect. However, no specific interaction problems have been identified in studies with common antihypertensive agents (e.g. beta-blockers and diuretics) or with digoxin, tolbutamide or warfarin.

The plasma level of lacidipine may be increased by simultaneous administration of cimetidine.

Lacidipine is highly protein bound (more than 95 %) to albumin and alpha-1-glycoprotein.

As with other dihydropyridines, lacidipine should not be taken with grapefruit juice as bioavailability may be altered.

In clinical studies in patients with a renal transplant treated with cyclosporin, lacidipine reversed the decrease in renal plasma flow and glomerular filtration rate induced by cyclosporin.

Lacidipine is known to be metabolised by cytochrome CYP3A4 and, therefore, significant inhibitors and inducers of CYP3A4 (eg. rifampicine, itraconazole) administered concurrently may interact with the metabolism and elimination of lacidipine.

Concomitant use of lacidipine and corticoides or tetracosactid might decrease antihypertensive effect.

4.6 Pregnancy and Lactation

Fertility
No Text.

Pregnancy
There are no data on the safety of lacidipine in human pregnancy.
Animal studies have shown no teratogenic effects or growth impairment (see 5.3 Preclinical safety data).

Lacidipine should only be used in pregnancy when the potential benefits for the mother outweigh the possibility of adverse effects in the foetus or neonate.

The possibility that lacidipine can cause relaxation of the uterine muscle at term should be considered (see 5.3 Preclinical safety data).

Lactation
Milk transfer studies in animals have shown that lacidipine (or its metabolites) are likely to be excreted into breast milk.

Lacidipine should only be used during lactation when the potential benefits for the mother outweigh the possibility of adverse effects in the foetus or neonate.
4.7 Ability to perform tasks that require judgment, motor or cognitive skills

...may cause dizziness. Patients should be warned not to drive or operate machinery if they experience dizziness or related symptoms.

4.8 Undesirable effects

Data from large clinical trials (internal and published) were used to determine the frequency of very common to uncommon adverse reactions. The following convention has been used for the classification of frequency:- very common ≥ 1/10, common ≥ 1/100 and <1/10, uncommon ≥ 1/1000 and <1/100, rare ≥ 1/10000 and < 1/1000, very rare <1/10000, not known (cannot be estimated from the available data).

Lacidipine is usually well tolerated. Some individuals may experience minor side-effects which are related to its known pharmacological action of peripheral vasodilation. Such effects, indicated by a hash (#), are usually transient and usually disappear with continued administration of lacidipine at the same dosage.

Nervous system disorders
Common #Headache, #dizziness
Very rare Tremor

Cardiac disorders
Common #Palpitation
Uncommon Aggravation of underlying angina
As with other dihydropyridines aggravation of underlying angina has been reported in a small number of individuals, especially at the start of treatment. This is more likely in patients with symptomatic ischaemic heart disease.

Vascular disorders
Common #Flushing

Gastrointestinal disorders
Common Stomach discomfort, nausea
Uncommon Gingival hyperplasia

Skin and subcutaneous tissue disorders
Common Skin rash (including erythema and itching)
Rare Angioedema, urticaria

Renal and urinary disorders
Common Polyuria

General disorders and administration site conditions
Common Asthenia, #oedema

Investigations
Common Reversible increase in alkaline phosphatase (clinically significant increases are uncommon)

Psychiatric disorders
Rare Disurbances of mood
4.9 Overdose

There have been no recorded cases of lacidipine overdosage.