SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lacidipine 4 mg Film-Coated Tablets

Pezius 4 mg Film-Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 4 mg lacidipine.

Excipient with known effect:

Each tablet contains 236 mg lactose (as lactose monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White coloured, oval shaped, film-coated tablet debossed with  on one side and '2' and '24' separated with a break line on the other side.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Lacidipine is indicated for the treatment of hypertension either alone or in combination with other antihypertensive agents, including ß-adrenoceptor antagonists, diuretics, and ACE-inhibitors.

4.2 Posology and method of administration

Posology

Adults:

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

The recommended initial dose is 2 mg once daily. The dose may be increased to 4 mg (and then, 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 3 to 4 weeks. Daily doses above 6 mg have not been shown to be significantly more effective.

Lacidipine should be taken at the same time each day, preferably in the morning.

Treatment with Lacidipine may be continued indefinitely.

Patients with hepatic impairment:
Lacidipine is metabolised primarily by the liver and therefore in patients with hepatic impairment, the bioavailability of Lacidipine may be increased and the hypotensive effect enhanced. These patients should be carefully monitored, and in severe cases, a dose reduction may be necessary.

Patients with kidney disease:
As Lacidipine is not cleared by the kidneys, the dose does not require modification in patients with kidney disease.

Paediatric population:
No experience has been gained with Lacidipine in children.

Method of administration
For oral administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Lacidipine should only be used with great care in patients with a previous allergic reaction to another dihydropyridine because there is a theoretical risk of cross-reactivity.

As with other calcium antagonists, Lacidipine should be discontinued in patients who develop cardiogenic shock and unstable angina. In addition, dihydropyridines have been shown to reduce coronary arterial blood-flow in patients with aortic stenosis and in such patients Lacidipine is contraindicated.

Lacidipine should not be used during or within one month of a myocardial infarction.

In case of rare hereditary conditions that may be incompatible with an excipient of the product (please refer to section 4.4 Special Warnings and Precautions for Use) the use of the product is contraindicated.

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.

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.

There is no evidence that lacidipine impairs glucose tolerance or alters diabetic control.

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

4.5 Interaction 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 (e.g. rifampicin, itraconazole) administered concurrently may interact with the metabolism and elimination of lacidipine.

Concomitant use of lacidipine and corticoids or tetracosactide might decrease antihypertensive effect.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Although some dihydropyridine compounds have been found to be teratogenic in animals, data in the rat and rabbit for lacidipine provide no evidence of a teratogenic effect. Using doses far above the therapeutic range, in animals lacidipine shows evidence of maternal toxicity resulting in increased pre- and post-implantation losses and possibly delayed ossification. Evidence from experimental animals has indicated that administration of lacidipine results in prolongation of gestational period and prolonged and difficult labour as a consequence of relaxation of uterine muscle.

There are no data on the safety of lacidipine in human pregnancy.

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.

Breast-feeding:

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 breastfeeding when the potential benefits for the mother outweigh the possibility of adverse effects in the foetus or neonate.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Lacidipine is generally 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.

The following convention has been utilised for the classification of undesirable effects:

Very common	≥ 1/10
Common	≥ 1/100, <1/10
Uncommon	≥1/1000, <1/100
Rare	≥1/10000, <1/1000
Very rare	<1/10000
Not known	Cannot be estimated from the available data

Adverse event frequencies have been estimated from spontaneous reports from post-marketing data.

Psychiatric disorders:

Depression	very rare

Nervous system disorders:

Dizziness#	common
Headache#	common
Tremor	very rare

Cardiac disorders:

Palpitations#	common
Tachycardia	common
Syncope	uncommon
Angina pectoris	uncommon

As with other dihydropyridines aggravation of underlying angina pectoris has been reported in a small number of individuals, especially at the start of treatment. This is more likely to happen in patients with symptomatic ischaemic heart disease. Lacidipine should be discontinued under medical supervision in patients who develop unstable angina.

Vascular disorders:

Flushing#	common
Hypotension	uncommon

Gastrointestinal disorders:

Abdominal discomfort	common
Nausea	common
Gingival	uncommon

hyperplasia

Skin and subcutaneous tissue disorders:

Rash	common
Erythema	common
Pruritus	common
Angioedema	rare
Urticaria	rare

Musculoskeletal and connective tissue disorders:

Muscle cramps	rare

Renal and urinary disorders:

Polyuria	common

General disorders and administration site conditions:

Asthenia	common
Oedema#	common

Investigations:

Blood alkaline phosphatase increased	common

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 Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard or search for MHRA Yellowcard in the Google Play or Apple App Store.

4.9 Overdose

Symptoms:

There have been no recorded cases of Lacidipine overdosage. The expected symptoms could comprise prolonged peripheral vasodilation associated with hypotension and tachycardia. Bradycardia or prolonged AV conduction could occur.

Therapy:

There is no specific antidote. Standard general measures for monitoring cardiac function and appropriate supportive and therapeutic measures should be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium channel blockers, Dihydropyridine derivatives, ATC code: C08CA09.

Mechanism of action:
Lacidipine is a specific and potent calcium antagonist with a predominant selectivity for calcium channels in the vascular smooth muscle.

Pharmacodynamic effects:
Its main action is to dilate peripheral arterioles, reducing peripheral vascular resistance and lowering blood pressure.

In a study of ten patients with a renal transplant, Lacidipine has been shown to prevent an acute decrease in renal plasma flow and glomerular filtration rate about six hours after administering oral cyclosporin. During the trough phase of cyclosporin treatment, there was no difference in renal plasma flow and glomerular filtration rate between patients with or without Lacidipine.

Following the oral administration of 4 mg lacidipine to volunteer subjects, a minimal prolongation of QTc interval has been observed (mean QTcF increase between 3.44 and 9.60 ms in young and elderly volunteers). This was not associated with any adverse clinical effects or cardiac arrhythmias on monitoring.

5.2 Pharmacokinetic properties

Absorption:
Lacidipine is a highly lipophilic compound; it is rapidly absorbed from the gastrointestinal tract following oral dosing. Absolute bioavailability averages about 10% due to extensive first-pass metabolism in the liver.

Peak plasma concentrations are reached between 30 and 150 minutes.

Metabolism:
The drug is eliminated primarily by hepatic metabolism (involving cytochrome P450 CYP3A4). There is no evidence that Lacidipine causes either induction or inhibition of hepatic enzymes.

The principal metabolites possess little, if any, pharmacodynamic activity.

Elimination:

Approximately 70% of the administered dose is eliminated as metabolites in the faeces and the remainder as metabolites in the urine.

The average terminal half-life of Lacidipine ranges from between 13 and 19 hours at steady state.

5.3 Preclinical safety data

In acute toxicity studies, Lacidipine has shown a wide safety margin.

In repeated dose toxicological studies, findings in animals, related to the safety profile of Lacidipine in man, were reversible and reflected the pharmacodynamic effect of Lacidipine.

No data of clinical relevance have been gained from *in vivo* and *in vitro* studies on reproduction toxicity, genetic toxicity or oncogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Povidone (K-30)

Crospovidone

Magnesium stearate

Film-coating:

Hypromellose 5cP (E464)

Titanium dioxide (E171)

Macrogol/PEG 400

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Alu/Alu blisters (OPA/Alu/PVC-Alu).

Pack sizes: 28

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Dr. Reddy's Laboratories (UK) Ltd,
410 Cambridge Science Park,
Milton Road,
Cambridge,
CB4 0PE,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 08553/0503

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/02/2025

10 DATE OF REVISION OF THE TEXT

03/02/2025