	PIL section: 2 What you need to know before you take Lacidipine tablets	
Extrapyramidal syndrome	SmPC and PIL only: SmPC Section: 4.8 Undesirable effects PIL section: 4 Possible side effects	None required.

Missing information		
Safety of treatment of malignant hypertension	SmPC only: SmPC Section: 4.4 Special warnings and special precautions for use	None required.
Safety in paediatric and adolescent patients (≤ 18 yrs of age)	SmPC and PIL only: SmPC Section: 4.2 (Posology and method of administration) PIL section: 2 What you need to know before you take Lacidipine tablets	None required.
Safety in pregnancy	SmPC and PIL only: SmPC Section: 4.6 Fertility, pregnancy and lactation 5.3 Preclinical safety data PIL section: 2 What you need to know before you take Lacidipine tablets	None required.

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Hypertension is a relatively common condition. It is well established that chronic, poorly controlled hypertension is a risk factor for cardiovascular morbidity and mortality, stroke and renal failure.

Chronic high blood pressure (BP) affects 20% to 50% of the adult population in developed countries (Bielecka-Dabrowa 2011). The condition is more frequent in men than in women and in elderly subjects, affecting more than 60% of those over 65 years-old (Pereira 2009, Wagner 2011, Lyra 2012).

There are genetic (age, race, sex, family history) and behavioural factors (smoking, obesity, alcoholism, sedentary lifestyle, stress, excessive salt consumption) that can affect the blood pressure (Lyra 2012).

High BP itself usually has no signs or symptoms. However, when the blood pressure stays high over time, it can damage the body in many ways. Generally, high BP can damage the heart and blood vessels leading to various serious cardiac and vascular disorders, such as heart attack, stroke or even death (Bielecka-Dabrowa 2011). Other health problems resulting from chronic high BP include kidney damage that can lead to their failure. High blood pressure is considered to be the leading risk factor for death in the world, causing an estimated 7.5 million deaths per year (13% of all deaths) (Reklaitiene 2012).

VI.2.2 Summary of treatment benefits

Lacidipine has been marketed in Europe for more than 20 years. The efficacy and safety of lacidipine has been investigated in numerous clinical studies, and is described in several review articles and standard literature. In the clinical studies efficacy and safety have been proven for the treatment of patients with the proposed indications. Along with well-established medical use, this active substance has acknowledged efficacy as well as an acceptable risk/benefit profile, in the claimed indications.

VI.2.3 Unknowns relating to treatment benefits

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

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Hypersensitivity reactions including skin rashes, itching and swelling	People with a history of allergies to the active ingredient or other ingredients in the medicine may experience allergic type reactions.	Yes, allergic reactions should be monitored for and action taken upon early signs and symptoms.
Reduction in the flow of blood through the heart in patients with existing restricted blood flow e.g. angina and heart attacks	As with other calcium antagonists, lacidipine should be used with caution in patients with poor cardiac reserve. Lacidipine should not be administered to patients after a recent myocardial infarction.	Yes, lacidipine should not be administered to patients following a recent heart attack or in circumstances where reduced blood flow to the heart is known.
Depression	Lacidipine may cause depression very rarely in some patients.	Yes, monitor for symptoms and report to doctor.
Increases in some liver enzymes	This is a potential adverse reaction with lacidipine. As the drug is metabolised in the liver this ADR could affect metabolism of the drug and cause other ADRs.	Yes, minimising the co-administration with drugs which affect liver enzymes and periodic monitoring of patients alkaline phosphatase levels.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Cardiac conduction disorders	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.
QT interval prolongation	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).
Extrapyramidal syndrome	The frequency of this ADR is not established. Extrapyramidal symptoms may occur due to the inhibition of calcium influx and dopaminergic antagonistic properties. The onset can be unpredictable although discontinuation of the medicine usually relieves the symptoms.

Missing information

Risk	What is known
Safety in treatment of malignant hypertension.	The efficacy and safety have not been established in the treatment of sudden onset hypertension.
Safety in paediatric and adolescent patients (≤ 18 yrs. of age)	The clinical studies that were undertaken have not established the safe use of lacidipine in a paediatric or adolescent population.
Safety in pregnancy	There are no clinical data on the use of this drug in pregnant women. Animal studies have shown no teratogenic effects or growth impairment. Nor has it shown any genotoxic potential in a battery of in vitro and in vivo tests. The only significant toxicological findings with lacidipine were reversible and consistent with the known pharmacological effects of calcium antagonists at high doses – decreased myocardial contractility and gingival hyperplasia in rats and dogs and constipation in rats. There was no evidence of carcinogenicity in mice. Like with other calcium channel antagonists, a carcinogenicity study has shown an increase in benign interstitial cell tumors in rats testes. The endocrine mechanisms believed to be involved in the production of interstitial hyperplasia and adenomas in rats are not relevant to humans. There is no evidence of developmental toxicity observed after administration of lacidipine in pregnant rats or rabbits.

Risk	What is known
	The possibility that lacidipine can cause relaxation of the uterine muscle at term should be considered.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable. This is the first Risk Management Plan for lacidipine for Double E.