6.2. Elements for a Public Summary

6.2.1. Overview of Disease Epidemiology

High blood pressure (hypertension)

High blood pressure increases the workload of the heart and arteries. If not treated, it can damage the blood vessels of the brain, heart, and kidneys, and may result in a stroke, heart failure, or kidney failure. High blood pressure increases the risk of heart disease, kidney disease and stroke. Even moderate elevation of arterial blood pressure is associated with a shortened life expectancy. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of associated health complications, although drug treatment is often necessary in people for whom lifestyle changes prove ineffective or insufficient.

Chest pain (angina)

Chest pain or angina is a heart condition resulting from a reduced blood flow to the heart muscles. The most common cause for this reduced blood flow is blocked or narrowed heart arteries. Angina can be experienced as a pressing, squeezing, heaviness, tightness or pain of the chest that sometimes can be felt in the neck, back, jaw, and left arm.

Chronic stable angina pectoris, the pain is triggered by a consistent high level of activity (like climbing stairs), which results in the heart working harder. Symptoms last a few minutes. Stable angina is a warning sign for an increased risk of more serious conditions such as heart attack or stroke.

Vasospastic (Prinzmetal's) angina, (also known as variant/unstable angina), an artery of the heart undergoes a temporary, sudden narrowing. This spasm results in a withholding of oxygen-rich blood to a part of the heart due to a decrease or cut-off of blood flow through the artery. This causes chest pain (angina) which may last from 5 – 30 minutes, which can also occur at rest.

If not treated, the risk for having a stroke or heart attack increases. Various medications in single or combined forms are prescribed for angina, however surgery is sometimes necessary. Diet and lifestyle changes are effective in preventing angina and preventing the worsening of symptoms.

6.2.2. Summary of Treatment Benefits

Amlodipine belongs to the class of medicines called calcium channel blockers. Calcium is necessary for muscle contraction, thus in blocking its transportation in the heart's arteries, heart muscles' arteries are relaxed and widened, resulting in an easier flow of blood through them. This prevents angina. This action in the rest of the body reduces blood pressure, which reduces the amount of work needed from the heart, further reducing angina in patients with coronary artery disease.

- High Blood Pressure

Amlodipine is used alone or in combination with other medications to lower blood pressure. This reduces the risk of stroke, heart attack and kidney disease. Benefits supporting this treatment have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes including amlodipine. Many antihypertensive medications during randomized controlled trials, showed a reduction of cardiovascular morbidity and mortality. These medications were from different pharmacologic classes and had different mechanisms of action. Thus it is concluded that reduction of blood pressure is responsible for these benefits.

- Chest Pain (Angina)

Amlodipine prevents chest pain by improving the blood supply to the heart muscles for them to get more oxygen. It does not provide immediate pain relief when taken for angina. Amlodipine treats the symptoms of chronic stable angina and treats Prinzmetal's angina. It may be used alone or in combination with other medications for the treatment of angina.

6.2.3. Unknowns Relating to Treatment Benefits

There is no unknown, of which the Marketing Authorisation Holder is aware, relating to treatment benefits.

6.2.4. Summary of Safety Concerns

Table 5. Important Identified Risks

Risk	What is Known	Preventability
Pancreatitis	Pancreatitis has been reported as an adverse event from some patients taking amlodipine.	Physician supervision and care
Low blood pressure (including fainting)	Low blood pressure may be associated with severe movement-dependent drop in blood pressure, that can lead to fainting and/or severe dizziness (such as when first standing up from a sitting or lying position), and potentially serious consequences including those related to falls.	Physician supervision and care
Heat attack [a]	Heart attack has been reported in patients taking amlodipine. Heart attack can be very serious.	Physician supervision and care. Patients should seek immediate medical attention for symptoms of heart attack.
Irregular heartbeat [a]	Irregular heartbeat has been reported in patients taking amlodipine. Irregular heartbeat can be serious.	Physician supervision and care. Patients should report symptoms of irregular heartbeat to their doctor.
Liver disorder (including hepatitis, jaundice or laboratory enzyme disorders)	Liver disorder (including hepatitis, jaundice or laboratory enzyme disorders) has been reported in patients taking amlodipine. Liver disorder can be very serious.	Liver disorder (including hepatitis, jaundice or laboratory enzyme disorders)

a: As with other calcium channel blockers, the development of heart attack and irregular heartbeat cannot be distinguished from the natural history of the underlying disease.

Table 6. Important Potential Risks

Risk	What is Known *(Including Reason Why it is Considered a Potential Risk)*
A buildup of fluid in the air spaces in the lungs. keeping oxygen from getting into the blood in patients with heart failure (pulmonary oedema)	In a follow-up, long term, study (PRAISE-2) of amlodipine in patients with moderate severe heart failure without clinical symptoms or objective findings suggestive or underlying heart blood vessel disease, amlodipine was associated with increased reports of pulmonary oedema.

Table 7. Missing Information

Risk	What is Known
Effect on Fertility	The effect of amlodipine on fertility has not been studied.
Safety during pregnancy and breast feeding	There are no adequate data on the use of amlodipine in pregnant women. Animal reproduction studies with have shown reproductive harm but no teratogenic effect. The potential risk for humans is unknown. Amlodipine should not be used during pregnancy. It is not known whether amlodipine is excreted into human milk. Amlodipine should not be used by breast feeding women.
Use in children less than 6 years old	The effect of amlodipine on blood pressure in children less than 6 years of age is not known.

6.2.5. 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, and the risks, and the 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.

The SmPC can be found in the Part VII Annex 2.

This medicine has no additional risk minimisation measures.

6.2.6. Summary of Additional Risk Minimization Measures by Safety Concerns

No additional risk minimization measures have been undertaken.

6.2.7. Planned Post Authorisation Development Plan (if Applicable)

Not applicable.

6.2.8. Summary of Changes to the Risk Management Plan Over Time

At the specific request of the MHRA, 4 new risks have been included as Important Risks. This RMP includes hypotension (including syncope), MI, arrhythmia and hepatitis (including hepatitis, jaundice, and elevated hepatic enzymes) as Important Identified Risks. As with other calcium channel blockers, the development of myocardial infarction and arrhythmia cannot be distinguished from the natural history of the underlying disease, for this antihypertensive.

6.3. REFERENCES

[1] Prospective Randomized Amlodipine Survival Evaluation 2 (PRAISE-2) DSMB Report and Executive Summary Report, July 2000