

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

High blood pressure (Essential hypertension)

Blood pressure is a measurement of the force against the walls of the arteries as heart pumps blood through body. Hypertension is another term used to describe high blood pressure. Hypertension affects about 1 billion people around the world According to a new report published by the European Commission, the occurrence of hypertension varied considerably by country. Countries in East Central Europe, particularly Bulgaria, Romania, and Slovakia, and the Mediterranean area (particularly Greece) reported the highest proportion ($\geq 50\%$) of people under long-term treatment for hypertension, where as in Belgium, The Netherlands, and Luxembourg (Benelux), hypertension was mentioned by $\leq 25\%$. The risk factors for getting high blood pressure includes obesity, smoking, too much alcohol, stress, diabetes (high sugar level in body) and family history of high blood pressure. High blood pressure increases chance of having a stroke (occurs when there is lack of blood supply to brain), heart attack, heart failure, kidney disease, or early death.

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 (blood vessel). 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.

VI.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 (Unstable angina). It may be used alone or in combination with other medications for the treatment of angina.

VI.2.3 Unknowns relating to treatment benefits

Data on safety and efficacy of amlodipine in children less than 6 years, use during pregnancy and breast feeding, and effect in hypertensive crisis has not been established.

VI.2.4 Summary of safety concerns**Important identified risks**

Risk	What is known	Preventability
Pulmonary oedema (An abnormal build-up of fluid in the lungs)	In a long-term, study in patients with severe heart failure, the reported incidence of pulmonary oedema was higher in the amlodipine treated group.	Patients with heart failure should be treated with caution.
Use in patients with impaired liver (hepatic) function	Dosage recommendations have not been established in patients with mild to moderate liver impairment; therefore dose selection should be cautious and should start at the lower end of the dosing range. The way the body absorbs, distributes and gets rid of amlodipine has not been studied in severe liver impairment. Amlodipine	You should inform your doctor if you have or have had liver disease.

	<p>should be initiated at the lowest dose and titrated slowly in patients with severe liver impairment.</p> <p>Amlodipine's concentration is prolonged in patients with impaired liver function.</p> <p>Slow dose titration and careful monitoring may be required in patients with severe liver impairment.</p>	
<p>Risk of cardiovascular events</p>	<p>Amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and death.</p> <p>The patient may develop cardiogenic shock (a condition where your heart is unable to supply enough blood to the body). The symptoms of cardiogenic shock are low blood pressure, low pulse and fast heartbeat.</p> <p>Heart attack is very rare (may affect up to 1 in 10,000 people) reported adverse reaction of amlodipine.</p> <p>Abnormal heartbeat is very rare reported adverse reaction of amlodipine.</p> <p>Palpitations (awareness of your heart beat) is a commonly (may affect up to 1 in 10 people) reported adverse</p>	<p>Do not take amlodipine tablets, if you are suffering from cardiogenic shock, have severe low blood pressure, heart failure after a heart attack and suffer from irregular heartbeat.</p> <p>Before taking Amlodipine tablets, tell your doctor if you have heart failure or have suffered a heart attack during the past month.</p> <p>Tell your doctor immediately if you experience any symptoms of heart attack or abnormal heartbeat after taking this medicine.</p> <p>If you get any side effects talk to your doctor or pharmacist.</p>

	reaction of amlodipine.	
Drug interaction with CYP3A4 inhibitors (Concomitant therapy with drugs which act as inhibitors of CYP3A4 hepatic enzymes)	<p>Amlodipine tablets may lower your blood pressure even more if you are already taking other medicines to treat your high blood pressure.</p> <p>Some medicines (including medicines obtained without prescription, herbal medications or natural products) may interact with Amlodipine. This means that the action of both medicines can be changed.</p>	<p>Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.</p> <p>In particular, tell your doctor if you are taking any of the following medicines:</p> <p>Medicines that can lower blood pressure, antifungal medicines used to treat skin and fungal infections, antiviral medicines used to treat HIV infections, medicine to treat depression, antibiotics.</p>

Important potential risks

Risk	What is known
Use in elderly patients	<p>Amlodipine, used at similar doses in elderly or younger patients, is equally well tolerated. Therefore normal dosage regimens are recommended, but increase of the dosage should take place with care.</p> <p>Concomitant therapy with drugs which act as inhibitors of CYP3A4 hepatic enzymes may lower blood pressure even more in the elderly.</p>

Breast cancer	None proposed
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Missing Information

Risk	What is known
Use in pregnancy and lactation	<p>Do not take amlodipine tablets, if you are pregnant or breast-feeding.</p> <p>The safety of amlodipine in human pregnancy has not been established. If you think you might be pregnant, or are planning to get pregnant, you must tell your doctor before you take amlodipine tablets.</p> <p>It is not known whether amlodipine is passed into breast milk. If you are breast-feeding or about to start breast-feeding you must tell your doctor before taking amlodipine tablets.</p> <p>Ask your doctor or pharmacist for advice before taking any medicine.</p>
Use in paediatric patients under 6 years old	No data available in children under the age of 6 years.
Effect on male fertility	Reversible biochemical changes in the head of spermatozoa have been reported in some patients treated by amlodipine type of medicines. Clinical data are insufficient regarding the potential effect of amlodipine on fertility. In one rat study, adverse effects were found on male fertility.
Use in hypertensive crisis	The safety and efficacy of amlodipine in hypertensive crisis has not been established.

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 (if applicable)

No studies planned.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety concern	Comment
Version 2.0	18-May-2016	<p>The safety concern “use in patients with severe hepatic impairment” upgraded to an important identified risk from missing information.</p> <p>Hepatitis and pancreatitis, Hypotension (Including syncope and cardiogenic shock), Myocardial infraction, and Arrhythmia omitted from important identified risk.</p> <p>The safety concern “Risk of cardiovascular events” added as important identified risk.</p> <p>The safety concern “Pulmonary oedema” upgraded to important identified risk from important potential risk.</p> <p>The safety concern “Use in elderly patients” added as important potential risk.</p> <p>The safety concern Use in hypertensive crisis” is added as missing information.</p>	<p>RMP has been updated based upon RMS Day 70 Preliminary Assessment Report of Amlodipin Accord, (SE/H/842/01-02/II/10) dated 21-Apr-2016</p> <p>In Part V.1-Risk minimisation measures by safety concern:</p> <p>Actual text of the SmPC sections included instead of reference to the SmPC section number.</p> <p>Editorial changes were made in to RMP.</p>