

VI.2 Elements for a Public Summary

Amlodipin Orion is indicated for the treatment of high blood pressure (hypertension), chronic and stable chest pain due to narrowing of the blood vessels of the heart muscle (chronic stable angina pectoris) and the more rare form of chest pain caused by cramping of the blood vessels of the heart muscle (vasospastic (Prinzmetal's) angina).

VI.2.1 Overview of disease epidemiology

High blood pressure (hypertension)

Hypertension is a chronic disease in which the blood pressure is sustainably elevated. Systolic blood pressure means the pressure inside the arteries (blood vessels that carry blood from heart into the tissues) during the contraction of the heart, whereas diastolic blood pressure can be described as the pressure inside the arteries during the relaxation and filling of the heart. Blood pressure is considered elevated, when systolic blood pressure in repeated blood pressure measurements exceeds 140 mmHg and/or diastolic blood pressure is over 90 mmHg. Hypertension has been estimated to affect approximately 26 % of the adult population and this proportion is considered to be increasing. The prevalence dramatically increases in patients older than 60 years. The age-related blood pressure rise for women exceeds that of men; the prevalence of hypertension was reported at 50% for white men and 55% for white women aged 70 years or older. Untreated hypertension increases risk of other diseases, such as stroke, heart attack, heart failure and impaired function of the kidneys. High blood pressure is also associated with a shortened life expectancy. Thus, treatment of hypertension is essential in terms of public health.

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. The prevalence of angina increases sharply with age in both sexes from 0,1-1% in women aged 45-54 to 10-15% in women aged 65-74 and from 2-5% in men aged 45-54 to 10-20% in men aged 65-74. Therefore, it can be estimated that the most European countries, 20 000 – 40 000 individuals of the population per million suffer from angina.

In chronic stable angina pectoris, the pain is triggered by a consistent high level of activity, 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.

In 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. It may be used alone or in combination with other medications for the treatment of angina.

VI.2.3 Unknowns relating to treatment benefits

None.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Risk of cardiovascular events	<p>In patients with heart failure, amlodipine may increase the risk of cardiovascular events and mortality. In a long-term study in patients with severe heart failure (NYHA class III and IV) the reported incidence of pulmonary oedema (a condition caused by excess fluid in the lungs) was higher in the amlodipine treated group than in the placebo group.</p> <p>Amlodipine may cause commonly palpitations (awareness of your heart beat). Irregular heartbeat (including slow heart rate (bradycardia), heart rhythm disorder caused by abnormal electrical signals in the lower chambers of the heart (ventricular tachycardia) and an irregular and often rapid heart rate that can increase the risk of stroke, heart failure and other heart-related complications</p>	<p>Amlodipin Orion should not be used in patients with; severe low blood pressure (hypotension); narrowing of the aortic heart valve (aortic stenosis);cardiogenic shock (a condition where heart is unable to supply enough blood to the body) or heart failure after a heart attack.</p> <p>In the elderly increase of the dosage should take place with care.</p> <p>Patients should be carefully monitored for irregular heartbeat (including slow heart rate (bradycardia), heart rhythm disorder caused by abnormal electrical signals in the lower chambers of the heart (ventricular tachycardia) and an irregular and often rapid heart rate that can increase the risk of stroke, heart failure and other</p>

Risk	What is known	Preventability
	(atrial fibrillation)) as an uncommon adverse event is suspected. Heart attack has been reported very rarely.	heart-related complications (atrial fibrillation).
Impaired function of the liver	In patients with impaired function of the liver the elimination of amlodipine is decreased. The pharmacokinetics of amlodipine have not been studied in patients with severe hepatic impairment.	Amlodipine should be initiated at the lower end of the dosing range and caution should be used, both on initial treatment and when increasing the dose. Slow dose titration and careful monitoring may be required in patients with severe hepatic impairment.
Excess fluid in the lungs (pulmonary oedema)	In a long-term study in patients with severe heart failure (NYHA class III and IV) the reported incidence of excess fluid in the lungs (pulmonary oedema) was shown to be higher in the amlodipine treated group than in the group receiving placebo.	Patients with heart failure should be treated with caution. Calcium channel blockers, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Drug interaction with CYP3A4 inhibitors	Concomitant use of amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors, azole antifungals, macrolides like erythromycin or clarithromycin, verapamil or diltiazem) may give rise to significant increase in amlodipine exposure, especially in the elderly. Clinical monitoring and dose adjustment may thus be required.
Drug interaction with CYP3A4 inducers	There is no data available regarding the effect of CYP3A4 inducers on amlodipine. The concomitant use of CYP3A4 inducers (e.g., rifampicin, hypericum perforatum) may give a lower plasma concentration of amlodipine. Amlodipine should be used with caution together with CYP3A4 inducers.

Missing information

Risk	What is known
Effect on male fertility	Clinical data are insufficient regarding the potential effect of amlodipine on fertility. In one rat study, adverse effects were found on male fertility.
Use during pregnancy and breast-feeding	There are no adequate data on the use of amlodipine in pregnant women. Animal reproduction studies have shown reproductive harm. The potential risk for humans is unknown. Use in pregnancy

Risk	What is known
	<p>is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and foetus. It is not known whether amlodipine is excreted into human milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with amlodipine should be made taking into account the benefit of breast-feeding to the child and the benefit of amlodipine therapy to the mother.</p>
Use in severely increased blood pressure (Hypertensive crisis)	The safety and efficacy of amlodipine in severely increased blood pressure (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. The Summary of Product Characteristics and the Package leaflet for this medicinal product can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

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

Not applicable.