VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Gout is a disease with painful, swollen joints caused by uric acid crystals. Gout is a complex form of arthritis and can affect anyone. Men are more likely to get gout, but women become increasingly susceptible to gout after menopause. Gout appears when uric acid builds up in the body. Eating plenty of certain types of foods, using certain types of medicines, and having treatment for cancer, can all make the uric acid level higher. The burden of gout in the United Kingdom is higher than previously thought, with approximately 1 in 40 adults being affected. [1] Where an increased incidence and prevalence of gout has been reported, it is generally attributed to trends in lifestyles leading to increases in gout risk factors, such as obesity, hypertension and alcohol consumption. [2]

Uric acid crystals deposited in the joints can cause pain, swelling, stiffness, and deformity, and impair movement. The crystals can also cause kidney stones. Most kidney stones pass out of the body, but sometimes they may get stuck in the urinary tract, block the flow of urine and cause great pain. [3]

Sometimes the excess uric acid precipitation within the kidney can result in to kidney failures. This is commonly seen in cancer patients, particularly after chemotherapy or radiation. [4]

Patients with hereditary enzyme deficiencies like Lesch-Nyhan syndrome suffer from neurological and behavioral abnormalities and the overproduction of uric acid. Patients with this conditions suffer from tensing of various muscles, jerking movements and flailing of the limbs. Patients usually cannot walk, require assistance sitting, and generally use a wheelchair.The prevalence of Lesch-Nyhan syndrome is approximately 1 in 380,000 individuals. This condition occurs with a similar frequency in all populations. [5]

Adenine phosphoribosyltransferase (APRT) deficiency is an inherited condition that affects the kidneys and urinary tract. APRT deficiency is estimated to affect 1 in 27,000 people in Japan. The condition is rarer in Europe, where it is thought to affect 1 in 50,000 to 100,000 people. [6]

VI.2.2 Summary of treatment benefits

Allopurinol is used to prevent or treat high uric acid levels in the blood. It reduces the amount of uric acid in the body by blocking one of the processes that makes it. This helps to stop the level of uric acid in the blood from becoming too high and causing problems like gout or kidney stones.

Allopurinol is indicted in for all forms of hyperuricaemia (high uric acid levels in the blood) not controllable by diet. Allopurinol is also used in secondary hyperuricaemia (high uric acid levels due to cancer, chemotherapy or genetic disorders).

VI.2.3 Unknowns relating to treatment benefits

Not applicable

VI.2.4 Summary of safety concerns

Table 12 Part VI - Summary table of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Serious hypersensitivity reactions	Serious hypersensitivity reactions involving fever, skin rash, joint pain, and abnormalities in blood and	This medicinal product should not be used in patients who are hypersensitive to allopurinol or to any of the other

	What is known	**Preventability**
	liver function tests (these may be signs of a multiorgan sensitivity disorder) are rare possible adverse reactions. Serious skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of allopurinol. Frequently, the rash can involve ulcers of the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These serious skin rashes are often preceded by influenza like symptoms fever, headache, body ache (flu-like symptoms). The rash may progress to widespread blistering and peeling of the skin. These serious skin reactions can be more common in people of Han Chinese or Thai origin. Very rarely acute anaphylactic shock has been reported. It is a severe disorder that can be life threatening without prompt treatment.	ingredients of this medicinal product. The patient should stop taking allopurinol and contact a doctor immediately if s/he experiences • an unexpected skin reaction (possibly in association with fever, swollen glands, joint pain, unusual blistering or bleeding, kidney problems or a sudden onset of fits). If the patient has an allergic reaction, s/he must stop taking allopurinol and see a doctor straight away. The signs may include: • skin rash, flaking skin, boils or sore lips and mouth • swelling of the face, hands, lips, tongue or throat • difficulty swallowing or breathing • very rarely signs may include sudden wheeziness, fluttering or tightness of the chest and collapse. • The patient must not take any more tablets unless doctor tells to do so.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Concomitant administration of ampicillin/amoxicillin	An increase in frequency of skin rash has been reported among patients receiving ampicillin or amoxicillin concurrently with allopurinol compared to patients who are not receiving both drugs. The cause of the reported association has not been established.
Administration during pregnancy and lactation	There is inadequate evidence of safety of allopurinol in human pregnancy. Animal reproductive toxicity studies have shown conflicting results. Reports indicate that allopurinol and oxipurinol are excreted in human breast milk. However, there are no data concerning the effects of allopurinol or its metabolites on the breast-fed baby.

Missing information

None

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) 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. 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

No studies planned.

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

The RMP was updated from version 1.0 to version 2.0 (this document) in line with the RMS Day 70 Preliminary Assessment Report for Allopurinol Vale (allopurinol), SE/H/1588/01-02/DC, dated 18-Jul-2016

Summary EU-Risk Management Plan