13 Part VI: Summary of the risk management plan (RMP) - Allopurinol, 100 mg and 300 mg, Tablets

This is a summary of the RMP for allopurinol, 100 mg and 300 mg, tablets. The RMP details important risks of allopurinol tablets, how these risks can be minimized, and how more information will be obtained about allopurinol tablets' risks and uncertainties (missing information).

Allopurinol tablets' summaries of product characteristics (SmPCs) and its package leaflet (PLs) give essential information to healthcare professionals (HCPs) and patients on how allopurinol tablets should be used.

Important new concerns or changes to the current ones will be included in updates of allopurinol tablets' RMP

13.1 Part VI: I. The medicine and what it is used for

For procedure: FI/H/0894/001-002

Adults

- All forms of hyperuricemia not controllable by diet, including secondary hyperuricemia of differing origin and clinical complications of hyperuricemia states, particularly manifest gout, urate nephropathy and for the dissolution and prevention of uric acid stones.
- The management of recurrent mixed calcium oxalate stones in concurrent hyperuricemia, when fluid, dietary and similar measures have failed.

Children and adolescents

- Secondary hyperuricemia of differing origin
- Uric acid nephropathy during treatment of leukemia
- Hereditary enzyme deficiency disorders, Lesch-Nyhan syndrome (partial or total hypoxanthin-guanine phosphoribosyl transferase deficiency) and adenine phosophoribosyl transferase deficiency.

For procedure: FI/H/0874/001-002

Allopurinol 100 mg

Adults

- All forms of hyperuricemia not controllable by diet, with serum uric acid values in the range of 535 µmol/l (9 mg/100 ml) and above and in clinical complications of hyperuricemia states, particularly manifest gout, urate nephropathy, for the dissolution and prevention of uric acid stones as well as for the prevention of the formation of calcium oxalate stones in concurrent hyperuricemia

Adults, children and adolescents ≥ 15 kg bodyweight

- Secondary hyperuricemia of differing origin

Children and adolescents ≥ 15 kg bodyweight

- Uric acid nephropathy during treatment of leukemia
- Hereditary enzyme deficiency disorders, Lesch-Nyhan syndrome (partial or total hypoxanthin-guanine phosphoribosyl transferase deficiency) and adenine phosophoribosyl transferase deficiency.

Allopurinol 300 mg

Adults

- All forms of hyperuricemia not controllable by diet, with serum uric acid values in the range of 535 µmol/l (9 mg/100 ml) and above and in clinical complications of hyperuricemia states, particularly manifest gout, urate nephropathy, for the dissolution and prevention of uric acid stones as well as for the prevention of the formation of calcium oxalate stones in concurrent hyperuricemia

Adults, children and adolescents ≥ 45 kg bodyweight

- Secondary hyperuricemia of differing origin

Children and adolescents ≥ 45 kg bodyweight

- Uric acid nephropathy during treatment of leukemia
- Hereditary enzyme deficiency disorders, Lesch-Nyhan syndrome (partial or total hypoxanthin-guanine phosphoribosyl transferase deficiency) and adenine phosophoribosyl transferase deficiency.

For procedure: IE/H/0425/001-002

Allopurinol is indicated for reducing urate/uric acid formation in conditions where urate/uric acid deposition has already occurred (e.g. gouty arthritis, skin tophi, nephrolithiasis) or is a predictable clinical risk (e.g. treatment of malignancy potentially leading to acute uric acid nephropathy).

The main clinical conditions where urate/uric acid deposition may occur are:

- Idiopathic gout;
- Uric acid lithiasis;
- Acute uric acid nephropathy;
- Neoplastic disease and myeloproliferative disease with high cell turnover rates, in which high urate levels occur either spontaneously, or after cytotoxic therapy;
- Certain enzyme disorders which lead to overproduction of urate, for example:
  - Hypoxanthine-guanine phosphoribosyltransferase, including Lesch-Nyhan syndrome;
  - Glucose-6-phosphatase including glycogen storage disease;
  - Phosphoribosylpyrophosphate synthetase;
  - Phosphoribosylpyrophosphate amidotransferase;
  - Adenine phosphoribosyltransferase;

Allopurinol is indicated for the management of 2, 8-dihydroxyadenine (2, 8-DHA) renal stones related to deficient activity of adenine phosphoribosyltranferase.

Allopurinol is indicated for the management of recurrent mixed calcium oxalate renal stones in the presence of hyperuricosuria, when fluid, dietary and similar measures have failed.

It contains allopurinol as the active substance and is given orally as tablets (100 mg and 300 mg).

13.2 Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of allopurinol tablets, together with measures to minimize such risks are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PLs and SmPCs addressed to patients and HCPs;
- Important advice on the medicine's packaging;
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimization* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including periodic safety update report (PSUR) assessment (if applicable) so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of allopurinol tablets is not yet available, it is listed under 'missing information' below.

13.2.1 Part VI – II.A: List of important risks and missing information

Important risks for allopurinol tablets are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of allopurinol tablets. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 13-1 List of important risks and missing information

List of important risks and missing information	
Important identified risk	Hypersensitivity reactions including Stevens-Johnson syndrome/toxic epidermal necrolysis
Important potential risk	None
Missing information	Use in pregnant women

13.2.2 Part VI – II.B: Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

13.2.3 Part VI – II.C: Post-authorization development plan

13.2.3.1 II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of allopurinol tablets.

13.2.3.2 II.C.2. Other studies in post-authorization development plan

There are no studies required for allopurinol tablets.