# Part II

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Allopurinol Tablets 300mg

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300mg of Allopurinol

For excipients, see 6.1

## 3 PHARMACEUTICAL FORM

Tablets
White biconvex tablets about 11mm in diameter. One face is marked with 'AP', a breakline and '300', the reverse carries the Roussel logo.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

1. In the management of conditions of excess body urate, including gout, neoplastic disease and associated treatment, enzyme disorders such as the Lesch – Nyhan Syndrome, renal calculi, renal failure, diuretic therapy and psoriasis.

2. In the prophylaxis and treatment of calcium renal lithiasis in patients with raised serum or urinary uric acid.

### 4.2 Posology and method of adminstration

DOSAGE:

Adults:
The usual daily dose is 300mg as a single dose with increments, as indicated by monitoring of serum and/or urinary uric acid, to the level necessary for optimum control, seldom in excess of 900mg. Dosage higher than 300mg should be given in divided doses not exceeding 300mg at any one time.

Children:
The usual daily dose is 10 to 20 mg/kg b.w.

To avoid an acute attack of gouty arthritis in the initial stages of treatment, colchicine or other appropriate agents should be given for at least a month. When used in neoplasia allopurinol therapy should be commenced before cytotoxics.

In renal insufficiency, dosage requirements must be reduced if creatinine clearance is less than 20ml/minute.

| **Creatinine Clearance** | **Dosage** |
|---|---|
| 10-20 ml/min | 100 to 200mg daily |
| <10ml/min | 100mg daily or at longer intervals |

If frequent renal dialysis is required allopurinol 300 to 400mg after each dialysis may be used in place of the above regimen.

ADMINISTRATION :

Oral

## 4.3 Contraindications

1. Use in patients hypersensitive to allopurinol.

2. As treatment for an acute attack of gout. Prophylactic therapy may be commenced on subsidence of the acute attack, provided that anti-inflammatory agents are concurrently used.

## 4.4 Special warnings and special precautions for use

1. An acute attack of gout may be precipitated in patients with xanthine deposition in tissues.

2. The drug should only be used with great caution in patients with renal or hepatic dysfunction. Dosage may require adjustment with creatinine clearance between 20 and 10ml/minute, a dose of 100 to 200mg daily is suggested. If the creatinine clearance is less than 10ml/min the dose is usually 100mg daily or at longer intervals.

3. There may be potential for interaction between allopurinol and the coumarin anti-coagulants.

## 4.5 Interaction with other medicinal products and other forms of interaction

1. Use of allopurinol concurrently with 6-mercaptopurine or azathioprine requires reduction in dosage of these drugs since the inhibition of xanthine oxidase will prolong their activity.

2. Allopurinol may be used concurrently with uricosuric agents, but if therapy is being changed to allopurinol, overlapping of treatment is necessary to ensure continuity of the hypouricaemic effect.

## 4.6 Pregnancy and lactation

Allopurinol should not be used during pregnancy unless considered essential by the physician. No data is available on excretion of allopurinol and its metabolites in breast milk.

## 4.7 Effects on ability to drive and use machines

Not applicable.

## 4.8 Undesirable effects

Adverse reactions in association with Allopurinol Tablets are rare in the overall treated population and mostly of a minor nature. The incidence is higher in the presence or renal and/or hepatic disorder.

*Skin and hypersensitivity reactions*

These are the most common reactions and may occur at any time during treatment. They may be pruritic, maculopapular, sometimes scaly, sometimes purpuric and rarely exfoliative. Allopurinol Tablets should be withdrawn immediately should such reactions occur. After recovery from mild reactions, Allopurinol Tablets may, if desired, be re-introduced at a small dose (e.g. 50mg/day) and gradually increased. If the rash recurs, Allopurinol Tablets should be permanently withdrawn as a more severe hypersensitivity reaction may occur. Skin reactions associated with exfoliation, fever, lymphadenopathy, arthralgia and/or eosinophilia resembling Stevens-Johnson syndrome and toxic

epidermal necrolysis occur rarely. Associated vasculitis and tissue response may be manifested in various ways including hepatitis, renal impairment and, very rarely, seizures. If such reactions do occur, it may be at any time during treatment. Allopurinol Tablets should be withdrawn immediately and permanently. Corticosteroids may be beneficial in overcoming hypersensitivity skin reactions. When generalised hypersensitivity reactions have occurred, renal and/or hepatic disorder has usually been present particularly when the outcome has been fatal.
Very rarely acute anaphylactic shock has been reported.

*Angioimmunoblastic lymphadenopathy*

Angioimmunoblastic lymphadenopathy has been described rarely following biopsy of a generalised lymphadenopathy. It appears to be reversible on withdrawal of Allopurinol Tablets.

*Hepatic function*

Rare cases of hepatic dysfunction ranging from asymptomatic rises in liver function tests to hepatitis (including hepatic necrosis and granulomatous hepatitis) have been reported without overt evidence of more generalised hypersensitivity.

*Gastrointestinal disorder*

In early clinical studies, nausea and vomiting were reported. Further reports suggest that this reaction is not a significant problem and can be avoided by taking Allopurinol Tablets after meals. Recurrent haematemesis has been reported as an extremely rare event, as has steatorrhoea.

*Blood and lymphatic system*

Occasional reports have been received of thrombocytopenia, agranulocytosis and aplastic anaemia, particularly in individuals with impaired renal and/or hepatic function, reinforcing the need for particular care in this group of patients.

*Miscellaneous*

The following complaints, have been reported occasionally; fever, general malaise, asthenia, headache, vertigo, ataxia, somnolence, coma, depression, paralysis, paraesthesiae, neuropathy, visual disorder, cataract, macular changes, taste perversion, stomatitis, changed bowel habit, infertility, impotence, diabetes mellitus, hyperlipaemia, furunculosis, alopecia, discoloured hair, angina, hypertension, bradycardia, oedema, uraemia, haematuria, angioedema, gynaecomastia.

## 4.9 Overdose

Ingestion of up to 22.5g allopurinol without adverse effect has been reported. Symptoms and signs including nausea, vomiting, diarrhoea and dizziness have been reported in a patient who ingested 20g allopurinol. Recovery followed general supportive measures.

*Management*

Massive absorption of Allopurinol Tablets may lead to considerable inhibition of xanthine oxidase activity, which should have no untoward effects unless affecting concomitant medication especially with 6-mercaptopurine and/or azathioprine. Adequate hydration to maintain optimum diuresis facilities excretion of allopurinol and its metabolites. If considered haemodialysis may be used.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Xanthine Oxidase inhibitor.

## 5.2 Pharmacokinetic properties

Allopurinol is readily absorbed from the gut with a half-life of 1 hour, it is rapidly converted to active metabolite oxpurinol (alloxanthine). Neither allopurinol nor oxypurinol is bound to plasma protein and excretion is mainly urinary. Oxypurinol is reabsorbed by the kidney tubules to give an effective half-life of 18-30 hours.

## 5.3 Preclinical safety data

None applicable

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Lactose
Maize Starch
Povidone
Stearic Acid
Sodium Starch Glycollate

## 6.2 Incompatibilities

Not applicable

## 6.3 Shelf Life

3 years.

## 6.4 Special precautions for storage

Store below 25$^{o}$C.

## 6.5 Nature and contents of container

Securitainers.
Allopurinol is available in the following pack sizes: 21, 100, 250 and 500 tablets.

Not all pack sizes may be marketed.

## 6.6 Instructions for use and handling

Not applicable.

# 7 MARKETING AUTHORISATION HOLDER

Roussel Laboratories Limited
Broadwater Park
Denham
Uxbridge
Middlesex UB9 5HP
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER

PA 6/38/2

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th July 1988

Date of last renewal: 25th July 2003

## 10 DATE OF REVISION OF THE TEXT

August 2004