SUMMARY OF PRODUCT CHARACTERISTICS

1  NAME OF THE MEDICINAL PRODUCT

Allopurinol 100mg Tablets

2  QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Allopurinol 100mg
Also contains lactose. For the full list of excipients, see section 6.1.

3  PHARMACEUTICAL FORM

Uncoated Tablets
White, biconvex tablets. Embossed ‘PV’ on one face and ‘A’ and ‘100’ on the other.

4  CLINICAL PARTICULARS

4.1  Therapeutic indications

Allopurinol is indicated for the main clinical manifestation of urate/uric acid deposition, these are gouty arthritis, skin tophi and/or renal involvement.
In the treatment of excess body urate associated with neoplastic disease, and its treatment, certain enzymes disorders (in particular Lesch-Nyhan syndrome) renal failure, renal calculus formation, diuretic therapy and psoriasis. In the prophylaxis and in the treatment of calcium renal lithiasis in patients with raised serum or urinary uric acid.

4.2  Posology and method of administration

The dosage should be adjusted by monitoring serum urate concentration and urinary urate/uric acid levels.

Route of administration: oral

Adults: Initial dose in the range 100mg to 200mg per day which may be taken as a single dose. Maintenance dose is 200mg to 600mg per day. Maximum single dose is 300mg. Doses in excess of 300mg should be administered in divided doses. It has rarely been found necessary to exceed 900mg per day. The dose
should be adjusted by monitoring serum uric acid and/or urinary uric acid levels at appropriate intervals until the desired effect is attained, which may take 1 to 3 weeks.

**Children:** 10-20mg/kg body weight/day use is mainly indicated in leukaemia and other malignant conditions and enzyme disorder such as Lesh-Nyhan syndrome.

**Elderly:** The dose should be maintained at the minimum, necessary to maintain normal serum and urinary urate levels.

**Initiation of therapy:** In the early stages of treatment with Allopurinol, as with uricosuric agents, an acute attack of gout arthritis may be precipitated. Therefore it is advisable to give a prophylactic dose of a suitable anti-inflammatory agent or colchicine (0.5mg, 3 times a day) for at least one month.

**Use with Uricosurics:** Allopurinol does not interfere with the action of uricosuric agents. When changing from uricosuric therapy to Allopurinol 1-3 weeks overlap of treatment is recommended to ensure a continuous hypouricaemic effect.

**Use in Neoplasia:** When giving Allopurinol to prevent uric acid in nephropathy in neoplastic condition, it is advisable to start treatment with Allopurinol before cytotoxic therapy.

Patients with hepatic disease: The dosage of allopurinol should be reduced in patients with hepatic disease.

Dose recommended in impaired renal function: Allopurinol and its metabolites are excreted via the kidney. Impairment of renal function may lead to retention of the drug and its metabolites with consequent prolongation of action. The amount and frequency may require reduction as indicated by monitoring serum uric acid levels. The following schedule is provided for guidance in adults:
- If creatinine clearance exceeds 20ml/min – give standard dose
- If creatinine clearance is between 20ml and 10ml/min – give 100 – 200mg/day.
- If creatinine clearance is less than 10ml/min – give 100mg/day at longer intervals

Dose recommended in renal dialysis: Allopurinol and its metabolites are removed by renal dialysis. If frequent dialysis is required an alternative schedule of 300 – 400mg Allopurinol after each dialysis with none in the interim should be considered.

**4.3 Contraindications:**

Should not be used in patients with a known intolerance to Allopurinol or to any other ingredients. Should not be used for treatment for acute attack of gout, nor immediately after an acute attack.

**4.4 Special warnings and precautions for use**
Allopurinol should be withdrawn immediately when a skin rash or other evidence of sensitivity occurs as this could result in more serious hypersensitivity reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis) (see section 4.8).

- Life-threatening cutaneous reactions Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of allopurinol.

- Patients should be advised of the signs and symptoms and monitored closely for skin reactions. The highest risk for occurrence of SJS or TEN is within the first weeks of treatment. (Adoption to individual drug if such data are available)

- If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesions) are present, allopurinol treatment should be discontinued.

- The best results in managing SJS and TEN come from early diagnosis and immediate discontinuation of any suspect drug. Early withdrawal is associated with a better prognosis.

- If the patient has developed SJS or TEN with the use of allopurinol, allopurinol must not be re-started in this patient at any time.

- Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) has also been reported with the use of allopurinol. DRESS is characterised by fever, eosinophilia, atypical circulating lymphocytes, lymphadenopathy and hepatitis.

**Hypersensitivity syndrome, SJS and TEN**

Allopurinol hypersensitivity reactions can manifest in many different ways, including maculopapular exanthema, hypersensitivity syndrome (also known as DRESS) and SJS/TEN. These reactions are clinical diagnoses, and their clinical presentations remain the basis for decision making. If such reactions occur at any time during treatment, allopurinol should be withdrawn immediately. Rechallenge should not be undertaken in patients with hypersensitivity syndrome and SJS/TEN. 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.

**HLA-B*5801 allele**

The HLA-B*5801 allele has been shown to be associated with the risk of developing allopurinol related hypersensitivity syndrome and SJS/TEN. The frequency of the HLA-B*5801 allele varies widely between ethnic populations: up to 20% in Han Chinese population, about 12% in the Korean population and 1-2% in individuals of Japanese or European origin. The use of genotyping as a screening tool to make decisions about treatment with allopurinol has not been established. If the patient is a known carrier of HLA-B*5801, the use of allopurinol may be considered if the benefits are thought to exceed risks. Extra vigilance for signs of hypersensitivity syndrome or SJS/TEN is required and the patient should be informed of the need to stop treatment immediately at the first appearance of symptoms (see section 4.8).

**Chronic renal impairment**

Patients with chronic renal impairment and concomitant diuretic use, in particular thiazides, may be at increased risk of developing hypersensitivity reactions including SJS/TEN associated with allopurinol. Extra vigilance for the signs of hypersensitivity
syndrome or SJS/TEN is required and the patient should be informed of the need to stop
treatment immediately and permanently at the first appearance of symptoms (see section
4.8).

**Acute gouty attacks**
Treatment with Allopurinol should not be started during an acute attack of gout has been
completely subsided, as further attacks may be precipitated.
Dosage should be reduced in the patients with renal or hepatic disorders.
Propylactic doses of a suitable anti-inflammatory (not aspirin or salicylates) should be
given concurrently. Fluid intake should ensure a urinary output of not less than 2 litres a
day and the urine rendered alkaline if uric acid overload is high.

**Hepatic or renal impairment**
Reduced doses should be used in patients with hepatic or renal impairment (see section
4.2). Patients under treatment for hypertension or cardiac insufficiency, for example
with diuretics or ACE inhibitors, may have some concomitant impairment of renal
function and allopurinol should be used with care in this group. Liver function should be
monitored, especially during the first few months, in patients with hepatic impairment.
Asymptomatic hyperuricaemia per se is generally not considered an indication for use of
allopurinol. Fluid and dietary modification with management of the underlying cause
may correct the condition.
In the early stages of treatment with Allopurinol, as with uricosuric agents, an acute
attack of gouty arthritis may be precipitated. Therefore it is advisable to give prophylaxis
with a suitable anti-inflammatory agent or colchicine for at least one month. The
literature should be consulted for details of appropriate dosage and precautions and
warnings.
If acute attacks develop in patients receiving allopurinol, treatment should continue at the
same dosage while the acute attack is treated with a suitable anti-inflammatory agent.

**Xanthine deposition**: A urinary output of not less than 2 litres a day must be maintained
in all patients receiving allopurinol and the urine rendered neutral or slightly alkaline if
uric acid overload is high. To reduce the risk of renal xanthine deposition, an adequate
fluid intake is required. Allopurinol should be used with care in patients under treatment
for any illness that may predispose to impairment of renal function such as hypertension,
cardiac insufficiency, diabetes mellitus. In conditions where the rate of urate formation is
greatly increased (e.g. malignant disease and its treatment, Lesch-Nyhan syndrome) the
absolute concentration of xanthine in urine could, in rare cases, rise sufficiently to allow
deposition in the urinary tract. This risk may be minimised by adequate hydration to
achieve optimal urine dilution.

**Impaction of uric acid renal stones**: Adequate therapy with Allopurinol will lead to
dissolution of large uric acid renal pelvic stones, with the remote possibility of impaction
in the ureter.
Neoplastic conditions: In neoplastic conditions, treatment with allopurinol (if required)
should be commenced before cytotoxic drugs are given.

**Lactose intolerance**: Allopurinol tablets contain lactose and therefore should not be
administered to patients with rare hereditary problems of galactose intolerance, the Lapp
lactase deficiency or glucose-galactose malabsorption.
Use in the elderly: the dose should be maintained at the minimum necessary to maintain serum and urinary urate levels.

4.5 Interaction with other medicinal products and other forms of interaction

Coumarin anticoagulants: Allopurinol may potentiate the effect of warfarin, dicoumarol and phenprocoumon. The dosage of these should be reduced when given concurrently.

Adenine: Evidence suggests that the plasma half-life of vidarabine (adenine arabinoside) is increased in the presence of allopurinol. When given concurrently, patients should be observed for enhanced toxic effect. There is no unequivocal evidence that allopurinol potentiates the activity of other cytotoxic drugs.

Salicylates and uricosuric agents: oxipurinol, the major metabolite of allopurinol and itself therapeutically active, is excreted by the kidney in a similar way to urate. When used with drugs which increase uricosuric activity such as probenecid or large doses of salicylates, Allopurinol therapeutic effect may be decreased, therefore the dose may have to be adjusted.

Antidiabetic agents: An increase in the half-life of chloropropamide, and a decrease in the half-life of tolbutamide have been described, but the effect on the hypoglycaemic response is uncertain. When given concurrently with chlorpropamide, there may be a risk of prolonged hypoglycaemia if renal function is impaired, because allopurinol and chlorpropamide may compete for excretion in the renal tubule.

Antacids: Allopurinol may fail to reduce the blood-uric-acid concentrations when given at the same time as aluminium hydroxide. Intake of antacids and allopurinol should not separated by less than 3 hours.

ACE Inhibitors: increased risk of toxicity when allopurinol given with captopril especially in renal impairment.

Antiepileptics: Allopurinol may inhibit hepatic oxidation of phenytoin but the clinical significance has not been demonstrated. Plasma carbamazepine concentrations can be gradually increased and the dose of carbamazepine may need to be reduced.

Theophylline: Inhibition of the metabolism of theophylline has been reported. The mechanism of the interaction may be explained by xanthine oxidase being involved in the biotransformation of theophylline in man. Theophylline levels should be monitored in patients starting or increasing allopurinol therapy.

Ampicillin / amoxicillin: An increase in the frequency of skin rash has been reported among patients receiving ampicillin or amoxicillin concurrently with allopurinol compared with patients who are not receiving both drugs. The cause of the reported association has not been established. However, it is recommended that in patients receiving allopurinol an alternative to ampicillin or amoxicillin is used where available.
Ciclosporin: Reports suggest that the plasma concentration of ciclosporin may be increased during concomitant treatment with allopurinol. The possibility of enhanced ciclosporin toxicity should be considered if the drugs are co-administered.

Diuretics: Increased risk of hypersensitivity when allopurinol given with thiazides and related diuretics especially in renal impairment.

Didanosine: In healthy volunteers and HIV patients receiving Didanosine, plasma Didanosine C\textsubscript{max} and AUC values were approximately doubled with concomitant allopurinol treatment (300 mg daily) without affecting terminal half life. Co-administration of these 2 drugs is generally not recommended. If concomitant use is unavoidable, a dose reduction of Didanosine may be required, and patients should be closely monitored.

Cytotoxics: allopurinol enhances effects and increase toxicity of azathioprine and mercaptopurine (reduce dose of azathioprine and mercaptopurine) avoidance of allopurinol advised by the manufacturer of capecitabine. Azathioprine is metabolised to 6-mercaptopurine which is inactivated by the action of xanthine oxidase. When 6-mercaptopurine or azathioprine is given concurrently with allopurinol, only one-quarter of the usual dose of 6-mercaptopurine or azathioprine should be given because inhibition of xanthine oxidase will prolong their activity.

Cyclophosphamide, doxorubicin, bleomycin, procarbazine, mechloroethamine: Enhanced bone marrow suppression by cyclophosphamide and other cytotoxic agents has been reported among patients with neoplastic disease (other than leukaemia), in the presence of allopurinol. However, in a well-controlled study of patients treated with cyclophosphamide, doxorubicin, bleomycin, procarbazine and/or mechloroethamine (chlormethine hydrochloride) allopurinol did not appear to increase the toxic reaction of these cytotoxic agents.

### 4.6 Fertility, pregnancy and lactation

There is no evidence that Allopurinol taken orally causes fatal abnormalities; however, as with all drugs, caution should be exercised in the use of Allopurinol in pregnancy.

Use in pregnancy only when there is no safer alternative and when the disease itself carries risk for the mother or unborn child.

Reports indicate that allopurinol and oxipurinol are excreted in breast milk and should not be given to nursing mothers. Concentrations of 1.4mg/litre allopurinol and 53.7mg/litre oxipurinol have been demonstrated in breast milk from women taking allopurinol 300mg/day. However, there are no data concerning the effects of allopurinol or its metabolites on the breast-fed baby.

### 4.7 Effects on ability to drive and use machines

Since adverse reactions such as somnolence, vertigo, ataxia and visual disturbances have been reported in patients receiving allopurinol, patients should exercise caution before driving, using machinery or participating in dangerous activities until they are reasonably certain that allopurinol does not adversely affect performance.
4.8 Undesirable effects

These are usually rare and mostly of a minor nature; the incidence is higher in the presence of renal and/or hepatic disorders.

For this product there is no modern clinical documentation which can be used as support for determining the frequency of undesirable effects. Undesirable effects may vary in their incidence depending on the dose received and also when given in combination with other therapeutic agents.

The frequency categories assigned to the adverse drug reactions below are estimates: for most reactions, suitable data for calculating incidence are not available. Adverse drug reactions identified through post-marketing surveillance were considered to be rare or very rare. The following convention has been used for the classification of frequency:

Very common (≥1/10 (≥10%)), Common (≥1/100 and <1/10 (≥1% and <10%)),
Uncommon (≥1/1000 and <1/100 (≥0.1% and <1%)), Rare (≥1/10,000 and <1/1000 (≥0.01% and <0.1%)), Very rare (<1/10,000 (<0.01%))

Adverse reactions in association with allopurinol are usually rare and mostly of a minor nature. The incidence is higher in the presence of renal and/or hepatic disorders.

Infections and infestations
Very rare Furunculosis

Blood and lymphatic system disorders
Very rare Agranulocytosis, aplastic anaemia, thrombocytopenia.
Not known leucopenia, eosinophilia, haemolytic anaemia

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.

Immune system disorders
Uncommon Hypersensitivity reactions
Very rare Anaphylaxis, angioimmunoblastic lymphadenopathy.
Angioimmunoblastic lymphadenopathy has been described very rarely following biopsy of a generalised lymphadenopathy. It appears to be reversible on withdrawal of allopurinol.

Not known Arthralgia
A delayed multi-organ hypersensitivity disorder (known as hypersensitivity syndrome or DRESS) with fever, rashes, vasculitis, lymphadenopathy, pseudo lymphoma, arthralgia, leucopenia, eosinophilia, hepato-splenomegaly, abnormal liver function tests and vanishing bile duct syndrome (destruction and disappearance of the intrahepatic bile ducts) occurring in various combinations. Other organs may also be affected (e.g. liver, lungs, kidneys, pancreas, myocardium, and colon). If such reactions do occur, it may be at any time during treatment, Allopurinol tablets should be withdrawn immediately and permanently.
Serious hypersensitivity reactions, Stevens - Johnson Syndrome and Toxic Epidermal Necrolysis occur rarely (see Skin and subcutaneous tissue disorders). Associated vasculitis and tissue response may be manifested in various ways including hepatitis, renal impairment (such as interstitial nephritis) and very rarely, epilepsy. Very rarely acute anaphylactic shock has been reported. If such reactions do occur, it may be at any time during treatment, Allopurinol 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. (see section 4.4).

Metabolism and nutrition disorders
Very rare Diabetes mellitus, hyperlipidaemia
Not known Exacerbation of gouty attacks (see section 4.4)

Psychiatric disorders
Very rare Depression

Nervous system disorders
Very rare Coma, paralysis, ataxia, neuropathy, paraesthesiae, somnolence, headache, taste perversion
Not known Dizziness

Eye disorders
Very rare Cataract, visual disorder, macular changes

Ear and labyrinth disorders
Very rare Vertigo

Cardiac disorders
Very rare Angina, bradycardia

Vascular disorders
Very rare Hypertension
Not known Vasculitis

Gastrointestinal disorders
Uncommon Vomiting, nausea
Very rare Recurrent haematemesis, steatorrhoea, stomatitis, changed bowel habit
Not known Diarrhoea, abdominal pain, gastrointestinal bleeding

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 after meals.

Hepatobiliary disorders
Uncommon Asymptomatic increases in liver function tests
Rare Hepatitis (including hepatic necrosis and granulomatous hepatitis)

Hepatic dysfunction has been reported without overt evidence of more generalised hypersensitivity.

**Skin and subcutaneous tissue disorders**

<table>
<thead>
<tr>
<th>Common</th>
<th>Rash</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare</td>
<td>Severe cutaneous adverse reactions (SCARs): Stevens-Johnson syndrome/toxic epidermal necrolysis</td>
</tr>
<tr>
<td>Very rare</td>
<td>Angioedema, fixed drug eruption, alopecia, discoloured hair</td>
</tr>
<tr>
<td>Not known</td>
<td>Skin reaction associated with eosinophilia, urticaria. Drug Rash with Eosinophilia and Systemic Symptoms has been reported. Some cases have had a fatal outcome.</td>
</tr>
</tbody>
</table>

Skin reactions 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, lymphadenopathy, arthralgia and/or eosinophilia resembling Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) and/or Lyell's have been reported (see section 4.4).

Allopurinol should be withdrawn immediately should such reactions occur. After recovery from mild reactions, Allopurinol may, if desired, be re-introduced at a small dose (e.g. 50mg/day) and gradually increased. If the rash recurs, Allopurinol should be permanently withdrawn as more severe hypersensitivity may occur (see Immune system disorders).

The HLA-B*5801 allele has been identified as a genetic risk factor for allopurinol associated SJS/TEN in retrospective, case-control, pharmacogenetic studies in patients of Han Chinese, Japanese and European descent. Up to 20-30% of some Han Chinese, African and Indian populations carry the HLA-B*5801 allele whereas only 1-2% of Northern European, US European and Japanese patients are estimated to be HLA-B*5801 carriers. However, the use of genotyping as a screening tool to make decisions about treatment with allopurinol has not been established.

The clinical diagnosis of SJS/TEN remains the basis for decision making. If such reactions occur at any time during treatment, allopurinol should be withdrawn immediately and permanently (see section 4.4).

Angioedema has been reported to occur with and without signs and symptoms of a more generalised hypersensitivity reaction.

**Renal and urinary disorders**

| Very rare | Haematuria, uraemia |
| Not Known | Nephrolithiasis |

**Reproductive system and breast disorders**

| Very rare | Male infertility, erectile dysfunction, impotence, gynaecomastia, nocturnal Emission |

**General disorders and administration site conditions**
Very rare  Oedema, general malaise, asthenia, fever
Not known  Chills
Fever has been reported to occur with and without signs and symptoms of a more generalised allopurinol hypersensitivity reaction (see immune system disorders)

Miscellaneous: exacerbation of acute gouty attacks may occur in the early stages of hypouricaemic therapy, see sub-section 4.2. In those conditions where the body’s miscible urate pool is greatly increased (eg malignant disease and its treatment; Lesch-Nyhan syndrome), the rise in the xanthine concentration resulting from the action of allopurinol may lead to tissue deposits of xanthine. Fluid intake should ensure adequate urinary output. Xanthine crystals have been seen in the muscle tissue of patients receiving allopurinol, but this appears to have no clinical significance.

**Reporting of suspected adverse reactions:**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme; website: www.mhra.gov.uk/yellowcard.

### 4.9 Overdose

No reports of over dosage or acute intoxication are available. Massive absorption of allopurinol may lead to considerable inhibition of xanthine oxidase activity may occur, which should have no untoward effects unless 6-mercaptopurine, adenine arabinoside and/or azathioprine is being taken concomitantly, which should lead to the risk of increased activity of these drugs.

Ingestion of up to 22.5 g allopurinol without adverse effect has been reported.

**Symptoms**
Nausea, vomiting, diarrhoea, dizziness, headache, somnolence and abdominal pain. Rarely, there may be renal insufficiency and hepatitis.

Symptoms and signs including nausea, vomiting, diarrhoea and dizziness have been reported in a patient who ingested 20 g allopurinol.

**Treatment**
The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose: 50g for adults; 1 g/kg for children) if the patient presents within 1 hour of ingestion of more than 50 mg/kg. If more than 50 mg/kg has been ingested check U&Es and LFTs.

Adequate hydration to maintain optimum diuresis facilitates excretion of Allopurinol and its metabolites. Other measures as indicated by the patient's clinical condition. Haemodialysis is unlikely to be required. Haemodialysis may be considered in patients with severe renal or hepatic impairment.

### 5.1 Pharmacodynamic properties
**Pharmacotherapeutic Group:** Antigout preparations inhibiting uric acid production

**ATC code:** M04 AA01

Allopurinol inhibits the action of xanthine oxidase and thus reduces the oxidation of hypoxanthine and xanthine to uric acid. The urinary purine load, normally almost entirely uric acid, is divided between hypoxanthine, xanthine and uric acid. The reduced concentration of uric acid in plasma facilitates the resolution of tophi and calculi. Hypoxanthine and xanthine may be re-utilized for nucleotide and nucleic acid synthesis, and purine biosynthesis may be reduced.

### 5.2 Pharmacokinetic Properties

Allopurinol is absorbed from the gastro-intestinal tract and is reported to have a plasma half life of about 1 hour. It is rapidly converted in the body into oxypurinol (alloxanthine) which is also an inhibitor of xanthine oxidase with a reported half life of 18 to 30 hours. Allopurinol and oxypurinol are not bound to serum proteins and are excreted mainly in the urine.

Allopurinol and oxipurinol clearance is greatly reduced in patients with poor renal function resulting in higher plasma levels in chronic therapy. A reduction in the dose of Allopurinol is therefore required in patients with renal impairment.

### 5.3 Preclinical safety data

**A. Mutagenicity**

Cytogenetic studies show that allopurinol does not induce chromosome aberrations in human blood cells *in vitro* at concentrations up to 100 micrograms/ml and *in vivo* at doses up to 600 mg/day for mean period of 40 months.

Allopurinol does not produce nitraso compounds *in vitro* or affect lymphocyte transformation *in vitro*.

Evidence from biochemical and other cytological investigations strongly suggests that allopurinol has no deleterious effects on DNA at any stage of the cell cycle and is not mutagenic.

**B. Carcinogenicity**

No evidence of carcinogenicity has been found in mice and rats treated with allopurinol for up to 2 years.

**C. Teratogenicity**

One study in mice receiving intraperitoneal doses of 50 or 100 mg/kg on days 10 or 13 of gestation resulted in foetal abnormalities, however in a similar study in rats at 120 mg/kg on day 12 of gestation no abnormalities were observed.

Extensive studies of high oral doses of allopurinol in mice up to 100 mg/kg/day, rats up to 200 mg/kg/day and rabbits up to 150 mg/kg/day during days 8 to 16 of gestation produced no teratogenic effects.

An *in vitro* study using foetal mouse salivary glands in culture to detect embryotoxicity indicated that allopurinol would not be expected to cause embryotoxicity without also causing maternal toxicity.
6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose
Starch
Polyethylene Glycol 4000
Povidone
Magnesium Stearate
Colloidal Silicon Dioxide
Microcrystalline Cellulose
Sodium Starch Glycollate

6.2. Incompatibilities

No major incompatibilities have been reported.

6.3. Shelf life

5 years

6.4. Special precautions for storage

Protect from light heat and moisture.
Store below 25°C

6.5 Nature and contents of container

Plastic securitainer with snap secure polypropylene lids containing Allopurinol Tablets. (Material of the container complies to EEC directives for plastic in contact with drugs and food stuff). Pack size available 14, 28, 30, 50, 56, 100, 250, 500 and 1000 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None
7 MARKETING AUTHORISATION HOLDER

Pharmvit limited
117 Bilton Road
Perivale
Greenford
Middlesex UB6 7HQ

8. MARKETING AUTHORISATION NUMBER

PL 04556/0005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29 July 1983 / 25 March 1993

10 DATE OF REVISION OF THE TEXT

11/10/2016