PRODUCT MONOGRAPH

Pr JAMP-Allopurinol
Allopurinol Tablets USP
100 mg, 200 mg and 300 mg

Xanthine Oxidase Inhibitor

Jamp Pharma Corporation
1380-203, Newton, Boucherville, Québec,
J4B 5H2

Control # 171829

Date of Preparation:
March 3, 2014
PRODUCT MONOGRAPH

PrJAMP-ALLOPURINOL

Allopurinol Tablets USP

100 mg, 200 mg and 300 mg

THERAPEUTIC CLASSIFICATION

Xanthine Oxidase Inhibitor

ACTIONS AND CLINICAL PHARMACOLOGY

Allopurinol is a structural analogue of hypoxanthine. Reduction in both the serum and urinary uric acid levels is brought about by allopurinol inhibiting the action of xanthine oxidase, the enzyme responsible for the conversion of hypoxanthine to xanthine and xanthine to uric acid. Allopurinol is metabolized to the corresponding xanthine analogue, oxypurinol, which is also an inhibitor of xanthine oxidase. The action of allopurinol in blocking formation of urate differs from that of uricosuric agents which lower the serum uric acid level by increasing urinary excretion of uric acid.

A blinded, randomized, two-sequence, two-treatment, two-period, crossover, single dose, bioequivalence study of JAMP-Allopurinol (Allopurinol) Tablets 300 mg by Jamp Pharma Corporation with Zyloprim® (Allopurinol) Tablets 300mg manufactured by M/s AA Pharma inc. Toronto, Canada- L4K 4N7, in normal, healthy, adult, male and female human subjects under fasting conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test*</th>
<th>Reference†</th>
<th>% Ratio of Geometric Means</th>
<th>90 % Confidence Interval</th>
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<tr>
<td>AUC0-t (ng*hr/mL)</td>
<td>5571.01 5875.22 (35.30)</td>
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<td>Cmax (ng/mL)</td>
<td>1922.22 2048.41 (36.78)</td>
<td>1741.55 1820.13 (31.09)</td>
<td>110.38</td>
<td>101.07-120.54</td>
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<td>Tmax (h)</td>
<td>1.63 (56.23)</td>
<td>1.37 (52.01)</td>
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</tbody>
</table>

* JAMP-Allopurinol, by Jamp Pharma Corporation
† Zyloprim® manufactured by M/s AA pharma inc. Toronto, Canada- L4K 4N7
‡ Expressed as the arithmetic mean (CV%) only
**INDICATIONS AND CLINICAL USE**

Treatment of gout, either primary, or secondary to hyperuricemia which occurs in blood dyscrasias and their therapy.

Treatment of primary or secondary uric acid nephropathy, with or without accompanying signs or symptoms of gout.

Prophylactically, to prevent tissue urate deposition or renal calculi in patients with leukemias, lymphomas or other malignancies, receiving antineoplastic treatment (radiation or cytotoxic drugs) which might induce increased uricemia levels. Also in the therapy and prophylaxis of acute urate nephropathy and resultant renal failure in patients with neoplastic disease who are particularly susceptible to hyperuricemia and uric acid stone formation (especially after radiation therapy or use of antineoplastic drugs).

Prevention of the occurrence and recurrence of uric acid stones or gravel and renal calcium lithiasis in patients with hyperuricemia and/or hyperuricosuria.

**CONTRAINDICATIONS**

Should not be given to patients who are hypersensitive to allopurinol or who have previously developed a severe reaction to this drug or to any components of the formulation. JAMP-ALLOPURINOL (allopurinol) is contraindicated in nursing mothers and in children (except in those with hyperuricemia secondary to malignancy).

**WARNINGS**

JAMP-ALLOPURINOL (allopurinol) should be discontinued at the appearance of a skin rash, as the rash may be, in some instances, followed by a more severe hypersensitivity reaction (see ADVERSE EFFECTS).

Periodic liver function tests should be performed in all patients on allopurinol therapy.

Reduced doses should be administered to patients with renal or hepatic impairment. The drug should be withdrawn if increased abnormalities in hepatic or renal functions appear. 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.

**Occupational Hazards:** Due to occasional occurrence of drowsiness, patients should be alerted to the need for precautions when engaging in activities where alertness is mandatory.

Adequate therapy with allopurinol will lead to dissolution of large uric acid renal pelvic stones, with the remote possibility of impaction in the ureter.
Asymptomatic hyperuricemia 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.

Mercaptopurine or Azathioprine with Allopurinol: In patients receiving mercaptopurine or azathioprine, the concomitant administration of 300 to 600 mg of allopurinol/day will require a reduction in dose to approximately one-third or one-fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of mercaptopurine or azathioprine should be made on the basis of therapeutic response and any toxic effects.

Pregnancy: JAMP-ALLOPURINOL is not recommended for use during pregnancy or in women of childbearing potential unless in the judgment of the physician, the potential benefits outweigh the possible risk to the fetus.

Children: JAMP-ALLOPURINOL should not be given to children with the exception of those with hyperuricemia secondary to malignancy or with Lesch-Nyhan syndrome, because safety and effectiveness have not been established in other conditions.

PRECAUTIONS

Allopurinol treatment should not be started until an acute attack of gout has completely subsided, as further attacks may be precipitated.

Acute gouty attacks may be precipitated at the start of treatment with allopurinol in new patients, and these may continue even after serum uric acid levels begin to fall. Prophylactic administration of colchicine is advisable, particularly in new patients and in those where the previous attack rate has been high. In addition, it is recommended that the patient start with a low dose of allopurinol (100 and 200 mg daily) and the dose be built up slowly until a serum uric acid level of 6 mg/100 mL or less is attained (see DOSAGE AND ADMINISTRATION). If acute gouty 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.

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 minimized by adequate hydration to achieve optimal urine dilution.

Lactation: Reports indicate that allopurinol and oxipurinol are excreted in human breast milk. Concentrations of 1.4 mg/L allopurinol and 53.7 mg/L oxipurinol have been demonstrated in breast milk from woman taking allopurinol 300 mg/day. However, there are no data concerning the effects of allopurinol or its metabolites on breast-fed babies.

Drug Interactions: Mercaptopurine or Azathioprine: (see WARNINGS).
Uricosurics and Salicylates: Renal clearance of oxypurinol, the major therapeutically active metabolite of allopurinol, is increased by uricosuric agents such as probenecid or large doses of salicylate and as a consequence the addition of a uricosuric agent may reduce the extent of inhibition of xanthine oxidase by oxypurinol. However, such combined therapy may be useful in achieving minimum serum uric acid levels provided that total urinary uric acid load does not exceed the competence of the patient’s renal function.

Coumarin Anticoagulants: It has been reported that under experimental conditions allopurinol prolongs the half-life of the anticoagulant, dicumarol. The clinical significance of this has not been established, but this interaction should be kept in mind when allopurinol is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

Chlorpropamide: In the presence of allopurinol, there may be competition in the renal tubule for the excretion of chlorpropamide. When renal function is poor, the recognized risk of prolonged hypoglycemic activity of chlorpropamide may be increased if allopurinol is given concomitantly.

Vidarabine: Evidence suggests that the plasma half-life of vidarabine is increased in the presence of allopurinol. When the two products are used concomitantly extra vigilance is necessary to recognize enhanced toxic effects.

Phenytoin: Allopurinol may inhibit hepatic oxidation of phenytoin but the clinical significance has not been demonstrated.

Theophylline: Inhibition of the metabolism of theophylline has been reported in normal subjects given relatively high doses of allopurinol (300 mg b.i.d.) under experimental conditions. The mechanism of the interaction may be explained by xanthine oxidase being involved in the biotransformation of theophylline in man. Although there have been no clinical reports of interaction, 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 to 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.

Cyclophosphamide, Doxorubicin, Bleomycin, Procarbazine and Mechlorethamine: Enhanced bone marrow suppression reported among patients with neoplastic disease, (other than leukemia), in the presence of allopurinol. However, in a well-controlled study of patients treated with cyclophosphamide, doxorubicin, bleomycin, procarbazine and/or mechlorethamine (mustine HCl) allopurinol did not appear to increase the toxic reaction of the cytotoxic agents.

Cyclosporin: Reports suggest that the plasma concentration of cyclosporin may be increased during concomitant treatment with allopurinol. The possibility of enhanced cyclosporin toxicity should be considered if the drugs are coadministered.
ADVERSE REACTIONS

Reporting Suspected Side Effects

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to:
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

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

Skin 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. The rash has been followed by severe hypersensitivity reactions. Allopurinol should be withdrawn immediately should such reactions occur. After recovery from mild reactions allopurinol may, if desired, be cautiously reintroduced at a small dose (e.g., 50 mg/day) and gradually increased. If the rash recurs, allopurinol should be permanently withdrawn.

Generalized Hypersensitivity: Skin reactions associated with exfoliation, fever, chills, nausea and vomiting, lymphadenopathy, arthralgia and/or eosinophilia resembling Stevens-Johnson and/or Lyell’s syndrome have occurred. Associated vasculitis and tissue response may be manifested in various ways including hepatitis, interstitial nephritis and very rarely, epilepsy. If they do occur, it may be at any time during treatment. Allopurinol should be withdrawn immediately and permanently.
Corticosteroids may be beneficial in overcoming such reactions. When generalized hypersensitivity reactions have occurred, renal and/or hepatic disorders have usually been present particularly when the outcome has been fatal.

**Angioimmunoblastic Lymphadenopathy:** Angioimmunoblastic lymphadenopathy has been described rarely following biopsy of a generalized lymphadenopathy. It appears to be reversible on withdrawal of allopurinol.

**Granulomatous Hepatitis:** Very rarely granulomatous hepatitis, without overt evidence of more generalized hypersensitivity has been described. It appears to be reversible on withdrawal of allopurinol.

**Gastrointestinal Disorders:** Diarrhea, intermittent abdominal pain, nausea and vomiting were reported. Gastrointestinal disorders diminish if allopurinol is taken after meals. Recurrent hematemesis has been reported as an extremely rare event, as has steatorrhea.

**Blood and Lymphatic System:** There have been occasional reports of reduction in the number of circulating formed elements of the blood, including agranulocytosis, thrombocytopenia and aplastic anemia, usually in association with renal and/or, hepatic disorders or in whom concomitant drugs have been administered which have a potential for causing these reactions.

**Miscellaneous:** The following adverse effects have been reported occasionally: fever, general malaise, asthenia, headache, vertigo, ataxia, somnolence, coma, depression, paralysis, paraesthesiae, taste perversion, stomatitis, changed bowel habit, infertility, hepatic necrosis, abnormal liver function tests, rise in BUN, hyperlipemia, visual disorder, cataracts, macular changes, neuropathy, impotence, diabetes mellitus, furunculosis, alopecia, discolored hair, angina, hypertension, bradycardia, hematuria, edema, uremia, drowsiness, peripheral neuritis, angioedema and gynecomastia.

### SYMPTOMS AND TREATMENT OF OVERDOSAGE

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<tr>
<th>For management of a suspected drug overdose contact your regional Poison Control Centre immediately.</th>
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Ingestion of up to 22.5 g allopurinol without adverse effect has been reported. Symptoms and signs including nausea, vomiting, diarrhea, and dizziness have been reported in a patient who ingested 20 g allopurinol. Recovery followed general supportive measures.

Massive absorption of allopurinol may lead to considerable inhibition of xanthine oxidase activity, which should have no untoward effects unless affecting concomitant medication, especially with mercaptopurine and/or azathioprine. No treatment is normally required provided the drug is withdrawn and adequate hydration is maintained to facilitate excretion of the drug. If considered necessary hemodialysis may be used. If, however, other forms of acute distress are observed, gastric lavage should be considered, otherwise the treatment is symptomatic.
DOSAGE AND ADMINISTRATION

Adults: General Considerations: JAMP-ALLOPURINOL (allopurinol) is administered orally. The total daily requirement should be divided into 1 to 3 doses. Daily doses up to and including 300 mg of JAMP-ALLOPURINOL may be taken once a-day after a meal. Larger doses should be administered as divided doses of not more than 300 mg. It should be noted that JAMP-ALLOPURINOL is generally better tolerated if taken following meals.

Treatment of Gout: The dose of JAMP-ALLOPURINOL (allopurinol) varies with the severity of the disease. The minimum effective dose is 100 to 200 mg. The average is 200 to 300 mg/day for patients with mild gout, 400 to 600 mg/day for patients with moderately severe tophaceous gout, and 700 to 800 mg in severe conditions. The maximal recommended dose is 800 mg/day in patients with normal renal function.

Since JAMP-ALLOPURINOL and its metabolites are excreted only by the kidney, accumulation of the drug can occur in renal failure and the dose of JAMP-ALLOPURINOL should consequently be reduced. With a creatinine clearance of 20 to 10 mL/min, a daily dosage of 200 mg of JAMP-ALLOPURINOL is suitable.

When the creatinine clearance is less than 10 mL/min, the daily dosage should not exceed 100 mg. With extreme renal impairment (creatinine clearance less than 3 mL/min), the interval between doses may also need to be lengthened. As no simple method of measuring the blood concentrations of JAMP-ALLOPURINOL is available, the correct size and frequency of dosage for maintaining the serum uric acid just within the normal range is best determined by using the serum uric acid level as an index.

Once the daily dose of JAMP-ALLOPURINOL necessary to produce the desired serum uric acid level has been determined, this dose should be continued until the serum uric acid level indicates a need for dosage adjustment.

Normal serum urate levels are achieved in 1 to 3 weeks. The upper limit of normal is about 6 mg % for men and postmenopausal women and 5 mg % for premenopausal women. By the selection of the appropriate dose, together with the use of uricosurics agents in certain patients, it is possible to reduce the serum uric level to normal and, if desired, to hold it as low as 2 to 3 mg %. Combined therapy of JAMP-ALLOPURINOL and uricosurics will often result in a reduction in dosage of both agents.

To reduce the possibility of an increase in acute attacks of gout during the early stages of JAMP-ALLOPURINOL administration, it is recommended that the patient start with a low dose of JAMP-ALLOPURINOL (100 to 200 mg daily) and increase at weekly intervals by 100 mg until a serum uric acid level of about 6 mg % or less is attained. Also, a maintenance dose of colchicine should be given prophylactically when allopurinol is begun, and a high fluid intake is advisable.
In patients who are being treated with uricosuric agents, colchicine and/or anti-inflammatory agents, it is wise to continue this therapy while adjusting the dosage of allopurinol until a normal serum uric acid level and freedom from acute attacks have been maintained for several months. If desired, the patient may then be transferred to allopurinol therapy exclusively.

**For the Prevention of Uric Acid Nephropathy During the Vigorous Therapy of Neoplastic Disease:** Treatment with 600 to 800 mg daily for 2 or 3 days prior to chemotherapy or X-irradiation is advisable. Treatment should be continued at a dosage adjusted to the serum uric acid level until there is no longer a threat of hyperuricemia and hyperuricosuria.

**JAMP-ALLOPURINOL (allopurinol) treatment can be maintained during the antimitotic therapy for prophylaxis of the hyperuricemia which may arise during the natural crises of the disease. In prolonged treatment, 300 to 400 mg of JAMP-ALLOPURINOL daily is usually enough to control the serum uric acid level.**

It is essential that a daily urinary output of 2 L or more be maintained during allopurinol therapy, and neutral or alkaline urine is desirable.

**Prophylaxis of Renal Calcium Lithiasis:** The recommended starting dose of JAMP-ALLOPURINOL (allopurinol) for the prevention of recurrent calcium stones is 200 to 300 mg daily as one dose or individual doses. Therapy should be continued indefinitely. Some patients have received maintenance dosages of 200 to 300 mg daily for more than 7 years. In some patients, the maintenance dosage may be reduced to 100 to 200 mg daily.

**Children (6 to 10 years of age):** For the treatment of secondary hyperuricemia associated with malignancies and in the Lesch-Nyhan syndrome, JAMP-ALLOPURINOL should be given in doses of 10 mg/kg/day. The response should be evaluated after approximately 48 hours by monitoring serum uric acid and/or urinary uric acid levels and adjusting the dose if necessary.
PHARMACEUTICAL INFORMATION

Drug Substance

Common/Proper Name: Allopurinol

Chemical Name: 4H-Pyrazolo [3,4-d]pyrimidin-4-one.

Structural Formula: 

![Structural Formula Image]

Molecular Formula: C₅H₄N₄O

Molecular Weight: 136.1 g/mol

Description: Allopurinol is a position isomer of the natural purine base hypoxanthine in which the carbon and nitrogen at the number 7 and number 8 positions in the purine nucleus are transferred. It is a white, odorless, tasteless powder, insoluble in cold water, soluble in about 250 parts of hot water and in dilute sodium hydroxide.

Composition

In addition to allopurinol, each tablet also contains the non-medicinal ingredients lactose monohydrate, corn starch, sodium starch glycolate, povidone and stearic acid.

**JAMP-ALLOPURINOL 200 & 300 mg:** In addition to the non-medicinal ingredients listed under composition, JAMP-ALLOPURINOL 200 and 300 mg tablets also contain the dye Sunset Yellow Aluminium Lake.

Stability and Storage Recommendations

Store at room temperature (15 -30°C).
AVAILABILITY OF DOSAGE FORMS

**JAMP-ALLOPURINOL 100 mg**: White to off white, colored, round, biconvex uncoated tablets with “AL” and “100” separated by breakline on one side and plain on the other side. Available in bottles of 30 and 1000 tablets.

**JAMP-ALLOPURINOL 200 mg**: Peach colored, round, biconvex uncoated tablets with “AL” and “200” separated by breakline on one side and plain on the other side. Available in bottles of 30 and 1000 tablets.

**JAMP-ALLOPURINOL 300 mg**: Peach colored, round, biconvex uncoated tablets with “AL” and “300” separated by breakline on one side and plain on the other side. Available in bottles of 30 and 1000 tablets.

PHARMACOLOGY

When taken orally, allopurinol is rapidly absorbed and rapidly metabolized. The main metabolite is oxypurinol, which is itself a xanthine oxidase inhibitor. Allopurinol and its metabolites are excreted by the kidney. The renal handling is such that allopurinol has a plasma half-life of about one hour, whereas that of oxypurinol exceeds 18 hours. Thus, the therapeutic effect can be achieved by a once-a-day dosage of JAMP-ALLOPURINOL in patients taking 300 mg or less per day.

Administration of allopurinol generally results in a fall in both serum and urinary uric acid within 2 to 3 days. The magnitude of the decrease can be adjusted to a certain extent by varying the dose of allopurinol. The serum uric acid levels fall gradually and therefore a week or more of allopurinol treatment may be necessary before the full effect is obtained. Uric acid returns to pre-treatment levels slowly, usually after a cessation of therapy. This is due primarily to the accumulation and slow clearance of oxypurinol. In some patients, particularly those with tophaceous gout, a significant fall in urinary uric acid excretion may not occur, possibly due to the mobilization of urate from tissue deposits as the serum uric acid levels begins to fall.

The combined increase in hypoxanthine and xanthine excreted in the urine is usually, but not always, considerably less than the accompanying decline in urinary uric acid. This may be due to pseudofeedback inhibition of purine biosynthesis by allopurinol ribotide.

It has been shown that reutilization of both hypoxanthine and xanthine for nucleotide and nucleic acid synthesis is markedly enhanced when their oxidations are inhibited by allopurinol. This reutilization and the normal feedback inhibition which would result from an increase in available purine nucleotides serve to regulate purine biosynthesis, and, in essence, the defect of the over-producer of uric acid is thereby compensated.
Innate deficiency of xanthine oxidase, which occurs in patients with xanthinuria, as in inborn error of metabolism has been shown to be compatible with comparative well being. While urinary levels of oxypurines attained with full doses of allopurinol may in exceptional cases equal those (250-600 mg/day) which in xanthinuric subjects have caused formation of urinary calculi, they usually fall in the range of 50-200 mg and no evidence of renal damage has been clinically observed. Xanthine crystalluria has been reported in a few exceptional cases. The serum concentration of oxypurines in patients receiving allopurinol is usually in the range of 0.3 mg to 0.4 mg % compared to a normal level of approximately 0.15 mg %. A maximum of 0.9 mg % was observed when the serum urate was lowered to less than 2 mg % by high doses of the drug. In one exceptional case, a value of 2.7 mg % was reached. These are far below the saturation level at which precipitation of xanthine or hypoxanthine would be expected to occur so that tissue deposition is unlikely and has not been observed to date. The solubilities of uric acid and xanthine in the serum are similar (about 7 mg %) while hypoxanthine is much more soluble. The finding that the renal clearance of oxypurines is at least ten times greater than that of uric acid explains the relatively low serum oxypurine concentration at a time when the serum uric acid level has decreased markedly. At serum oxypurine levels of 0.3 to 0.9 mg %, oxypurine: inulin clearance ratios were between 0.7 and 1.9. The glomerular filtration rate and urate clearance in patients receiving allopurinol do not differ significantly from those obtained prior to therapy. The rapid renal clearance of oxypurines suggests that allopurinol therapy should be of value in allowing a patient with gout to increase his total purine excretion.

TOXICOLOGY

ACUTE ORAL TOXICITY (LD$_{50}$)
Rats: greater than 1100 mg/kg
Mice: greater than 953 mg/kg

SUBACUTE TOXICITY

In a 13-week feeding experiment in rats at a drug level of 72 mg/kg/day, 2 of 10 rats died; at 225 mg/kg/day, 4 to 10 died before the completion of the experiment. Both groups exhibited renal tubular damage due to the deposition of xanthine that was more extensive at the higher dose. In chronic feeding experiments, rats showed no toxic effects at a level of 14 mg/kg/day after one year. At a level of 24 mg/kg/day for one year, the rats showed very slight depression of weight gain and food intake, and five out of ten of the animals showed minor changes in the kidney tubules of the type exhibited by the rats on the higher dose described above.

Dogs survived oral dosing at 30 mg/kg/day for one year with nil to minor changes in the kidney and no other significant abnormalities. At 90 mg/kg/day for one year, there was some accumulation of xanthine in the kidneys with resultant chronic irritation and slight tubular changes. Occasional hemosiderin-like deposits were seen in the reticuloendothelial system. A higher dose (270 mg/kg/day) resulted in large concentrations in the renal pelves, with severe
destructive changes in the kidney secondary to xanthine accumulation. The deposit of xanthine appears to be a function of both the metabolic turnover of purines (which is proportionately larger in the smaller animals) and the degree of inhibition of xanthine oxidase.

TERATOGENICITY

Reproductive studies in rats and rabbits indicated that allopurinol did not affect litter size, the mean weight of the progeny at birth or at three weeks postpartum, nor did it cause an increase in animals born dead or with malformations.
BIBLIOGRAPHY


32. Product Monograph for Zyloprim® (Allopurinol) 100 mg, 200 mg and 300 mg tablets, AA PHARMA INC., Control # 141409. Date of Preparation: September 15, 2010.