The chemical name for allopurinol sodium is 1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one monosodium salt. It is a white amorphous powder with a molecular weight of 208.26 g/mole.

The pH of allopurinol sodium is 5.3.

PHARMACOLOGY

Allopurinol is a xanthine oxidase inhibitor. It reduces the uric acid production by inhibiting the key enzyme xanthine oxidase. The chemical name for allopurinol sodium is 1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one monosodium salt. It is a white amorphous powder with a molecular weight of 208.26 g/mole.

The pH of allopurinol sodium is 5.3.

PHARMACOKINETICS

Allopurinol is metabolized to the corresponding xanthine analogue, oxypurinol (alloxanthine), which also is an inhibitor of xanthine oxidase.

Reutilization of both hypoxanthine and xanthine for nucleotide and nucleic acid synthesis is markedly enhanced when their oxidative metabolism is blocked. Allopurinol selectively inhibits xanthine oxidase.

Table: Allopurinol Pharmacokinetic Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Allopurinol</th>
<th>Oxypurinol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (mcg/mL)</td>
<td>1.58 ± 0.22</td>
<td>0.53 ± 0.10</td>
</tr>
<tr>
<td>T1/2 (hr)</td>
<td>3.89 ± 1.41</td>
<td>3.10 ± 1.49</td>
</tr>
<tr>
<td>Vss (L/kg)†</td>
<td>0.84 ± 0.13</td>
<td>0.87 ± 0.13</td>
</tr>
<tr>
<td>CL (L/day)</td>
<td>12.2 ± 3.11</td>
<td>13.1 ± 2.24</td>
</tr>
<tr>
<td>Vd (L/kg)††</td>
<td>24.8 ± 19.7</td>
<td>52.2 ± 15.1</td>
</tr>
</tbody>
</table>

CL = Clearance; Vd = Volume of Distribution; Vss = Volume of Distribution (Steady-State)

†Absolte Bioavailability

††Relative Bioavailability

PRECAUTIONS

Drug Interactions:
The following drug interactions were observed in some patients undergoing treatment with oral allopurinol.

Allopurinol and its primary active metabolite, oxypurinol, are eliminated by the kidneys. Therefore, in patients with renal impairment or those receiving uricosuric agents, the dosage of allopurinol may need to be adjusted. Concurrent administration of uricosuric agents and allopurinol, however, is not contraindicated.

PRECAUTIONS

General: A rapid rise to sufficient plasma levels of oxypurinol and urine uric acid concentrations is usual. Therefore, in patients on allopurinol, routine uric acid and oxypurinol levels should be measured at frequent intervals until steady state conditions have been established.

In patients with hyperuricemia due to malignancy, plasma uric acid levels have been reported to rise within weeks to months after the initiation of allopurinol therapy. The plasma uric acid concentration at the time of treatment initiation, although of value in the clinical context, is not a reliable predictor of the magnitude of the therapeutic response.

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<th>Note</th>
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CONTRAINDICATIONS AND USAGE

Allopurinol Sodium for Injection is indicated for the management of patients with leukemia, lymphoma, and solid tumor malignancies who are receiving cancer therapy which causes elevations of serum and urinary uric acid levels and who cannot tolerate oral therapy.

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CONTRAINDICATIONS

Patients with hepatic failure or renal insufficiency should not be started on this drug.

WARNINGS

ALLOPURINOL SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR OTHER SIGNS WHICH MAY INDICATE AN ALLERGIC REACTION. In some instances with oral allopurinol, a skin rash may be followed by more severe hypersensitivity reactions, including toxic epidermal necrolysis (lyell’s syndrome), and generalized exfoliative dermatitis. In patients receiving methylxanthine or azathioprine, the concurrent administration of 300 to 600 mg of allopurinol for injection per day will require a reduction in dose to approximately one-third to one-fourth of the usual dose of methylxanthine or azathioprine. Subsequent adjustment of dose of methylxanthine or azathioprine should be made on the basis of therapeutic response and the appearance of adverse effects (see PRECAUTIONS-Drug Interactions).

The following drug interactions were observed in some patients undergoing treatment with oral allopurinol.

Allopurinol inhibits the enzymatic oxidation of mercaptopurine and azathioprine to 6-thiouric acid. This oxidation is catalyzed by xanthine oxidase. Allopurinol inhibits xanthine oxidase and thus prevents these 6-thiouric acid metabolites from being formed.

Urinary uric acid concentrations may increase in patients receiving diuretics. Diuretics such as thiazides and loop diuretics can increase uric acid production, leading to an increase in serum uric acid levels. This effect is most pronounced in patients with renal impairment or those receiving uricosuric agents. oxypurinol.

DIABETES MELLITUS: Patients with diabetes mellitus may require dosage adjustment. In diabetic patients taking allopurinol, allopurinol therapy should be discontinued in the presence of ketoacidosis. A fall in the serum uric acid level is usually followed by a rise in the blood glucose level. The cause of this reaction has not been established.

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Cytotoxic Agents: Enhanced bone marrow suppression by cyclophosphamide and other cytotoxic agents has been reported among patients with neoplastic disease, except leukemia, in the presence of allopurinol. However, in a well-controlled study of patients with lymphoma on combination therapy, allopurinol did not influence the bone marrow toxicity of patients treated with cyclophosphamide, doxorubicin, bleomycin, procarbazine, and/or mechlorethamine.

Corticosteroids: The half-life of cyclosporine in the plasma may be decreased by allopurinol, since allopurinol and other propenylpurines may compete for excretion in the renal tubule. The risk of hyperuricemia secondary to this interaction may be increased if allopurinol and cyclosporine are given concomitantly in the presence of renal insufficiency.

Cyclophosphamide: Reports indicate that cyclophosphamide levels may be increased during concurrent treatment with allopurinol sodium for injection. Monitoring of cyclophosphene levels and possible adjustment of cyclophosphene dosage should be considered in these cases if they are co-administered.

Drug Laboratory Test Interactions: Allopurinol is not known to alter the accuracy of laboratory tests.

Carcinogenesis, Mutagenesis and Impairment of Fertility:

Carcinogenesis: Allopurinol administered intravenously at doses up to 20 mg/kg/day to mice and rats for the majority of their life span. There was no evidence of tumors in male or female mice or male rats, respectively. There was no evidence of tumors in female rats. In male rats, benign and malignant tumors of the prostate occurred at incidences significantly higher than controls. This drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Carcinogenesis, Mutagenesis and Impairment of Fertility:

Mutagenesis:

Impairment of Fertility:

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