This enzyme is required for the conversion of hypoxanthine, an end product of purine, to uric acid. A deficiency of the enzyme, xanthine oxidase, results in hyperuricemia and resultant deposition of monosodium urate, which causes the symptoms of gout. Patients with gout require dietary restrictions to prevent the overproduction of uric acid by inhibiting the biochemical reactions involved in xanthine metabolism.

ZYLOPRIM is a structural analogue of the natural purine base, hypoxanthine. It is an inhibitor of xanthine oxidase, the enzyme responsible for the conversion of hypoxanthine to xanthine and of xanthine to uric acid, the end product of purine metabolism in man. ZYLOPRIM is metabolized to the corre- sponding xanthine oxidase inhibitors, alloxanthine, xanthine, and oxipurinol, which also are inhibitors of xanthine oxidase.

It has been shown that reutilization of both hypoxanthine and xanthine by hypoxanthine and xanthine oxidase activity is markedly enhanced when their oxidation is inhibited by ZYLOPRIM. ZYLOPRIM is a competitive and irreversible inhibitor of xanthine oxidase activity, with a competitive, non-competitive, or mixed mechanism of inhibition, depending on the enzyme concentration and temperature.

It is a USP-grade, USP-referenced, USP-compliant material. It is a USP-grade, USP-referenced, USP-compliant material. It is a USP-grade, USP-referenced, USP-compliant material. It is a USP-grade, USP-referenced, USP-compliant material.
Allopurinol and oxipurinol have been found in the milk of a mother who was receiving ZYLOPRIM. Since the effect of allopurinol on the nursing infant is unknown, caution should be exercised when ZYLOPRIM is administered to a nursing woman.

Pediatric Use: ZYLOPRIM is rarely indicated for use in children with the exception of those with hyperuricemia secondary to myeloproliferative disorders. When it is indicated, the dose should be even more conservatively adjusted in those patients on such combined therapy if diminished renal function is detected.

The most frequent adverse reactions to ZYLOPRIM are skin rash. Skin reactions can be severe and sometimes fatal. Therefore, treatment with ZYLOPRIM should be discontinued immediately if a rash develops (see WARNINGS).

Drug/Laboratory Test Interactions: Allopurinol and oxipurinol have been found in the milk of a mother who was receiving ZYLOPRIM. Since the effect of allopurinol on the nursing infant is unknown, caution should be exercised when ZYLOPRIM is administered to a nursing woman.

Enhanced bone marrow suppression by cyclophosphamide and other cytotoxic agents has been reported among patients receiving ZYLOPRIM and cyclosporine. Therefore, close monitoring of cyclosporine levels and possible adjustment of cyclosporine dosage should be exercised when ZYLOPRIM is administered to a nursing woman.

An increase in the frequency of skin rash has been reported among patients receiving ampicillin or amoxicillin concurrently with ZYLOPRIM compared to patients who are not receiving both drugs. The cause of the reported association has not been established.

While adjusting the dosage of ZYLOPRIM in patients who are being treated with colchicine and/or anti-inflammatory agents, it is wise to continue the latter therapy until serum uric acid has been normalized and there has been freedom from acute gouty attacks for several months.

In transferring a patient from a uricosuric agent to ZYLOPRIM, the dose of the uricosuric agent should be gradually reduced over a period of several weeks and the dose of ZYLOPRIM gradually increased to the required dose needed to maintain a normal serum uric acid level. It should also be noted that ZYLOPRIM is generally better tolerated than colchicine when given as an oral contraceptive. The correct size and frequency of dosage for maintaining the serum uric acid level is best determined by using the serum uric acid level as an index.

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 is advisable together with a high fluid intake. Otherwise similar considerations to the above recommendations for treating patients with gout govern the regulation of dosage for maintenance purposes in secondary hyperuricemia.

OVDOSAGE: Massive overdosage or acute poisoning by ZYLOPRIM has not been reported in humans.

In mice, the intraperitoneal (IP) LD₅₀ of 160 mg/kg given intraperitoneally (IP) with deaths delayed up to 5 days and 700 mg/kg orally (PO) (approximately 140 times the usual human dose of ZYLOPRIM) with deaths delayed up to 24 days. In rats, the acute LD₅₀ is 750 mg/kg IP and 6000 mg/kg PO (approximately 1200 times the human dose).

In the absence of renal failure, and dosage levels should be altered if anuria occurs, the frequency of dosage intervals should be lengthened.

OPTIC neuritis, confusion, dizziness, vertigo, foot drop, decrease in libido, depression, anemia, tinutis, asthma, insomnia.

Body As a Whole: Rash, fever, chills, arthralgias, intermittent abdominal pain, gastritis, dyspepsia.

Gastrointestinal: Diarrhea, nausea, alkaline phosphatase increased, SGOT/SGPT increased.

Metabolic and Nutritional: Acute attacks of gout.

Skin and Appendages: Rash, maculopapular rash.

Early clinical studies and incidence rates from early clinical trials and voluntary reports since marketing of ZYLOPRIM show that the incidence of these adverse reactions is now less than 1%. The explanation for this decrease has not been determined.

Most Common Reactions * Probably Causally Related: Gastrointestinal: Diarrhea, nausea, alkaline phosphatase increased, SGOT/SGPT increased.

The dose of ZYLOPRIM recommended for management of recurrent calcium oxalate stones in hyperuricosuric patients is 200 to 300 mg/day in divided doses or as the single equivalent. This dose may be adjusted up or down depending upon the resultant control of the hyperuricosuria based upon subsequent urinary calcium and oxalate excretion.

In the absence of renal failure, and dosage levels should be altered if anuria occurs, the frequency of dosage intervals should be lengthened.

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Body As a Whole: Rash, fever, chills, arthralgias, intermittent abdominal pain, gastritis, dyspepsia.

Gastrointestinal: Diarrhea, nausea, alkaline phosphatase increased, SGOT/SGPT increased.

Metabolic and Nutritional: Acute attacks of gout.

Skin and Appendages: Rash, maculopapular rash.

Teratogenic Effects: PREGNANCY CATEGORY C. Reproduction studies in rats and rabbits at doses up to 100 mg/kg have shown no evidence of teratogenicity. There is a published report of a study in pregnant mice given 50 or 100 mg/kg allopurinol but not in those given 500 mg/kg. There were increased numbers of fetal deaths in dams given 100 mg/kg allopurinol but not in those given 5 mg/kg. There were increased numbers of external malformations in fetuses at both doses of allopurinol on gestation day 10 and increased numbers of skeletal malformations in fetuses at both doses on gestation day 13.

The acute oral LD₅₀ in rats based on body weight is 700 mg/kg PO (approximately 140 times the usual human dose of ZYLOPRIM) with deaths delayed up to 24 days. In mice, the acute LD₅₀ is 160 mg/kg given intraperitoneally (IP) with deaths delayed up to 5 days and 700 mg/kg orally (PO) (approximately 140 times the usual human dose of ZYLOPRIM) with deaths delayed up to 24 days. In rats, the acute LD₅₀ is 750 mg/kg IP and 6000 mg/kg PO (approximately 1200 times the human dose).

In the absence of renal failure, and dosage levels should be altered if anuria occurs, the frequency of dosage intervals should be lengthened.

The response is evaluated after approximately 48 hours of therapy and a dosage adjustment is made if necessary.

HOW SUPPLIED: 100-mg (white) scored, flat cylindrical tablets imprinted with "ZYLOPRIM 100" on a raised hexagon, bottles of 100 (NDC 65483-991-10).

Store at 15° to 25°C (59° to 77°F) in a dry place.

300-mg (peach) scored, flat, cylindrical tablets imprinted with "ZYLOPRIM 300" on a raised hexagon, bottles of 100 (NDC 65483-993-10) and 500 (NDC 65483-995-50).

Store at 15° to 25°C (59° to 77°F) in a dry place and protect from light.

PROMETHEUS LABORATORIES INC.
Manufactured by: DSM Pharmaceuticals, Inc.
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For Prometheus Laboratories Inc. San Diego, CA 92121

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