

ZYLORIC

- **Drug Class Description**
Xanthine oxidase inhibitors.
- **Generic Name**
Allopurinol
- **Presentation**
Tablet
- **Description**
Zyloric 100 mg Tablets Zyloric 300 mg Tablets

Indications

Zyloric is indicated for reducing urate/uric acid formation in conditions where urate/uric acid deposition has already occurred (e.g. gouty arthritis, skin tophi, nephrolithiasis) or is a predictable clinical risk (e.g. treatment of malignancy potentially leading to acute uric acid nephropathy).

The main clinical conditions where urate/uric acid deposition may occur are: idiopathic gout; uric acid lithiasis; acute uric acid nephropathy; neoplastic disease and myeloproliferative disease with high cell turnover rates, in which high urate levels occur either spontaneously, or after cytotoxic therapy; certain enzyme disorders which lead to overproduction of urate, for example: hypoxanthine-guanine phosphoribosyltransferase, including Lesch-Nyhan syndrome; glucose-6-phosphatase including glycogen storage disease; phosphoribosylpyrophosphate synthetase, phosphoribosylpyrophosphate amidotransferase; adenine phosphoribosyltransferase.

Zyloric is indicated for management of 2, 8-dihydroxyadenine (2, 8-DHA) renal stones related to deficient activity of adenine phosphoribosyltransferase. Zyloric is indicated for the management of recurrent mixed calcium oxalate renal stones in the presence of hyperuricosuria, when fluid, dietary and similar measures have failed.

Adult Dosage

Zyloric should be introduced at low dosage e.g. 100mg/day to reduce the risk of adverse reactions and increased only if the serum urate response is unsatisfactory. Extra caution should be exercised if renal function is poor. The following dosage schedules are suggested:

- 100 to 200 mg daily in mild conditions,
- 300 to 600 mg daily in moderately severe conditions,
- 700 to 900 mg daily in severe conditions.

If dosage on an mg/kg bodyweight basis is required, 2 to 10 mg/kg bodyweight/day should be used.

Dosage in renal impairment: Since allopurinol and its metabolites are excreted by the kidney, impaired renal function may lead to retention of the drug and/or its metabolites with consequent prolongation of plasma half-lives. In severe renal insufficiency, it may be advisable to use less than 100 mg per day or to use single doses of 100mg at longer intervals than one day.

Allopurinol and its metabolites are removed by renal dialysis. If dialysis is required two to three times a week consideration should be given to an alternative dosage schedule of 300-400 mg Zyloric immediately after each dialysis with none in the interim.

Dosage in hepatic impairment: Reduced doses should be used in patients with hepatic impairment. Periodic liver function tests are recommended during the early stages of therapy.

Treatment of high urate turnover conditions, e.g. neoplasia, Lesch-Nyhan syndrome: It is advisable to correct existing hyperuricaemia and/or hyperuricosuria with Zyloric before starting cytotoxic therapy. It is important to ensure adequate hydration to maintain optimum diuresis and to attempt alkalinisation of urine to increase solubility of urinary urate/uric acid. Dosage of Zyloric should be at the lower end of the recommended dosage schedule.

If urate nephropathy or other pathology has compromised renal function, the advice given in *Dosage in renal impairment* should be followed.

These steps may reduce the risk of xanthine and/or oxipurinol deposition complicating the clinical situation.

Monitoring Advice: The dosage should be adjusted by monitoring serum urate concentrations and urinary urate/uric acid levels at appropriate intervals.

Instructions for Use:

Zyloric may be taken orally once a day after a meal. It is well tolerated, especially after food. Should the daily dosage exceed 300 mg and gastrointestinal intolerance be manifested, a divided doses regimen may be appropriate.

Child Dosage

Children under 15 years: 10 to 20 mg/kg bodyweight/day up to a maximum of 400 mg daily. Use in children is rarely indicated, except in malignant conditions (especially leukaemia) and certain enzyme disorders such as Lesch-Nyhan syndrome.

Elderly Dosage

In the absence of specific data, the lowest dosage which produces satisfactory urate reduction should be used.

Special Precautions

Zyloric should be withdrawn *immediately* when a skin rash or other evidence of sensitivity occurs. Reduced doses should be used in patients with hepatic or renal impairment. 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.

Asymptomatic hyperuricaemia 'per se' is generally not considered an indication for use of Zyloric. Fluid and dietary modification with management of the underlying cause may correct the condition.

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

In the early stages of treatment with Zyloric, 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: 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 Zyloric will lead to dissolution of large uric acid renal pelvic stones, with the remote possibility of impaction in the ureters.