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OXYPURINOL DRUG MEASUREMENT INFORMATION SHEET

Oxypurinol is the single active metabolite of allopurinol. Oxypurinol is measured instead of allopurinol as it is responsible for most of the inhibition of the reduced form of xanthine oxidase and subsequent reduction in uric acid. It is eliminated more slowly than allopurinol.

WHEN TO CONSIDER TDM

- Patients not achieving desired serum uric acid concentration (< 0.36 mmol/l) who are taking reasonable doses of allopurinol. [1,2]
- To assess patient adherence with allopurinol therapy. [1]

SAMPLE COLLECTION TIME

6-9 hours after allopurinol dose.

THERAPEUTIC RANGE

- Suggested oxypurinol target for controlling hyperuricaemia is 5-22.8 mg/L. [2,3]
- Target oxypurinol concentrations between 20-30 mg/L may be necessary, if serum urate concentration is not <0.36 mmol/L. [2]

TOXIC RANGE

- A target for toxicity has not been defined, but concentrations above the therapeutic range may be associated with toxicity.
- Toxicity may also be associated with:
  - a high starting dose of allopurinol
  - rapid dose escalation of allopurinol
  - concomitant diuretics [see note 1]
  - patients at risk of hypersensitivity reactions e.g. certain ethnic groups with HLA-B* 5801 gene particularly of Han-Chinese ancestry [see note 2]. [4]

ADDITIONAL COMMENTS

- Note 1. Diuretics such as frusemide may increase uric acid levels and cause “resistance” to allopurinol. Patients taking frusemide may require higher doses of allopurinol compared with patients not receiving diuretics.
- Note 2. In patients of Chinese ancestry discuss alternative therapy or genetic testing with specialist.[4]

SAMPLE COLLECTION, TRANSPORT AND COST

- Wait 5 to 6 days after commencing/changing therapy to reach steady state before collecting blood for analysis. Blood samples for TDM can be collected earlier if efficacy or toxicity are concerns.

- Collect a 5 mL EDTA (purple top) tube 6-9 hour after the dose. Do not use tubes with gel separator as gel can bind drugs giving a falsely low result.
- Send in an Esky with an ice brick. If sample transport delayed for 12 h, freeze plasma sample as soon as possible after collection and send frozen.
- Assay is performed once a week.

PHARMACOKINETICS OF OXYPURINOL[5]

Elimination half life t½	23 hours [Range 9-38 hours]
Cl after oral administration	0.31ml/min/kg
After oral administration	0.62L/kg

DOSING CONSIDERATIONS

Renal Impairment	Determines starting dose
Pharmacogenomics	Ethnic groups with HLA-B* 5801 (Han Chinese)
Critical Drug Interaction	Allopurinol reduces metabolism of 6-mercaptopurine or azathioprine and increases risk of severe bone marrow toxicity.[6]

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