Uricosuric agents: These drugs increase uric acid excretion by a direct action on the renal tubule. They remain useful as prophylaxis for patients with severe recurrent gout who have severe adverse reactions to allopurinol. Common examples: Probenecid and Sulfinpyrazone (which also has NSAID activity). Benzbromarone is also available for treatment of patients with renal impairment.

PROBENECID: This uricosuric agent is given orally. In low doses, it causes a decrease in distal tubular secretion of uric acid but in larger therapeutic doses, it increases its excretion, by blocking tubular reabsorption. After treatment for some months, the serum uric acid may return to normal levels.

Adverse reactions: Probenecid is relatively non-toxic and is well tolerated. Occasionally, it causes dyspepsia, skin rashes and deposition of urate crystals in the renal tubules/pelvis; this risk can be minimised by maintaining a high volume of alkaline urine.

The drug inhibits the renal excretion of drugs such as penicillin, indomethacin, methotrexate and dapsone. It also impairs heparin metabolism thus reducing the dose of heparin necessary for anticoagulation.

SULFINPYRAZONE: This is a sulfoxide derivative of phenylbutazone with some anti-inflammatory activity but marked uricosuric property. This effect is dose related. Like probenecid its smaller dose prevents the tubular secretion of uric acid while higher dose promotes its excretion. It is administered orally in doses of 100-200 mg tid. The daily dose should not exceed 600 mg.

Adverse reactions: Vomiting, upper abdominal discomfort and skin rashes. May cause bone marrow depression. Sulfinpyrazone inhibits platelet aggregation.

Both probenecid and sulfinpyrazone are ineffective in the presence of impaired renal function.

Benzbromarone, a benzofuran compound, is another uricosuric drug. It is potent and is claimed to be effective even when the GFR is reduced to 25-50 % of normal.

AZAPROPAZONE: This uricosuric agent has weak analgesic, antipyretic and anti- inflammatory actions; it is a weak inhibitor of cyclooxygenase. The drug is rapidly and almost completely absorbed from the gut. It is relatively toxic.

The dose in acute gout is 600 mg four times on the first day, followed by 1800 mg a day in divided doses until the acute attack has subsided; the maintenance dose is 1200 mg a day in

divided doses. It has also been used for the treatment of Rheumatoid Arthritis and Osteo arthritis.

Uricosuric drugs can be hazardous in: • Urate overproducers; Those with urine flow consistently less than 1 ml/min

• Those with creatinine clearance less than 50 ml/min; and

• Those with history of uric acid or calcium stones

Aspirin, an analgesic, relieves joint pains. Although it has a uricosuric action, the dose required for persistent uricosuria is large, which is unacceptable. In smaller doses it acts as anti-uricosuric and also blocks the uricosuric effect of other drugs.

Salicylates, therefore, should be avoided in gout.

Drugs Increasing Metabolism Urate oxidase (uricase) metabolizes insoluble uric acid to soluble allantoin in the birds. This enzyme is absent in humans.

Recombinant urate oxidase is now available as Rasburicase and Pegloticase