Mercaptopurine Jan JPP

Day 1: A metabolite of azathioprine, #mercaptopurine was discovered to be an immunosuppressant circa 1950s. The role for #mercaptopurine developed in leukaemias (acute and maintenance therapy) and inflammatory bowel disease (IBD) for maintenance of remission for Crohn’s and ulcerative colitis (IBD unlicensed role).

(cont) Dose; significant individual variations in kinetics eg drug metabolism and in dynamics such as intracellular uptake and breakdown,mean an individual approach. Adult acute chemotherapy 2.5-5mg/kg PO once daily, maintenance 1.5-2.5mg/kg/day. IBD 1-1.5mg/kg (British National Formulary states lower can be effective e.g some IBD sites state 0.75-1.5mg/kg/day. Use unlicensed in children & chemotherapy dose is customised, IBD as per adult.

(cont) Rapidly dividing cells are most affected, such as tumours and bone marrow blood cells, some of which control inflammation. When used in inflammatory bowel conditions, the effects/full effects may not be experienced for three, or even six months.

Day 3: Key kinetics; oral bioavailability is variable and affected by some food (drug is taken 1 hour before or 2 hours after milk/dairy products). There is extensive metabolism by multiple pathways. Polymorphisms are relevant as they can predict adverse drug reactions such as TPMT deficiency. Elimination is triphasic; t ½ at 45 mins, 2.5 hours and 10 hours

Day 4: The toxic compounds formed from cell uptake of #mercaptopurine are broken down to non-toxic metabolites by enzymes such as TPMT, which is subject to genetic polymorphisms.TPMT testing is recommended before starting. Less than 1% population have TMPT deficiency (use alternative drug), but up to 11% have reduced levels, which still increases the risk of toxicity (lower dose).

Day 6: DDIs; Many common drugs increase risk of hepatotoxicity eg flucloxacillin, statins, valproate. Monitor INR with warfarin. Xanthine oxidase breaks down #mercaptopurine, so gout drugs e.g allopurinol & febuxostat can increase risk toxicity. If combination necessary, reduce mercaptopurine dose by 25%

Day 7: Interesting fact. Dairy avoidance (i hour before or 2 hours after dairy) is recommended because cow’s milk is high in xanthine oxidase which starts to break down the drug, making less bioavailable.

With the help of Prescribing and Therapeutics Training Ltd and the Journal of Prescribing Practice, you can earn your 1-hour CPD certificate. Complete the additional reading suggested below and then answer the ten questions. Please submit the answers to reesprescribe@gmail.com as a numbered list with TRUE/FALSE or the correct A,B,C,D option. If you achieve 8 or more out of ten on the questions, a CPD certificate will be emailed to you.

NOTE: there is only one correct answer for each question.

2. Why does the dose for mercaptopurine need to be reduced if allopurinol is also prescribed?

A. Because allopurinol prevents mercaptopurine being taken up by cells

B. Because allopurinol inhibits one of the enzymes that breaks down mercaptopurine, increasing the risk of toxicity

C. Because allopurinol induces one of the enzymes that breaks down mercaptopurine, so the therapeutic effect is lost

D. Because some people have a reaction that causes a lack of allopurinol breakdown

4.Mercaptopurine is an evidence-based intervention for leukaemias and inflammatory bowel disease, but it is not licensed for use in either condition

TRUE or FALSE

8. Why does mercaptopurine have some target selectivity?

A. The fastest dividing cells are the most affected

B. The slowest dividing cells are the most affected

C. Only tumour cells take up the drug

D. Mercaptopurine only binds to bone marrow stem cells

9. Cow’s milk products contain the enzyme xanthine oxidase, which breaks down mercaptopurine, hence dairy products can affect absorption TRUE or FALSE?