CPD March 2023: Carbimazole

[[A person smiling for the camera

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Day 1 Sulphur-containing compounds were found to be thyroid-toxic in the 1940s which led to propylthiouracil use. A 2nd thiouracil analogue ‘methimazole’ was found & its prodrug #carbimazole was licensed in 1953, as believed less toxic (not so)

Day 2: #carbimazole is used for hyperthyroidism for all ages. Adult start dose 20-60mg daily (divide) & child dose re age/weight; all regimens based on time to euthyroid, then reduce to maintenance dose. Also used for the ‘blocking-replacement’ regimen in combination for 6-18 months with levothyroxine to prevent hypothyroidism

Day 3: Oral absorption unaffected by food; metabolite cmax 1-2 hours. Low Vd as concentrates in thyroid gland. Crosses placenta & present in breast milk. 10% entero-hepatic recycling & contraindicated if severe hepatic impairment. T½ 5-6 hrs (prolonged in hyperthyroidism). Renal excretion ~ 90% as mostly unchanged drug

Day 4: The full MOA for #carbimazole is not fully understood; there is reduced uptake of iodine in thyroid gland & it also opposes iodination by inhibition of thyroid peroxidases; these actions lead to thyroid suppression & reduced thyroxine synthesis. Symptoms can take a few weeks to abate

Day 5: Poor frequency data for ADEs. Common include nausea, headache, dizziness. Rare include agranulocytosis. Bone marrow suppression (BMS) & blood disorders can be fatal; pre-existing significant haematological conditions preclude use. Advise re signs of BMS requiring urgent attention e.g fever, bruising. Note #carbimazole can worsen goitre (NOT exhaustive)

Day 6: #carbimazole was licensed pre-vigilance data. No drug-drug interaction denoted as ‘severe’ in BNF. As vitamin K antagonist it could increase anti-coagulation (monitor); slowing kinetic processes could alter drug levels, so increased lithium, digoxin, prednisolone levels (NOT exhaustive)

Day 7: Propylthiouracil is 1st line in USA, as less placental transfer. #carbimazole not 1st-line in UK for pregnancy as potential for foetal harm, especially during 1st trimester \* Effective contraception advised where child-bearing potential. The SPC was altered 2018 following EU safety recommendations, but acknowledges evidence is ‘based on human experience from epidemiological studies & spontaneous reporting’.

CPD

CPD: In addition to the tweets, read the BNF treatment summary on hyperthyroidism and the monograph for carbimazole, as well as the Summary of Product Characteristics for carbimazole

<https://bnf.nice.org.uk/treatment-summaries/hyperthyroidism/>

<https://bnf.nice.org.uk/drugs/carbimazole/>

<https://www.medicines.org.uk/emc/product/4266/smpc>

1. Carbimazole was discovered as an anti-thyroid function drug in the 1970s

TRUE or FALSE

1. Carbimazole is a prodrug

TRUE or FALSE

1. Carbimazole is not first-line in pregnancy

TRUE or FALSE

1. Which of the following is TRUE?
2. Carbimazole concentrates in the pituitary gland
3. Carbimazole is broken down extensively in the liver
4. Carbimazole has very high protein binding characteristics
5. Carbimazole crosses the placenta
6. Which of the following is a rare adverse drug effect (ADE)
7. Aplastic anaemia
8. Agranulocytosis
9. Rash
10. Loss of taste
11. Which of the following best describes the mechanism of action for carbimazole?
12. It inhibits thyroid peroxidase function
13. It is directly cytotoxic to thyroid producing cells
14. It limits absorption of dietary iodine
15. It causes immune suppression stopping any attack on the thyroid gland
16. Carbimazole usually takes months to years to improve symptoms

TRUE or FALSE

1. Carbimazole has no listed ‘severe’ drug-drug interactions listed in the BNF

TRUE or FALSE

1. Counselling about the relevance of signs/symptoms such as severe sore throat, fever, bruising etc is important because these can indicate bone marrow suppression

TRUE or FALSE

1. Carbimazole can cause congenital malformations if used in pregnancy

TRUE or FALSE