Antithyroid drugs in pregnancy

Radioactive iodine therapy is contra-indicated during pregnancy. Propylthiouracil and carbimazole can be given but the blocking-replacement regimen is **not** suitable. Carbimazole is associated with congenital defects, including aplasia cutis of the neonate, therefore propylthiouracil remains the drug of choice during the first trimester of pregnancy. In the second trimester, consider switching to carbimazole because of the potential risk of hepatotoxicity with propylthiouracil. Both propylthiouracil and carbimazole cross the placenta and in high doses may cause fetal goitre and hypothyroidism—the lowest dose that will control the hyperthyroid state should be used (requirements in Graves' disease tend to fall during pregnancy). See also *Important safety information* in the carbimazole below drug monograph.

Antithyroid drugs in neonates

Neonatal hyperthyroidism is treated with carbimazole or propylthiouracil, usually for 8 to 12 weeks. In severe symptomatic disease iodine may be needed to block the thyroid and propranolol required to treat peripheral symptoms.

Other drugs used for Hyperthyroidism Metoprolol tartrate, p. 113

ANTITHYROID DRUGS › SULFUR-CONTAINING IMIDAZOLES

Carbimazole

22-Nov-2019

- **INDICATIONS AND DOSE**

Hyperthyroidism (blocking-replacement regimen) in combination with levothyroxine

- BY MOUTH
- Child: Therapy usually given for 12 to 24 months (consult product literature or local protocols)

Hyperthyroidism (including Graves' disease)

- BY MOUTH
- Neonate: Initially 750 micrograms/kg daily until patient is euthyroid, usually after 8 to 12 weeks, then gradually reduce to a maintenance dose of 30–60% of the initial dose; higher initial doses (up to 1 mg/kg daily) are occasionally required, particularly in thyrotoxic crisis, dose may be given in single or divided doses.
- Child 1 month-11 years: Initially 750 micrograms/kg daily until patient is euthyroid, usually after 4–8 weeks, then gradually reduce to a maintenance dose of 30–60% of the initial dose; higher initial doses are occasionally required, particularly in thyrotoxic crisis, dose may be given in single or divided doses; maximum 30 mg per day
- Child 12-17 years: Initially 30 mg daily until euthyroid, usually after 4–8 weeks, then gradually reduce to a maintenance dose of 30–60% of the initial dose; higher initial doses are occasionally required, particularly in thyrotoxic crisis, dose may be given in single or divided doses

DOSE EQUIVALENCE AND CONVERSION

- When substituting, carbimazole 1 mg is considered equivalent to propylthiouracil 10 mg but the dose may need adjusting according to response.

IMPORTANT SAFETY INFORMATION

NEUTROPENIA AND AGRANULOCYTOSIS

Manufacturer advises of the importance of recognising bone marrow suppression induced by carbimazole and the need to stop treatment promptly.

- Patient should be asked to report symptoms and signs suggestive of infection, especially sore throat.
- A white blood cell count should be performed if there is any clinical evidence of infection.
- Carbimazole should be stopped promptly if there is clinical or laboratory evidence of neutropenia.

MHRA/CHM ADVICE: CARBIMAZOLE: INCREASED RISK OF CONGENITAL MALFORMATIONS; STRENGTHENED ADVICE ON CONTRACEPTION (FEBRUARY 2019)

Carbimazole is associated with an increased risk of congenital malformations when used during pregnancy, especially in the first trimester and at high doses (daily dose of 15 mg or more).

Women of childbearing potential should use effective contraception during treatment with carbimazole. It should only be considered in pregnancy after a thorough benefit-risk assessment, and at the lowest effective dose without additional administration of thyroid hormones—close maternal, fetal, and neonatal monitoring is recommended.

MHRA/CHM ADVICE: CARBIMAZOLE: RISK OF ACUTE PANCREATITIS (FEBRUARY 2019)

Cases of acute pancreatitis have been reported during treatment with carbimazole. It should be stopped immediately and permanently if acute pancreatitis occurs.

Carbimazole should not be used in patients with a history of acute pancreatitis associated with previous treatment—re-exposure may result in life-threatening acute pancreatitis with a decreased time to onset.

- **CONTRA-INDICATIONS** Severe blood disorders
- **INTERACTIONS** → Appendix 1: carbimazole
- **SIDE-EFFECTS**
  - **Rare or very rare** Bone marrow disorders · haemolytic anaemia · severe cutaneous adverse reactions (SCARs) · thrombocytopenia
  - **Frequency not known** Agranulocytosis · alopecia · angioedema · dyspepsia · eosinophilia · fever · gastrointestinal disorder · generalised lymphadenopathy · haemorrhage · headache · hepatic disorders · insulin autoimmune syndrome · leucopenia · malaise · myopathy · nausea · nerve disorders · neutropenia · pancreatitis acute (discontinue permanently) · salivary gland enlargement · skin reactions · taste loss
- **CONCEPTION AND CONTRACEPTION** The MHRA advises that females of childbearing potential should use effective contraception during treatment.
- **PREGNANCY** The MHRA advises consider use only after a thorough benefit-risk assessment. See *Important Safety Information* and Antithyroid drugs p. 521 for further information.
- **BREAST FEEDING** Present in breast milk but this does not preclude breast-feeding as long as neonatal development is closely monitored and the lowest effective dose is used. Amount in milk may be sufficient to affect neonatal thyroid function therefore lowest effective dose should be used.
- **HEPATIC IMPAIRMENT** Manufacturer advises use with caution in mild to moderate insufficiency—half-life may be prolonged; avoid in severe insufficiency.
- **PATIENT AND CARER ADVICE** Warn patient or carers to tell doctor **immediately** if sore throat, mouth ulcers, bruising, fever, malaise, or non-specific illness develops.
  Medicines for Children leaflet: Carbimazole for hyperthyroidism
  www.medicinesforchildren.org.uk/carbimazole-hyperthyroidism