consult product literature; discontinue permanently if hepatic enzymes at least 3 times the upper limit of normal.

- **CONCEPTION AND CONTRACEPTION** Effective contraception must be used in women of child-bearing potential.
- **PREGNANCY** Manufacturer advises avoid—teratogenic in *animal* studies.
- **BREAST FEEDING** Manufacturer advises avoid—present in breast milk.
- **HEPATIC IMPAIRMENT** Manufacturer advises avoid.
- **MONITORING REQUIREMENTS**
  - Monitor ECG before and one week after initiation, and then as clinically indicated thereafter.
  - Adrenal insufficiency Monitor adrenal function within one week of initiation, then regularly thereafter. When cortisol levels are normalised or close to target and effective dose established, monitor every 3–6 months as there is a risk of autoimmune disease development or exacerbation after normalisation of cortisol levels. If symptoms suggestive of adrenal insufficiency such as fatigue, anorexia, nausea, vomiting, hypotension, hyponatraemia, hyperkalaemia, and/or hypoglycaemia occur, measure cortisol levels and discontinue treatment temporarily (can be resumed thereafter at lower dose) or reduce dose and if necessary, initiate corticosteroid substitution.
  - Hepatotoxicity Monitor liver function before initiation of treatment, then weekly for 1 month after initiation, then monthly for 6 months—more frequently if dose adjusted or abnormal liver function detected.
- **PATIENT AND CARER ADVICE** Patients or their carers should be told how to recognise signs of liver disorder, and advised to discontinue treatment and seek prompt medical attention if symptoms such as anorexia, nausea, vomiting, fatigue, jaundice, abdominal pain, or dark urine develop. Patients or their carers should also be told how to recognise signs of adrenal insufficiency.
  Driving and skilled tasks Dizziness and somnolence may affect the performance of skilled tasks (e.g. driving).

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug. Forms available from special-order manufacturers include: oral suspension

Tablet

CAUTIONARY AND ADVISORY LABELS 2, 5, 21

- Ketoconazole (non-proprietary) ▼
  Ketoconazole 200 mg Ketoconazole 200mg tablets | 60 tablet PoM £480.00 DT = £480.00

Metyrapone

- **DRUG ACTION** Metyrapone is a competitive inhibitor of 11β-hydroxylation in the adrenal cortex; the resulting inhibition of cortisol (and to a lesser extent aldosterone) production leads to an increase in ACTH production which, in turn, leads to increased synthesis and release of cortisol precursors. Metyrapone may be used as a test of anterior pituitary function.

- **INDICATIONS AND DOSE**

Differential diagnosis of ACTH-dependent Cushing's syndrome (specialist supervision in hospital)

- BY MOUTH
- Child: 15 mg/kg every 4 hours for 6 doses, alternatively 300 mg/m^2 every 4 hours for 6 doses; usual dose 250–750 mg every 4 hours

Management of Cushing's syndrome (specialist supervision in hospital)

- BY MOUTH
- Child: Usual dose 0.25–6 g daily, dose to be tailored to cortisol production, dose is either low, and tailored to cortisol production, or high, in which case corticosteroid replacement therapy is also needed

- **CONTRA-INDICATIONS** Adrenocortical insufficiency
- **CAUTIONS** Avoid in Acute porphyrias p. 652 · gross hypopituitarism (risk of precipitating acute adrenal failure) · hypertension on long-term administration · hypothyroidism (delayed response)
- **INTERACTIONS** → Appendix 1: metyrapone
- **SIDE-EFFECTS**
  - **Common or very common** Dizziness · headache · hypotension · nausea · sedation · vomiting
  - **Rare or very rare** Abdominal pain · adrenal insufficiency · allergic dermatitis · hirsutism
  - **Frequency not known** Alopecia · bone marrow failure · hypertension
- **PREGNANCY** Avoid (may impair biosynthesis of fetal-placental steroids).
- **BREAST FEEDING** Avoid—no information available.
- **HEPATIC IMPAIRMENT** Manufacturer advises caution (risk of delayed response).
- **PATIENT AND CARER ADVICE**
  Driving and skilled tasks Drowsiness may affect the performance of skilled tasks (e.g. driving).

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Capsule

CAUTIONARY AND ADVISORY LABELS 21

- Metopirone (HRA Pharma UK Ltd)
  Metyrapone 250 mg Metopirone 250mg capsules | 100 capsule PoM £363.66 DT = £363.66

3 Diabetes mellitus and hypoglycaemia

3.1 Diabetes mellitus

Diabetes

05-Jun-2017

Description of condition

Diabetes mellitus is a group of metabolic disorders in which persistent hyperglycaemia is caused by deficient insulin secretion or by resistance to the action of insulin. This leads to the abnormalities of carbohydrate, fat and protein metabolism that are characteristic of diabetes mellitus.

Type 1 diabetes mellitus p. 482 and Type 2 diabetes mellitus p. 485 are the two most common classifications of diabetes. Other common types of diabetes are gestational diabetes (develops during pregnancy and resolves after delivery) and secondary diabetes (may be caused by pancreatic damage, hepatic cirrhosis, or endocrine disease). Treatment with endocrine, antiviral or antipsychotic drugs may also cause secondary diabetes. In children, conditions such as cystic fibrosis can lead to diabetes; monogenic diabetes (previously known as maturity onset diabetes in the young) can also occur due to a single gene defect.

Driving

Information on the requirements for driving vehicles by young people receiving treatment for diabetes is available in the BNF or from the DVLA at www.gov.uk/guidance/diabetes-mellitus-assessing-fitness-to-drive.

Alcohol

Adolescents and their carers should be made aware that alcohol can make the signs of hypoglycaemia less clear, and can cause delayed hypoglycaemia; (note: specialist sources