mitotane. The dose of glucocorticoid should be increased in case of shock, trauma, or infection.

- **PATIENT AND CARER ADVICE** Patients should be warned to contact doctor immediately if injury, infection, or illness occurs (because of risk of acute adrenal insufficiency).
  Driving and skilled tasks Central nervous system toxicity may affect performance of skilled tasks (e.g. driving).

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.
  Tablet
  CAUTIONARY AND ADVISORY LABELS 2, 10, 21
  - **Lysodren** (HRA Pharma UK Ltd)
    Mitotane 500 mg Lysodren 500mg tablets | 100 tablet PoM £590.97

Pegaspargase

16-Mar-2017

- **DRUG ACTION** Pegaspargase breaks down the amino acid L-asparagine, thereby interfering with the growth of malignant cells, which are unable to synthesise L-asparagine.

- **INDICATIONS AND DOSE**
  Acute lymphoblastic leukaemia (in combination with other antineoplastic drugs) (specialist use only)
  - BY INTRAMUSCULAR INJECTION, OR BY INTRAVENOUS INFUSION
  - Neonate: 82.5 units/kg every 14 days.
  - Child (body surface area up to 0.6 m^2): 82.5 units/kg every 14 days
  - Child (body surface area 0.6 m^2 and above): 2500 units/m^2 every 14 days

IMPORTANT SAFETY INFORMATION
Be aware that doses are calculated either using units/kg or units/m^2, depending on the size of the child.

- **CONTRA-INDICATIONS** History of pancreatitis · history of serious haemorrhagic event with previous L-asparaginase therapy · history of serious thrombosis with previous L-asparaginase therapy
- **CAUTIONS** Concomitant use of other hepatotoxic drugs (particularly in pre-existing hepatic impairment)—monitor hepatic function · diabetes (may raise blood glucose) · hypersensitivity reactions · marked decrease of leukocyte count at start of treatment is possible—may be associated with significant rise in serum uric acid and development of uric acid nephropathy

  CAUTIONS, FURTHER INFORMATION
  - Hypersensitivity reactions Serious hypersensitivity reactions, including life-threatening anaphylaxis, can occur—pegaspargase should only be administered when appropriately trained staff and resuscitation facilities are immediately available; manufacturer advises patients should be closely monitored for signs of hypersensitivity during treatment and for an hour after administration. In the event of a hypersensitivity reaction, treatment should be stopped immediately and appropriate management initiated.
- **INTERACTIONS** → Appendix 1: pegaspargase
- **SIDE-EFFECTS**
  - **Common or very common** Abdominal pain · bone marrow depression · diarrhoea · hyperglycaemia · hypersensitivity · hypoxia · pain in extremity · pancreatitis (discontinue if suspected and do not restart if confirmed) · peripheral neuropathy · rash · seizure · stomatitis · syncope · thrombosis (discontinue) · vomiting
  - **Rare or very rare** Acute kidney injury · posterior reversible encephalopathy syndrome (PRES) · tremor
  - **Frequency not known** Confusion · diabetic ketoacidosis · drowsiness · hepatobiliary disorder · hyperammonaemia (monitor if symptoms present) · toxic epidermal necrolysis

  SIDE-EFFECTS, FURTHER INFORMATION There have been rare reports of cholestasis, icterus, hepatic cell necrosis and hepatic failure with fatal outcome in patients receiving pegaspargase.
- **CONCEPTION AND CONTRACEPTION** Manufacturer advises effective contraception in men and women of child-bearing potential during treatment and for at least 6 months after discontinuing treatment; pegaspargase may reduce effectiveness of oral contraceptives—additional precautions (e.g. barrier method) are required, see also *Pregnancy and reproductive function* in Cytotoxic drugs p. 551.
- **PREGNANCY** Manufacturer advises avoid unless essential. See also *Pregnancy and reproductive function* in Cytotoxic drugs p. 551.
- **BREAST FEEDING** Manufacturer advises avoid—no information available.
- **HEPATIC IMPAIRMENT** Manufacturer advises avoid in severe impairment.
- **MONITORING REQUIREMENTS**
  - Manufacturer advises trough serum asparaginase activity levels may be measured before the next administration of pegaspargase; consider switching to a different asparaginase preparation if target levels not reached—seek expert advice.
  - Manufacturer advises monitor plasma and urine glucose levels during treatment; monitor coagulation profile at baseline and periodically during and after treatment (particularly with concomitant use of other drugs that inhibit coagulation); monitor serum amylase.
- **DIRECTIONS FOR ADMINISTRATION** Manufacturer advises *for intramuscular injection*, volumes over 2 mL must be divided between more than one site.
- **HANDLING AND STORAGE** Manufacturer advises store in a refrigerator between 2–8°C.
- **PATIENT AND CARER ADVICE**
  Pancreatitis Manufacturer advises patients and carers should be told how to recognise signs and symptoms of pancreatitis and advised to seek medical attention if symptoms such as persistent, severe abdominal pain develop.
  Driving and skilled tasks Manufacturer advises patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of confusion and somnolence.
- **NATIONAL FUNDING/ACCESS DECISIONS**
  NICE decisions
  - **Pegaspargase for treating acute lymphoblastic leukaemia (September 2016)** NICE TA408
    Pegaspargase, as part of antineoplastic combination therapy, is recommended as an option for treating acute lymphoblastic leukaemia only in patients with untreated newly diagnosed disease.
    Patients whose treatment was started within the NHS before this guidance was published may continue treatment until they and their clinician consider it appropriate to stop.
    www.nice.org.uk/guidance/ta408

  Scottish Medicines Consortium (SMC) decisions
  The *Scottish Medicines Consortium* has advised (October 2016) that pegaspargase (*Oncaspar*®) is accepted for use within NHS Scotland as a component of antineoplastic combination therapy in acute lymphoblastic leukaemia.