**WARNINGS AND PRECAUTIONS**

- **Adrenal Crisis in the Setting of Shock or Severe Trauma**

  In patients taking LYSODREN, adrenal crisis occurs in the setting of shock or severe trauma and response to shock is impaired. Administer intravenous hydrocortisone, monitor for escalating signs of shock and discontinue LYSODREN until recovery. (2.3, 5.1)

- **Drug Interactions**

  7.1 CYP3A4 Substrates

  Mitotane is a strong inducer of cytochrome P450 3A4 (CYP3A4). Monitor patients for a change in dosage requirements for the concomitant drug when administering LYSODREN to patients receiving drugs that are substrates of CYP3A4.

- **Warfarin**

  When administering coumarin-type anticoagulants to patients receiving LYSODREN, monitor coagulation tests and adjust the anticoagulant dose as needed.

**USE IN SPECIFIC POPULATIONS**

- **Drug Interactions**

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- **Warfarin**

  When administering coumarin-type anticoagulants to patients receiving LYSODREN, monitor coagulation tests and adjust the anticoagulant dose as needed.
LYSODREN (mitotane) is an oral adrenal cytotoxic agent. The chemical name is: (±)-1,1-dichloro-2-(o-chlorophenyl)-2-(p-chlorophenyl) ethane (also known as 1,1-DDD). The chemical structure is:

Mitotane is a white granular solid composed of clear colorless crystals. It is tasteless and has a slight pleasant aromatic odor. It is soluble in ethanol and has a molecular weight of 320.05.

Inactive ingredients in LYSODREN are: microcrystalline cellulose, polyethylene glycol 3350, silicon dioxide, and starch.

CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Mitotane is an adrenal cytotoxic agent with an unknown mechanism of action. Mitotane modifies the peripheral metabolism of steroids and directly suppresses the adrenal cortex. A reduction in 17-hydroxycorticosteroids in the absence of decreased corticosteroid concentrations and increased formation of 6-β-hydroxycortisol have been reported.

12.2 Pharmacodynamics
The pharmacodynamics of mitotane are unknown.

12.3 Pharmacokinetics
Absorption
Following oral administration of LYSODREN, 40% of the dose is absorbed.

Distribution
Mitotane is found in most tissues of the body; however, fat is the primary site of distribution.

Elimination
Following discontinuation of mitotane, the plasma terminal half-life ranges from 18 to 159 days (median 53 days).

Metabolism
Mitotane is converted to a water-soluble metabolite.

Excretion
No unchanged mitotane is found in urine or bile. Approximately 10% of the administered dose is recovered in the urine as a water-soluble metabolite. A variable amount of metabolite (15%-17%) is excreted in the bile.

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
The carcinogenicity and mutagenicity of mitotane are unknown.

REFERENCES
1. 1. OSHA. http://www.osha.gov/SLTC/hazardousdrugs/index.html

HOW SUPPLIED/STORAGE AND HANDLING

LYSODREN tablets are supplied as 500 mg white, round, biconvex, scored tablets, bisected on one side and imprinted with “BL” over “L1” on the other side.

100 tablets per bottle: NDC 76336-3080-60

Store bottles at 25°C (77°F); excursions permitted between 15°C and 30°C (59°F-86°F).

Mitotane is a cytotoxic drug. Follow applicable special handling and disposal procedures [see References (15)].