BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.21.163

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	October 2, 2020
Subject:	Lysodren	**Page:**	1 of 4

Last Review Date: June 13, 2024

Lysodren

Description

Lysodren (mitotane)

Background
Lysodren (mitotane) is an adrenal cytotoxic agent with an unknown mechanism of action. Lysodren modifies the peripheral metabolism of steroids and directly suppresses the adrenal cortex. This leads to a reduction in 17-hydroxycorticosteroids in the absence of decreased corticosteroid concentrations and increased formation of 6-β-hydroxycortisol (1).

Regulatory Status
FDA-approved indication: Lysodren is an adrenal cytotoxic agent indicated for the treatment of inoperable, functional or nonfunctional, adrenocortical carcinoma (ACC) (1).

Lysodren dose should be increased incrementally to achieve a blood concentration of 14 to 20 mg/L, or as tolerated (1).

Lysodren has a boxed warning regarding adrenal crisis in the setting of shock, severe trauma, or infection. Patients taking Lysodren are at increased risk for developing adrenal crisis in the setting of shock, severe trauma, or infection that may lead to death. IF shock, severe trauma, or infection occurs or develops, temporarily discontinue Lysodren and administer exogenous steroids (1).

Lysodren also has warnings regarding CNS toxicity and adrenal insufficiency. Mitotane plasma concentrations exceeding 20 mcg/mL are associated with a greater incidence of CNS toxicity.

Free cortisol and corticotropin (ACTH) levels should be measured to achieve optimal steroid replacement (1).

Lysodren can cause fetal harm when administered to a pregnant woman. Pregnant women should be advised of the potential risk to a fetus. Females of reproductive potential should be advised to use effective contraception during treatment with Lysodren and after discontinuation of treatment for as long as mitotane plasma levels are detectable (1).

The safety and effectiveness of Lysodren in pediatric patients have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Lysodren may be considered **medically necessary** if the conditions indicated below are met.

Lysodren may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Adrenocortical carcinoma (ACC)

AND ALL of the following:

a. The tumor is inoperable
b. Prescriber agrees to monitor the patient for signs and symptoms of adrenal crisis in the setting of shock, severe trauma, or infection
c. Prescriber agrees to monitor for CNS toxicity
d. Prescriber agrees to monitor free cortisol and corticotropin (ACTH) levels
e. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Lysodren and after

discontinuation of treatment for as long as mitotane plasma levels are detectable

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Adrenocortical carcinoma (ACC)

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor the patient for signs and symptoms of adrenal crisis in the setting of shock, severe trauma, or infection
c. Prescriber agrees to monitor for CNS toxicity
d. Prescriber agrees to monitor free cortisol and corticotropin (ACTH) levels
e. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Lysodren and after discontinuation of treatment for as long as mitotane plasma levels are detectable

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary
Lysodren (mitotane) is an adrenal cytotoxic agent with an unknown mechanism of action indicated for the treatment of inoperable, functional or nonfunctional, adrenocortical carcinoma (ACC). Lysodren modifies the peripheral metabolism of steroids and directly suppresses the adrenal cortex. This leads to a reduction in 17-hydroxycorticosteroids in the absence of decreased corticosteroid concentrations and increased formation of 6-β-hydroxycortisol (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Lysodren while maintaining optimal therapeutic outcomes.

References
1. Lysodren [package insert]. Farmingdale, NJ: Direct Success Inc.; January 2024.
2. NCCN Drugs & Biologics Compendium® Mitotane 2024. National Comprehensive Cancer Network, Inc. Accessed on April 11, 2024.

Policy History

Date	Action
October 2020	Addition to PA
December 2020	Annual review
June 2021	Annual review and reference update
June 2022	Annual review and reference update
June 2023	Annual review and reference update
June 2024	Annual editorial review and reference update. Adjusted diagnosis to andrenocortical carcinoma (ACC) and also updated boxed warning to include adrenal crisis during infection

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.