

Drug Policy

Policy: Impacted Drugs:	Gonadotropin-Releasing Hormone Agonists – Injectable Long-Acting Products Lupaneta Pack (leuprolide acetate for IM depot suspension; norethindrone acetate oral tablets co-packaged) Lupron Depot (leuprolide acetate IM for depot suspension)	Annual Review Date: 01/18/2024 Last Revised Date: 01/18/2024
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OVERVIEW

Lupaneta Pack is indicated for initial management of the painful symptoms of **endometriosis** and for management of recurrence of symptoms.^{1,2}

Lupron Depot (3.75 mg intramuscular (IM) injection every month, 11.25 mg IM injection every 3 months) is indicated for the following conditions:^{3,4}

- Preoperative hematologic improvement of women with **anemia caused by uterine leiomyomata** (fibroids) for whom 3 months of hormonal suppression is deemed necessary. (Lupron Depot in combination with iron therapy).
- **Endometriosis**, including pain relief and reduction of endometriotic lesions (Lupron Depot monotherapy).
- **Endometriosis**, initial management of the painful symptoms of endometriosis and management of recurrence of symptoms (Lupron Depot in combination with norethindrone acetate 5 mg daily).

Lupron Depot (7.5 mg IM injection every month, 22.5 mg IM injection every 3 months, 30 mg IM injection every 4 months, and 45 mg IM injection every 6 months) is indicated for the **palliative treatment of advanced prostate cancer**.⁵

Duration of Treatment:

- Lupaneta Pack: Initial treatment course is limited to 6 months; a single retreatment course of up to 6 months is allowed. Total duration of treatment is limited to 12 months.^{1,2}
- Lupron Depot 3.75 mg and 11.25 mg:^{3,4}
 - Endometriosis: For the first 6 months of treatment, Lupron Depot may be used as monotherapy or in combination with norethindrone acetate. If retreatment is needed, Lupron Depot must be used in combination with norethindrone acetate (for 6 months). Total duration of treatment is limited to 12 months.
 - Uterine leiomyomata (fibroids): Recommended duration of treatment is up to 3 months.
- Lupron Depot 7.5 mg, 22.5 mg, 30 mg, and 45 mg: Labeling does not specify a treatment duration.

In addition to the approved indications, GnRH agonists such as leuprolide long-acting, have been used for other conditions and various guidelines (e.g., guidelines from the National Comprehensive Cancer Center [NCCN]) discuss its use.

POLICY STATEMENT

This policy involves the use of Lupaneta Pack and Lupron-Depot. Prior authorization is recommended for pharmacy benefit coverage of Lupaneta Pack and Lupron-Depot. Approval is recommended for those who meet the conditions of coverage

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in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Lupaneta Pack and Lupron-Depot as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Lupaneta Pack and Lupron-Depot be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lupaneta Pack and Lupron-Depot is recommended in those who meet the following criteria:

1. **Prostate Cancer**

Criteria. Approve Lupron Depot 7.5 mg, 22.5 mg, 30 mg, or 45 mg for 1 year if prescribed by or in consultation with an oncologist AND the patient has tried Eligard.

2. **Endometriosis**

Criteria. Approve Lupron Depot (3.75 mg or 11.25 mg) or Lupaneta Pack for 1 year if the patient has tried one of the following (A, B, or C):

- A) A contraceptive (e.g., combination oral contraceptives, levonorgestrel-releasing intrauterine systems [e.g., Mirena®, Liletta®]), OR
- B) An oral progesterone (e.g., norethindrone tablets), OR
- C) A depo-medroxyprogesterone injection, unless contraindicated.

NOTE: An exception to the requirement for a trial of the above therapies can be made if the patient has previously used a gonadotropin-releasing hormone [GnRH] agonist (e.g., Lupron-Depot) or antagonist (e.g., Orilissa).

3. **Uterine Leiomyomata (fibroids)**

Criteria. Approve Lupron Depot 3.75 mg or 11.25 mg for 3 months.

NOTE: Response to therapy is required for continuation of therapy.

Initial Approval/ Extended Approval.

See specific approval duration listed under each approved use.

OTHER USES WITH SUPPORTIVE EVIDENCE

4. **Gender Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male [FTM] or Male-To-Female [MTF])**

Criteria. Approve Lupron Depot for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients.

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NOTE: Response to therapy is required for continuation of therapy.

5. Ovarian Cancer (Lupron Depot)

Criteria. Approve Lupron Depot 3.75 mg, 7.5 mg, 11.25 mg, or 22.5 mg for 1 year if prescribed by or in consultation with an oncologist.

6. Breast Cancer

Criteria. Approve Lupron Depot 3.75 mg or 11.25 mg for 1 year if prescribed by or in consultation with a hematologist or oncologist.

7. Preserve Ovarian Function/Fertility in Patients undergoing Chemotherapy

Criteria. Approve Lupron Depot 3.75 mg or 11.25 mg for 1 year if prescribed by or in consultation with an oncologist.

8. Prophylaxis or Treatment of Uterine Bleeding or Menstrual Suppression in Patients with Hematologic Malignancy, or, Undergoing Cancer Treatment, or Prior to Bone Marrow/Stem Cell Transplantation (BMT/SCT)

Criteria. Approve Lupron Depot 3.75 mg or 11.25 mg for 1 year if prescribed by or in consultation with a hematologist or oncologist.

9. Abnormal Uterine Bleeding

Criteria. Approve Lupron Depot 3.75 mg or 11.25 mg for up to 3 months of therapy.

10. Head and Neck Cancer – Salivary Gland Tumors

Criteria. Approve Lupron Depot 3.75 mg, 7.5 mg, 11.25mg, or 22.5 mg for 1 year if the patient meets the following criteria (A, B, and C):

- A) Patient has recurrent, unresectable, or metastatic disease; AND
- B) Patient has androgen receptor (AR)-positive disease; AND
- C) The medication is prescribed by or in consultation with an oncologist.

11. Patients with another indication that is not listed but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation

Criteria. Prescriber will provide specific diagnosis for documentation. Approve.

Initial Approval/ Extended Approval.

See specific approval duration listed under each approved use.

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CONDITIONS NOT RECOMMENDED FOR APPROVAL

Lupaneta Pack and Lupron-Depot have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

- 1. Hirsutism.** The Endocrine Society guidelines (2018) on the treatment of hirsutism in premenopausal women suggest against using GnRH agonists except in women with severe forms of hyperandrogenemia, such as ovarian hyperthecosis, who have had a suboptimal response to oral contraceptives and antiandrogens.²¹
- 2. Menstrual Migraine.** A review article notes that GnRH analogs are effective in eliminating menstrual migraines, but their use is limited due to the significant adverse effects of estrogen deficiency, including severe vasomotor symptoms, sleep disruption, and a marked reduction in bone density.^{22,23}
- 3. Premenstrual Syndrome (PMS).** On occasion, GnRH analogs are recommended as an aid in the diagnosis of PMS.²⁴ Use of GnRH analogs results in profound cycle suppression and elimination of PMS symptoms, but these agents should not be used routinely. GnRH analogs are recommended only as a third-line treatment or for the most refractory patients.
- 4. Polycystic Ovarian Syndrome (PCOS).** PCOS guidelines from the Endocrine Society (2013)²⁵ and review articles^{26,27} do not recommend this as a treatment modality.
- 5.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company.

Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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3. Lupron Depot® – 3.75 mg [prescribing information]. North Chicago, IL: AbbVie Inc.; February 2021.
4. Lupron Depot® –11.25 mg [prescribing information]. North Chicago, IL: AbbVie Inc.; March 2020.
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