Clinical Policy: Olaratumab (Lartruvo)

Reference Number: ERX.SPA.284
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Olaratumab (Lartruvo®) is a platelet-derived growth factor receptor alpha (PDGFR-α) blocking antibody.

FDA Approved Indication(s)*
Lartruvo is indicated, in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.

Limitation(s) of use: This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

***Eli Lilly and Co, manufacturer of Lartruvo, was issued a letter revoking the approval to manufacture and market Lartruvo (*see Appendix E*).**

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Lartruvo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Soft Tissue Sarcoma

1. Authorization is not permitted. Member may not initiate therapy with Lartruvo (*see Appendix E*). If member is currently using Lartruvo, proceed to section II. A. Soft Tissue Sarcoma for continued therapy criteria.

Approval duration: Not applicable

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Soft Tissue Sarcoma (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Lartruvo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member has not had disease progression on Lartruvo;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 15 mg/kg on Days 1 and 8 of each 21-day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
PDGFR-α: platelet-derived growth factor receptor alpha
STS: soft tissue sarcoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
doxorubicin HCL (Adriamycin®)	Labeled dosing regimen for metastatic STS: • As a single agent: 60 to 75 mg/m^2 IV every 21 days. • In combination with other chemotherapy drugs: 40 to 75 mg/m^2 IV every 21 to 28 days. • Consider use of the lower doxorubicin dose in the recommended dose range or longer intervals between cycles for heavily pretreated patients, elderly patients, or obese patients. • Cumulative doses above 550 mg/m^2 are associated with an increased risk of cardiomyopathy.	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Black Box Warnings
None reported

Appendix D: STS Subtypes
- Sarcomas are divided into STS and sarcomas of bone.
- More than 50 STS histologic subtypes have been identified. Common subtypes include undifferentiated sarcoma, gastrointestinal stromal tumor, liposarcoma, and leiomyosarcoma.
- The most common anatomic STS locations are extremities, trunk, visceral, retroperitoneum, and head and neck. Rhabdomyosarcoma is the most common STS of children and adolescents and is less common in adults.

Appendix E: ANNOUNCE Trial: NCCN and FDA update
- NCCN no longer recommends Lartruvo in combination with doxorubicin as a treatment option for:
  - Soft tissue sarcoma subtypes with non-specific histologies (soft tissue sarcoma [version 2.2019]). The following language has been deleted from the guideline: For use in STS histologies for which an anthracycline-containing regimen is appropriate.
  - Uterine sarcoma (uterine neoplasms [version 3.2019])

- January 18, 2019: Eli Lilly reported in a press release that the confirmatory study required as a condition of Lartruvo's accelerated approval, entitled "Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of Doxorubicin Plus Olaratumab Versus Doxorubicin Plus Placebo in Patients With Advanced or Metastatic Soft Tissue Sarcoma" (ANNOUNCE trial), "did not meet the primary endpoints of overall survival in the full study population or in the leiomyosarcoma subpopulation."
- January 24th, 2019 updated: In light of this information, the FDA recommends that patients who are currently receiving Lartruvo should consult with their healthcare provider about whether to remain on the treatment. The FDA also recommends that Lartruvo should not be initiated in new patients outside of an investigational study.
- September 27, 2019: Eli Lilly requested withdrawal (revocation), in writing, of the BLA for Lartruvo (BLA 761038) because the ANNOUNCE trial failed to demonstrate improvement in overall survival for olaratumab in combination with doxorubicin compared to doxorubicin alone. In that letter, Eli Lilly waived its opportunity for a hearing.
- February 25, 2020: the FDA issued a letter to Eli Lilly revoking the approval to manufacture and market Lartruvo.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
STS	15 mg/kg IV over 60 minutes on Days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity. For first 8 cycles, Lartruvo is administered with doxorubicin. Refer to doxorubicin prescribing information for dosing/dose modifications.	15 mg/kg per infusion

VI. Product Availability

Single-dose vial: 500 mg/50 mL, 190 mg/19 mL

VII. References

1. Lartruvo Prescribing Information. Indianapolis, IN: Eli Lilly and Company; August 2018. Available at http://pi.lilly.com/us/lartruvo-uspi.pdf. Accessed June 30, 2021.
2. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2021. Available at: http://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed June 30, 2021.
3. National Comprehensive Cancer Network. Uterine Neoplasms Version 3.2021. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed June 30, 2021.
4. Doxorubicin Prescribing Information. New York, NY: Pfizer, Inc. May 2020. Available at: http://labeling.pfizer.com/showlabeling.aspx?id=530. Accessed June 30, 2021.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/.
6. Tap WD, Jones RL, Van Tine BA, et al. Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial [published correction appears in Lancet. 2016 Jul 30;388(10043):464]. Lancet. 2016;388(10043):488-497.
7. Eli Lilly and Co.; Announcement of the Revocation of the Biologics License for Lartruvo. July 2020. Available at: https://www.federalregister.gov/documents/2020/07/17/2020-15516/eli-lilly-and-co-announcement-of-the-revocation-of-the-biologics-license-for-lartruvo. Accessed October 22, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	08.07.18	11.18
4Q 2019 annual review: removed uterine sarcoma from criteria since NCCN no longer recommends Lartruvo + doxorubicin for that use; updated Appendix D to state NCCN guidelines' removal of doxorubicin and olaratumab as a combination therapy for non-specific STS and uterine sarcoma; references reviewed and updated.	08.09.19	11.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.17.20	11.20
Removed initial approval criteria for soft tissue sarcoma; added criteria to continuation approval for soft tissue sarcoma requiring patient has not had disease progression on Lartruvo; added Appendix E: FDA update due to ANNOUNCE trial results; references reviewed and updated.	11.10.20	02.21
4Q 2021 annual review: no significant changes; references reviewed and updated.	06.30.21	11.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.