Clinical Policy: Olaratumab (Lartruvo)

Reference Number: CP.PHAR.326
Effective Date: 03.01.17
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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 was 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 was approved under accelerated approval. Continued approval for this indication was contingent upon verification and description of clinical benefit in the confirmatory trial.

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***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.

It is the policy of health plans affiliated with Centene Corporation® that Lartruvo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

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

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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. Patient 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, 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 for all relevant lines of business 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/m2 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.
- On 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, and 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 July 29, 2022.
2. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2022. Available at: http://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed July 29, 2022.
3. National Comprehensive Cancer Network. Uterine Neoplasms Version 1.2022. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed July 29, 2022.
4. Doxorubicin Prescribing Information. New York, NY: Pfizer, Inc. May 2020. Available at: http://labeling.pfizer.com/showlabeling.aspx?id=530. Accessed July 29, 2022.

5. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; 2022. Available at: http://www.clinicalkeys.com/pharmacology.
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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9285	Injection, olaratumab, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: no significant changes; NCCN and FDA-approved uses summarized for improved clarity; specialist involvement in care and continuation of care added; references reviewed and updated.	08.07.18	11.18
4Q 2019 annual review: removed uterine sarcoma from criteria; updated Appendix D to state NCCN guidelines' removal of doxorubicin and olaratumab as a combination therapy for STS and uterine sarcoma; references reviewed and updated.	08.09.19	11.19
4Q 2020 annual review: modified HIM-Medical Benefit to HIM line of business; no significant changes; references reviewed and updated.	08.17.20	11.20
Added Commercial line of business; 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 to HIM.PHAR.21 revised to HIM.PA.154; 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
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.29.22	11.22

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.