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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	May 21, 2021
Subject:	Zynlonta	**Page:**	1 of 5

Last Review Date: March 8, 2024

Zynlonta

Description

Zynlonta (loncastuximab tesirine-lpyl)

Background
Zynlonta (loncastuximab tesirine-lpyl) is an antibody-drug conjugate (ADC) targeting CD19. The monoclonal IgG1 kappa antibody component binds to human CD19, a transmembrane protein expressed on the surface of cells of B-lineage origin. The small molecule component is SG3199, a PBD dimer and alkylating agent. Upon binding to CD19, Zynlonta is internalized followed by release of SG3199 via proteolytic cleavage. The released SG3199 binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks, subsequently inducing cell death (1).

Regulatory Status
FDA-approved indication: Zynlonta is a CD19-directed antibody and alkylating agent conjugate indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma (1).

Unless contraindicated, dexamethasone should be administered at 4 mg orally or intravenously twice daily for 3 days beginning the day before administering Zynlonta. If dexamethasone administration does not begin the day before Zynlonta, dexamethasone should begin at least 2 hours prior to administration of Zynlonta (1).

Serious effusion and edema can occur in patients treated with Zynlonta. Patients should be monitored for new or worsening edema or effusions (1).

Zynlonta can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. Complete blood counts (CBC) should be monitored throughout treatment. Prophylactic granulocyte colony-stimulating factor administration may be considered as applicable (1).

Fatal and serious infections, including opportunistic infections, occurred in patients treated with Zynlonta. Patients should be monitored for signs and symptoms of infection (1).

Zynlonta may cause embryo-fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to use effective contraception during treatment with Zynlonta and for 9 months after the last dose. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Zynlonta and for 6 months after the last dose (1).

The safety and effectiveness of Zynlonta in pediatric patients less than 18 years of age have not been established (1).

Related policies
Monjuvi

Policy

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

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

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

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Relapsed or refractory large B-cell lymphoma, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma
    a. Patient has previously received two or more lines of systemic therapy

AND ALL of the following:

a. Patient will be given dexamethasone before Zynlonta infusion **OR** the patient has a contraindication to dexamethasone
b. Prescriber agrees to monitor complete blood counts (CBC) for myelosuppression
c. Prescriber agrees to monitor the patient for infections
d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zynlonta and for 9 months after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zynlonta and for 6 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Relapsed or refractory large B-cell lymphoma, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma

AND ALL of the following:

a. Patient will be given dexamethasone before Zynlonta infusion **OR** the patient has a contraindication to dexamethasone
b. Prescriber agrees to monitor complete blood counts (CBC) for myelosuppression

c. Prescriber agrees to monitor the patient for infections
d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zynlonta and for 9 months after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zynlonta and for 6 months after the last dose

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Zynlonta (loncastuximab tesirine-lpyl) is an antibody-drug conjugate (ADC) targeting CD19. The monoclonal IgG1 kappa antibody component binds to human CD19, a transmembrane protein expressed on the surface of cells of B-lineage origin. The small molecule component is SG3199, a PBD dimer and alkylating agent. Upon binding to CD19, Zynlonta is internalized followed by release of SG3199 via proteolytic cleavage. The released SG3199 binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks, subsequently inducing cell death. The safety and effectiveness of Zynlonta in pediatric patients less than 18 years of age have not been established (1).

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

References

1. Zynlonta [package insert]. Murray Hill, NJ: ADC Therapeutics America; October 2022.

2. NCCN Drugs & Biologics Compendium® Loncastuximab tesirine-lpyl 2024. National Comprehensive Cancer Network, Inc. Accessed on January 22, 2024.

Policy History

Date	Action
May 2021	Addition to PA
September 2021	Annual review and reference update
December 2022	Annual review and reference update
March 2023	Annual review and reference update
September 2023	Annual review and reference update
December 2023	Annual review and reference update
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.