

POLICY: Oncology – Adcetris® (brentuximab injection for intravenous use – Seattle Genetics, Inc.)

APPROVAL DATE: 09/25/2019

OVERVIEW

Adcetris is a CD30-directed antibody, produced in Chinese hamster ovary cells, conjugated with monomethyl auristatin E (MMAE).¹ CD30 is expressed on systemic anaplastic large cell lymphoma cells and on Hodgkin Reed-Sternberg cells in classical Hodgkin lymphoma and MMAE is a microtubule-disrupting agent. The anticancer activity is due to the binding of Adcetris to the CD30 receptor, followed by internalization and release of MMAE. MMAE then binds to tubulin disrupting the microtubule network leading to cell cycle arrest and apoptosis.

Adcetris is FDA-approved for the treatment of adults with:

- Previously untreated Stage III or IV classical Hodgkin lymphoma, in combination with doxorubicin, vinblastine, and dacarbazine.
- Classical Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation consolidation.
- Classical Hodgkin lymphoma after failure of autologous hematopoietic stem cell transplantation or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not autologous hematopoietic stem cell transplantation candidates.
- Previously untreated systemic anaplastic large cell lymphoma or other CD30-expressing peripheral T-cell lymphomas, including angioimmunoblastic T-cell lymphoma and peripheral T-cell lymphomas not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone.
- Systemic anaplastic large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen.
- Primary cutaneous anaplastic large cell lymphoma or CD30-expressing mycosis fungoides who have received prior systemic therapy.¹

Guidelines

The National Comprehensive Cancer Network (NCCN) Hodgkin Lymphoma Clinical Practice Guidelines (version 2.2019 – July 15, 2019) recommend Adcetris for the treatment of classical Hodgkin Lymphoma in combination with chemotherapy, as second-line or subsequent therapy for relapsed or refractory disease, as maintenance therapy following high-dose therapy and autologous stem cell rescue for relapsed or refractory disease, or as palliative therapy.^{2,3}

The NCCN T-Cell Lymphomas Clinical Practice Guidelines (version 2.2019 – December 17, 2018) recommend Adcetris as a preferred first-line therapy in combination with CHP (cyclophosphamide, doxorubicin, prednisone) for the treatment of CD30+ anaplastic large cell lymphoma (ALCL), CD30+ peripheral T-cell lymphoma, CD30+ angioimmunoblastic T-cell lymphoma, CD30+ enteropathy-associated T-cell lymphoma, CD30+ monomorphic epitheliotropic intestinal T-cell lymphoma, CD30+ nodal peripheral T-cell lymphoma with TFH phenotype, CD30+ hepatosplenic gamma-delta T-cell lymphoma, or CD30+ follicular T-cell lymphoma.^{2,4} As a single agent for subsequent therapy for relapsed/refractory ALCL, CD30+ peripheral T-cell lymphoma, CD30+ hepatosplenic gamma-delta T-cell lymphoma, CD30+ extranodal NK/T-cell lymphoma – nasal type, or CD30+ angioimmunoblastic T-cell lymphoma. As a component of CHP for the treatment of CD30+ adult T-cell leukemia/lymphoma. As a single agent or in combination with CHP for the adjuvant treatment of CD30+ breast implant-associated ALCL.

The NCCN Primary Cutaneous Lymphomas Clinical Practices Guidelines (version 2.2019 – December 17, 2018) recommend Adcetris for the systemic therapy of CD30+: mycosis fungoides/Sezary syndrome, primary cutaneous anaplastic large cell lymphoma, and lymphomatoid papulosis.^{2,5}

The NCCN B-Cell Lymphomas Clinical Practice Guidelines (version 4.2019 – June 18,2019) recommend Adcetris for the second-line or subsequent treatment of histologic transformation of follicular lymphoma to CD30+ diffuse large B-cell lymphoma (DLBCL), histologic transformation of marginal zone lymphoma to CD30+ DLBCL, CD30+ DLBCL, CD30+ high-grade B-cell lymphoma, CD30+ AIDS-related B-cell lymphoma, and CD30+ post-transplant lymphoproliferative disorders.^{2,6}

Other Uses With Supportive Evidence

A phase II study assessed the efficacy of Adcetris in patients with relapsed/refractory B-cell CD30+ non-Hodgkin lymphoma.⁷ Patients received Adcetris 1.8 mg/kg intravenously every 3 weeks until disease progression, unacceptable adverse events, or study closure. The overall response rate in patients with diffuse large B-cell lymphoma was 44% (n = 21/48) and 26% (n = 5/19) in patients with other B-cell lymphomas.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Adcetris. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Adcetris as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Adcetris to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Adcetris is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Hodgkin Lymphoma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
 - A) The patient is \geq 18 years of age; AND
 - B) The patient has classical Hodgkin lymphoma; AND
 - C) Adcetris is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens (A and B):

- A) Each individual dose must not exceed 1.8 mg/kg or a maximum of 180 mg administered by intravenous infusion; AND
- B) The dose is administered no more frequently than once every 2 weeks.¹

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2. **T-Cell Lymphoma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
 - A) The patient is \geq 18 years of age; AND
 - B) Adcetris is used for CD30+ T-cell lymphoma.
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(Note: Examples include CD30+ systemic anaplastic large cell lymphoma, CD30+ angioimmunoblastic T-cell lymphoma, CD30+ peripheral T-cell lymphoma not otherwise specified, CD30+ mycosis fungoides/Sezary syndrome, CD30+ primary cutaneous anaplastic large cell lymphoma, CD30+ lymphomatoid papulosis, CD30+ breast implant-associated anaplastic large cell lymphoma, CD30+ T-cell leukemia/lymphoma);^{1,2,4,5} AND

C) Adcetris is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens (A and B):

A) Each individual dose must not exceed 1.8 mg/kg or a maximum of 180 mg administered by intravenous infusion; AND

B) The dose is administered no more frequently than once every 3 weeks.¹

Other Uses with Supportive Evidence

3. B-Cell Lymphoma. Approve for 1 year if the patient meets the following criteria (A, B, and C):

A) The patient is \geq 18 years of age; AND

B) Adcetris is used as second-line or subsequent therapy for CD30+ B-cell lymphoma.

(Note: Examples include CD30+ diffuse large B-cell lymphoma, CD30+ post-transplant lymphoproliferative disorders, CD30+ AIDS-related B-cell lymphoma, CD30+ high-grade B-cell lymphoma);^{2,6} AND

C) Adcetris is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens (A and B):

A) Each individual dose must not exceed 1.8 mg/kg or a maximum of 180 mg administered by intravenous infusion; AND

B) The dose is administered no more frequently than once every 3 weeks.^{1,7}

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Adcetris has not been shown to be effective, or there are limited or preliminary data or safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Authorization Criteria (FDA-approved indications and Other Uses with Supportive Evidence). Criteria will be updated as new published data are available.

REFERENCES

1. Adcetris® injection [prescribing information]. Bothell, WA: Seattle Genetics, Inc.; November 2018.
2. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 16, 2019. Search term: brentuximab.
3. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – July 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 16, 2019.
4. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 2.2019 – December 17, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 16, 2019.
5. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (Version 2.2019 – December 17, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 16, 2019.
6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 4.2019 – June 18, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 16, 2019.
7. Jacobsen ED, Sharman JP, Oki Y, et al. Brentuximab vedotin demonstrates objective responses in a phase 2 study of relapsed/refractory DLBCL with variable CD30 expression. *Blood*. 2015;125:1394-1402.

HISTORY

| Type of Revision | Summary of Changes | Approval Date |
|-------------------------|--|----------------------|
| New policy | -- | 01/03/2019 |
| revisions | Updated the Guideline section with new T-cell lymphoma guidelines, criteria were not changed. Removed the Duration of Therapy and Note to Nurse Clinician sections. | NA |
| Early Annual | Hodgkin lymphoma – removed criteria for use as primary treatment, in relapsed disease, for maintenance therapy, and as palliative care. T-cell lymphoma – Added CD30+ lymphomatoid papulosis to the list of examples. | 09/25/2019 |