BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 7, 2013
Subject:	Adcetris	**Page:**	1 of 6

Last Review Date: March 12, 2021

Adcetris

Description

Adcetris (brentuximab vedotin)

Background
Adcetris (brentuximab vedotin) is a CD30-directed antibody-drug conjugate consisting of three components: a chimeric IgG1 antibody specific for human CD30, the microtubule-disrupting agent MMAE, and a protease-cleavable linker that covalently attaches MMAE to the antibody. Binding of MMAE to tubulin disrupts the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic death of the cells (1).

Regulatory Status
FDA-approved indication: Adcetris is a CD30-directed antibody-drug conjugate indicated for the treatment of patients with: (1)

1. Classical Hodgkin's lymphoma after failure of autologous hematopoietic stem cell transplant (auto-HSCT) or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
2. Classical HL at high risk of relapse or progression as post-auto-HSCT consolidation
3. Systemic anaplastic large cell lymphoma (sALCL) after failure of at least 1 prior multi-agent chemotherapy regimen
4. Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy
5. Previously untreated Stage III or IV classical Hodgkin's lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
6. Previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell

lymphoma and PTCL, not otherwise specified, in combination with cyclophosphamide, doxorubicin and prednisone

Adcetris has a boxed warning for progressive multifocal leukoencephalopathy. JC virus infection resulting in progressive multifocal leukoencephalopathy (PML) and death can occur in patients receiving Adcetris (1).

The use of Adcetris is associated with development of peripheral neuropathy and neutropenia, in which case a dose modification may be required. Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain or weakness. Complete blood counts should be monitored prior to each dose of Adcetris and more frequently for patients with Grade 3 or 4 neutropenia. Patients with rapidly proliferating tumor and high tumor burden may be at increased risk of tumor lysis syndrome (1).

Based on mechanism of action and findings in animals, Adcetris can cause fetal harm when administered to pregnant women. Female patients of reproductive potential should be advised of the potential risk to a fetus and to avoid pregnancy (1).

Safety and effectiveness of Adcetris in pediatric patients have not been established (1).

Related policies

Policy

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

Adcetris may be considered **medically necessary** in patients that are 18 years of age or older with Hodgkin lymphoma, systemic anaplastic large cell lymphoma (sALCL), primary cutaneous anaplastic large cell lymphoma (pcALCL), CD30 expressing mycosis fungoides (MF), or previously untreated systemic anaplastic large cell lymphomas (sALCL) or other CD30-expressing peripheral cell T cell lymphomas (PTCL); and if the conditions indicated below are met.

Adcetris may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have ONE of the following:

1. Classical Hodgkin's lymphoma

   AND ONE of the following:
   a. Failure of autologous hematopoietic stem cell transplant (auto-HSCT)
   b. Failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
   c. Patients at high risk of relapse or progression as post-auto-HSCT consolidation
   d. Previously untreated Stage III or IV **AND** used in combination with doxorubicin, vinblastine, and dacarbazine

2. Systemic anaplastic large cell lymphoma (sALCL)
   a. Failure at least one prior multi-agent chemotherapy regimen
   OR
   a. Previously untreated **AND** used in combination with cyclophosphamide, doxorubicin and prednisone

3. Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30 expressing mycosis fungoides (MF)
   a. Patient has received prior systemic therapy

4. CD-30 expressing peripheral T-cell lymphomas (PTCL) including angioimmunoblastic T-cell lymphoma and PTCL, not otherwise specified
   a. Previously untreated **AND** used in combination with cyclophosphamide, doxorubicin and prednisone

AND the following for **ALL** indications:
a. Prescriber agrees to monitor patient for the development of JC virus infection resulting in PML and will discontinue use if a diagnosis of PML is confirmed

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsed classical Hodgkin's lymphoma
2. Classical Hodgkin Lymphoma
    a. Patient has received **NO** more than 16 cycles of treatment
3. Relapsed systemic anaplastic large cell lymphoma (sALCL)
4. Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30 expressing mycosis fungoides (MF)
    a. Patient has received **NO** more than 16 cycles of treatment

AND following for **ALL** indications:

a. Prescriber agrees to monitor patient for the development of JC virus infection resulting in PML and will discontinue use if a diagnosis of PML is confirmed

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months for previously untreated stage 3 or 4 Classical Hodgkin's lymphoma and previously untreated systemic ALCL or other CD30- expressing PTCL

12 months for all other diagnoses

Prior – Approval *Renewal* Limits

Duration ***No renewal*** for previously untreated stage 3 or 4 Classical Hodgkin's lymphoma and previously untreated systemic ALCL or other CD30- expressing PTCL

Maximum of 16 cycles - Classical Hodgkin Lymphoma and Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30 expressing mycosis fungoides (MF)

12 months for all other diagnoses

Rationale

Summary

Adcetris (brentuximab vedotin) is FDA indicated for the treatment of patients with Hodgkin lymphoma after failure of autologous hematopoietic stem cell transplant (auto-HSCT) or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates. Adcetris is also indicated for patients with classical HL at high risk of relapse or progression as post-auto- HSCT consolidation or previously untreated Stage III or IV classical HL, in combination with chemotherapy. Adcetris is also indicated for the treatment of patients with systemic anaplastic large cell lymphoma (ALCL) or primary cutaneous anaplastic large cell lymphoma and CD30-expressing mycosis fungoides. The use of Adcetris is associated with development of peripheral neuropathy, neutropenia, tumor lysis syndrome, and progressive multifocal leukoencephalopathy (PML) (1).

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

References

1. Adcetris [package insert]. Bothell, WA: Seattle Genetics, Inc.; October 2019.

Policy History

Date	Action
April 2012	New Policy
March 2013	Annual editorial review and reference update
March 2014	Annual review and reference update
March 2015	Annual review and reference update
August 2015	Addition of classical HL at high risk of relapse or progression as post-auto-HSCT consolidation and the addition of age 65 and older patients
September 2015	Annual Review
June 2016	Annual editorial review and reference update Policy number change from 5.04.19 to 5.21.19

June 2017	Annual editorial review and reference update Addition of requirement: Prescriber agrees to monitor patient for the development of JC virus infection resulting in PML and will discontinue use if a diagnosis of PML is confirmed
December 2017	Addition of primary cutaneous anaplastic large cell lymphoma and CD30-expressing mycosis fungoides
March 2018	Annual review
May 2018	Addition of new indication: Previously untreated Stage III or IV classical HL, in combination with chemotherapy
June 2018	Annual review
November 2018	Addition of new indication : First line therapy of CD 30- expressing peripheral T cell lymphomas (PTCLs) to be used with cyclophosphamide, doxorubicin, and prednisone Change to Stage III or IV classical Hodgkin lymphoma from used in combination with chemotherapy to used in combination with doxorubicin, vinblastine, and dacarbazine
March 2019	Annual review
March 2021	Annual editorial review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.