ADCETRIS® (brentuximab vedotin)

DOSAGE AND ADMINISTRATION GUIDE

Select Important Safety Information

BOXED WARNING

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML): JC virus infection resulting in PML and death can occur in ADCETRIS-treated patients.

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Please see additional Important Safety Information here and full Prescribing Information, including BOXED WARNING at adcetrispro.com

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Approved indications for CD30-expressing lymphomas

ADCETRIS® (brentuximab vedotin) is indicated for the treatment of:

Previously untreated Stage III/IV cHL

- Adult patients with previously untreated Stage III/IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine.

Previously untreated high risk cHL

- Pediatric patients 2 years and older with previously untreated high risk cHL, in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide.

cHL post-auto-HSCT consolidation

- Adult patients with cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation.

Relapsed cHL

- Adult patients with cHL after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates.

Previously untreated sALCL or other CD30-expressing PTCL

- Adult patients with 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.

Relapsed sALCL

- Adult patients with sALCL after failure of at least one prior multi-agent chemotherapy regimen.

Relapsed pcALCL or CD30-expressing MF

- Adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy.

Select Important Safety Information

BOXED WARNING

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Important Safety Information

BOXED WARNING

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML): JC virus infection resulting in PML and death can occur in ADCETRIS-treated patients.

CONTRAINDICATION

Contraindicated with concomitant bleomycin due to pulmonary toxicity (e.g., interstitial infiltration and/or inflammation).

WARNINGS AND PRECAUTIONS

Peripheral neuropathy (PN): ADCETRIS causes PN that is predominantly sensory. Cases of motor PN have also been reported. ADCETRIS-induced PN is cumulative. Monitor for symptoms such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness. Patients experiencing new or worsening PN may require a delay, change in dose, or discontinuation of ADCETRIS.

Anaphylaxis and infusion reactions: Infusion-related reactions (IRR), including anaphylaxis, have occurred with ADCETRIS. Monitor patients during infusion. If an IRR occurs, interrupt the infusion and institute appropriate medical management. If anaphylaxis occurs, immediately and permanently discontinue the infusion and administer appropriate medical therapy. Premedicate patients with a prior IRR before subsequent infusions. Premedication may include acetaminophen, an antihistamine, and a corticosteroid.

Hematologic toxicities: Fatal and serious cases of febrile neutropenia have been reported with ADCETRIS. Prolonged (≥1 week) severe neutropenia and Grade 3 or 4 thrombocytopenia or anemia can occur with ADCETRIS.

Administer G-CSF primary prophylaxis beginning with Cycle 1 for adult patients who receive ADCETRIS in combination with chemotherapy for previously untreated Stage III/IV cHL or previously untreated PTCL, and pediatric patients who receive ADCETRIS in combination with chemotherapy for previously untreated high risk cHL.

Monitor complete blood counts prior to each ADCETRIS dose. Monitor more frequently for patients with Grade 3 or 4 neutropenia. Monitor patients for fever. If Grade 3 or 4 neutropenia develops, consider dose delays, reductions, discontinuation, or G-CSF prophylaxis with subsequent doses.

Serious infections and opportunistic infections: Infections such as pneumonia, bacteremia, and sepsis or septic shock (including fatal outcomes) have been reported in ADCETRIS-treated patients. Closely monitor patients during treatment for infections.

Tumor lysis syndrome: Patients with rapidly proliferating tumor and high tumor burden may be at increased risk. Monitor closely and take appropriate measures.

Increased toxicity in the presence of severe renal impairment: The frequency of ≥Grade 3 adverse reactions and deaths was greater in patients with severe renal impairment. Avoid use in patients with severe renal impairment.

Increased toxicity in the presence of moderate or severe hepatic impairment: The frequency of ≥Grade 3 adverse reactions and deaths was greater in patients with moderate or severe hepatic impairment. Avoid use in patients with moderate or severe hepatic impairment.

Hepatotoxicity: Fatal and serious cases have occurred in ADCETRIS-treated patients. Cases were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin, and occurred after the first ADCETRIS dose or rechallenge. Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may increase the risk. Monitor liver enzymes and bilirubin. Patients with new, worsening, or recurrent hepatotoxicity may require a delay, change in dose, or discontinuation of ADCETRIS.

PML: Fatal cases of JC virus infection resulting in PML have been reported in ADCETRIS-treated patients. First onset of symptoms occurred at various times from initiation of ADCETRIS, with some cases occurring within 3 months of initial exposure. In addition to ADCETRIS therapy, other possible contributory factors include prior therapies and underlying disease that may cause immunosuppression. Consider PML diagnosis in patients with new-onset signs and symptoms of central nervous system abnormalities. Hold ADCETRIS if PML is suspected and discontinue ADCETRIS if PML is confirmed.

Pulmonary toxicity: Fatal and serious events of noninfectious pulmonary toxicity, including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome, have been reported. Monitor patients for signs and symptoms, including cough and dyspnea. In the event of new or worsening pulmonary symptoms, hold ADCETRIS dosing during evaluation and until symptomatic improvement.

Serious dermatologic reactions: Fatal and serious cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with ADCETRIS. If SJS or TEN occurs, discontinue ADCETRIS and administer appropriate medical therapy.

Gastrointestinal (GI) complications: Fatal and serious cases of acute pancreatitis have been reported. Other fatal and serious GI complications include perforation, hemorrhage, erosion, ulcer, intestinal obstruction, enterocolitis, neutropenic colitis, and ileus. Lymphoma with preexisting GI involvement may increase the risk of perforation. In the event of new or worsening GI symptoms, including severe abdominal pain, perform a prompt diagnostic evaluation and treat appropriately.

Hyperglycemia: Serious cases, such as new-onset hyperglycemia, exacerbation of preexisting diabetes mellitus, and ketoacidosis (including fatal outcomes) have been reported with ADCETRIS. Hyperglycemia occurred more frequently in patients with high body mass index or diabetes. Monitor serum glucose and if hyperglycemia develops, administer anti-hyperglycemic medications as clinically indicated.

Embryo-fetal toxicity: Based on the mechanism of action and animal studies, ADCETRIS can cause fetal harm. Advise females of reproductive potential of this potential risk, to use effective contraception during ADCETRIS treatment and for 2 months after the last dose of ADCETRIS. Advise male patients with female partners of reproductive potential to use effective contraception during ADCETRIS treatment and for 4 months after the last dose of ADCETRIS.

ADVERSE REACTIONS

The most common adverse reactions (≥20% in any study) are peripheral neuropathy, fatigue, nausea, diarrhea, neutropenia, upper respiratory tract infection, pyrexia, constipation, vomiting, alopecia, decreased weight, abdominal pain, anemia, stomatitis, lymphopenia, mucositis, thrombocytopenia, and febrile neutropenia.

DRUG INTERACTIONS

Concomitant use of strong CYP3A4 inhibitors has the potential to affect the exposure to monomethyl auristatin E (MMAE). Closely monitor adverse reactions.

USE IN SPECIAL POPULATIONS

Lactation: Breastfeeding is not recommended during ADCETRIS treatment.

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ADCETRIS®
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FOR ADULTS

Previously untreated Stage III/IV cHL

Recommended dosage[1]

ADCETRIS 1.2 mg/kg up to a maximum of 120 mg*
in combination with doxorubicin, vinblastine, and dacarbazine

Intravenous infusion over 30 minutes

Every 2 weeks until a maximum of 12 doses, disease progression, or unacceptable toxicity

G-CSF primary prophylaxis beginning with Cycle 1

- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products[1]**

See next page for dosage modifications.

cHL = classical Hodgkin lymphoma.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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FOR ADULTS

Previously untreated Stage III/IV cHL

Dose modifications[1]

Renal impairment		• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use
Hepatic impairment		• **Mild (Child-Pugh A):** 0.9 mg/kg up to a maximum of 90 mg* every 2 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use
Neutropenia	Grade 3 or 4:	• Administer G-CSF prophylaxis in subsequent cycles for patients not receiving primary G-CSF
	Grade 2:	• **Reduce** dose to 0.9 mg/kg up to a maximum of 90 mg* every 2 weeks
Peripheral neuropathy	Grade 3:	• **Hold** ADCETRIS dosing until improvement to Grade 2 or lower • **Restart** at 0.9 mg/kg up to a maximum of 90 mg* every 2 weeks • **Consider modifying** the dose of other neurotoxic chemotherapy agents
	Grade 4:	• **Discontinue**

CrCL = creatinine clearance; G-CSF = granulocyte–colony stimulating factor.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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FOR ADULTS

Previously untreated Stage III/IV cHL

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (any grade)†: 91% A+AVD vs 89% ABVD • Febrile neutropenia (any grade): 19% A+AVD vs 8% ABVD

Peripheral neuropathy (PN)[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• Peripheral sensory neuropathy (any grade): 65% A+AVD vs 41% ABVD • Peripheral motor neuropathy (any grade): 11% A+AVD vs 4% ABVD

A+AVD = ADCETRIS + doxorubicin, vinblastine, dacarbazine;
ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine.

*Data from trial (ECHELON-1) in 1321 previously untreated patients with Stage III or IV cHL: 662 in the A+AVD arm and 659 in the ABVD arm.

†Derived from laboratory values and adverse reaction data; data are included for clinical relevance irrespective of rate between arms.

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FOR ADULTS

Previously untreated Stage III/IV cHL

Dose delays and discontinuations*[1]

- Adverse reactions that led to dose delays of one or more drugs in more than 5% of A+AVD-treated patients were neutropenia (21%) and febrile neutropenia (8%)
- Adverse reactions led to treatment discontinuation of one or more drugs in 13% of A+AVD-treated patients
  - 7% of patients treated with A+AVD discontinued due to peripheral neuropathy

*Data from phase 3 trial (ECHELON-1) in 1321 previously untreated patients with Stage III or IV cHL: 662 in the A+AVD arm and 659 in the ABVD arm.

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FOR PEDIATRIC PATIENTS 2 YEARS AND OLDER

Previously untreated high risk cHL

Recommended dosage[1]

ADCETRIS 1.8 mg/kg up to a maximum of 180 mg*
in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide

Intravenous infusion over 30 minutes

Every 3 weeks until a maximum of 5 doses

G-CSF primary prophylaxis beginning with Cycle 1

- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products[1]**

See next page for dosage modifications.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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Previously untreated high risk cHL

Dose modifications[1]

Renal impairment	• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use	
Hepatic impairment	• **Mild (Child-Pugh A):** 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use	
Neutropenia	Grade 3 or 4:	• **Reduce** dose to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks in patients who are unable to start a cycle >5 weeks after the start of the previous cycle (>2-week delay) due to neutropenia
Peripheral neuropathy†	Grade 2:	• **Reduce** dose of vincristine per prescribing information • **Continue** dosing with ADCETRIS • If neuropathy improves to Grade ≤1 by day 8 of next cycle, then resume vincristine at full dose
	Grade 3:	• **Discontinue** vincristine • **First occurrence: Hold** ADCETRIS dosing until improvement to ≤Grade 2 then restart at 1.2 mg/kg up to a maximum of 120 mg* • **Second occurrence: Hold** until improvement to ≤Grade 2 then restart at 0.8 mg/kg up to a maximum of 80 mg* • **Third occurrence: Discontinue** ADCETRIS
	Grade 4:	• **Discontinue** ADCETRIS and vincristine

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

†Peripheral neuropathy was assessed using the Balis scale.

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Previously untreated high risk cHL

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (Grade 3): 8% A+AVEPC vs 4.4% ABVE-PC; (Grade 4) 43% A+AVEPC vs 36% ABVE-PC • Febrile neutropenia (Grade 3): 28% A+AVEPC vs 31% ABVE-PC; (Grade 4) 3.4% A+AVEPC vs 1.7% ABVE-PC

Peripheral neuropathy (PN)†[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• Peripheral sensory neuropathy (any grade): 81% A+AVEPC • Peripheral motor neuropathy (any grade): 29% A+AVEPC

ABVE-PC = adriamycin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide; AVEPC = adriamycin, vincristine, etoposide, prednisone, cyclophosphamide.

*Data from open-label trial (AHOD1331) in 600 previously untreated patients with high-risk cHL: 300 in the A+AVEPC arm and 300 in the ABVE-PC arm.

†Peripheral neuropathy was assessed using the Balis scale.

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FOR ADULTS

cHL post-auto-HSCT consolidation

Recommended dosage[1]

ADCETRIS 1.8 mg/kg up to a maximum of 180 mg*

Intravenous infusion over 30 minutes

Every 3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity

- Initiate ADCETRIS treatment within 4-6 weeks post-auto-HSCT or upon recovery from auto-HSCT[1]
- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products**[1]

See next page for dosage modifications.

HSCT = hematopoietic stem cell transplantation.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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FOR ADULTS

cHL post-auto-HSCT consolidation

Dose modifications[1]

Renal impairment		• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use
Hepatic impairment		• **Mild (Child-Pugh A):** 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use
Neutropenia	Grade 3 or 4:	• **Hold** dosing until improvement to baseline or Grade 2 or lower • **Consider** G-CSF prophylaxis for subsequent cycles
	Recurrent Grade 4 despite G-CSF prophylaxis:	• **Consider** discontinuation or dose reduction to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks
Peripheral neuropathy	New or worsening Grade 2 or 3:	• **Hold** ADCETRIS dosing until improvement to baseline or Grade 1 • **Restart** at 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks
	Grade 4:	• **Discontinue**

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

cHL post-auto-HSCT consolidation

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (any grade)†: 78% ADCETRIS vs 34% placebo

Peripheral neuropathy (PN)[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• Peripheral sensory neuropathy (any grade): 56% ADCETRIS vs 16% placebo • Peripheral motor neuropathy (any grade): 23% ADCETRIS vs 2% placebo

*Data from trial (AETHERA) in 327 patients with cHL at high risk of relapse or disease progression post-auto-HSCT: 167 in the ADCETRIS arm and 160 in the placebo arm.

†Derived from laboratory values and adverse reaction data.

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FOR ADULTS

cHL post-auto-HSCT consolidation

Dose delays and discontinuations*[1]

- Adverse reactions that led to dose delays in more than 5% of ADCETRIS-treated patients were neutropenia (22%), peripheral sensory neuropathy (16%), upper respiratory tract infection (6%), and peripheral motor neuropathy (6%)
- Adverse reactions led to treatment discontinuation in 32% of ADCETRIS-treated patients
  - Adverse reactions that led to treatment discontinuation in 2 or more patients were peripheral sensory neuropathy (14%), peripheral motor neuropathy (7%), acute respiratory distress syndrome (1%), paresthesia (1%), and vomiting (1%)

*Data from phase 3 trial (AETHERA) in 327 patients with cHL at high risk of relapse or disease progression post-auto-HSCT: 167 in the ADCETRIS arm and 160 in the placebo arm.

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FOR ADULTS

Relapsed cHL

Recommended dosage[1]

ADCETRIS 1.8 mg/kg up to a maximum of 180 mg*

Intravenous infusion over 30 minutes

Every 3 weeks until disease progression or unacceptable toxicity

- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products[1]**

See next page for dosage modifications.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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ADCETRIS® brentuximab vedotin | injection 50 mg

Relapsed cHL

Dose modifications[1]

Renal impairment		• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use	
Hepatic impairment		• **Mild (Child-Pugh A):** 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use	
Neutropenia	Grade 3 or 4:	• **Hold** dosing until improvement to baseline or Grade 2 or lower • **Consider** G-CSF prophylaxis for subsequent cycles	
	Recurrent Grade 4 despite G-CSF prophylaxis:	• **Consider** discontinuation or dose reduction to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks	
Peripheral neuropathy	New or worsening Grade 2 or 3:	• **Hold** ADCETRIS dosing until improvement to baseline or Grade 1 • **Restart** at 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks	
	Grade 4:	• **Discontinue**	

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

Relapsed cHL

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (any grade)†: 54%

*Data from open-label, single-arm trial in 102 patients with cHL who relapsed after auto-HSCT and were treated with ADCETRIS.

†Derived from laboratory values and adverse reaction data.

Peripheral neuropathy (PN)[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• Peripheral sensory neuropathy (any grade): 52% ADCETRIS • Peripheral motor neuropathy (any grade): 16% ADCETRIS

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Relapsed cHL

Dose delays and discontinuations*[1]

- Adverse reactions that led to dose delays in more than 5% of ADCETRIS-treated patients were neutropenia (16%) and peripheral sensory neuropathy (13%)
- Adverse reactions led to treatment discontinuation in 20% of ADCETRIS-treated patients
  - Adverse reactions that led to treatment discontinuation in 2 or more patients were peripheral sensory neuropathy (6%) and peripheral motor neuropathy (3%)

*Data from phase 2, open-label, single-arm trial in 102 patients with cHL who relapsed after auto-HSCT and were treated with ADCETRIS.

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ADCETRIS® brentuximab vedotin | injection 50 mg

FOR ADULTS

Previously untreated sALCL or other CD30-expressing PTCL

Recommended dosage[1]

ADCETRIS 1.8 mg/kg up to a maximum of 180 mg*
in combination with cyclophosphamide, doxorubicin, and prednisone

Intravenous infusion over 30 minutes

Every 3 weeks with each cycle of chemotherapy for 6 to 8 doses

G-CSF primary prophylaxis beginning with Cycle 1

- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products[1]**

See next page for dosage modifications.

sALCL=systemic anaplastic large cell lymphoma.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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ADCETRIS® brentuximab vedotin | injection 50 mg

FOR ADULTS

Previously untreated sALCL or other CD30-expressing PTCL

Dose modifications[1]

Renal impairment		• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use
Hepatic impairment		• **Mild (Child-Pugh A):** 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use
Neutropenia	Grade 3 or 4:	• Administer G-CSF prophylaxis in subsequent cycles for patients not receiving primary G-CSF
Peripheral neuropathy	Sensory:	• **Grade 2: Continue** at normal recommended dose • **Grade 3: Reduce** to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Grade 4: Discontinue**
	Motor:	• **Grade 2: Reduce** to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Grade 3 or 4: Discontinue**

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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ADCETRIS® brentuximab vedotin | injection 50 mg

FOR ADULTS

Previously untreated sALCL or other CD30-expressing PTCL

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (any grade)†: 59% A+CHP vs 58% CHOP • Febrile neutropenia (any grade): 19% A+CHP vs 16% CHOP

Peripheral neuropathy (PN)[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• New or worsening PN (any grade): 52% A+CHP vs 55% CHOP • For A+CHP (by maximum grade): 34% Grade 1, 15% Grade 2, 3% Grade 3, <1% Grade 4 • PN was predominantly sensory with A+CHP (94% sensory, 16% motor)

A+CHP = ADCETRIS + cyclophosphamide, doxorubicin, and prednisone; CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone.

*Data from trial (ECHELON-2) in 449 previously untreated patients with CD30-expressing PTCL: 223 in the A+CHP arm and 226 in the CHOP arm.

†Derived from laboratory values and adverse reaction data. Laboratory values were obtained at the start of each cycle and end of treatment.

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FOR ADULTS

Previously untreated sALCL or other CD30-expressing PTCL

Dose delay, dose reduction, and discontinuations*[1]

- In A+CHP patients, adverse reactions led to dose delays of ADCETRIS in 25% of patients, dose reduction in 9% (most often for peripheral neuropathy), and discontinuation of ADCETRIS with or without the other CHP components in 7% (most often from peripheral neuropathy and infection)

*Data from phase 3 trial (ECHELON-2) in 449 previously untreated patients with CD30-expressing PTCL: 223 in the A+CHP arm and 226 in the CHOP arm.

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FOR ADULTS

Relapsed sALCL

Recommended dosage[1]

ADCETRIS 1.8 mg/kg up to a maximum of 180 mg*

Intravenous infusion over 30 minutes

Every 3 weeks until disease progression or unacceptable toxicity

- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products[1]**

See next page for dosage modifications.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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ADCETRIS® brentuximab vedotin | injection 50 mg

Relapsed sALCL

Dose modifications[1]

	Renal impairment		• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use
	Hepatic impairment		• **Mild (Child-Pugh A):** 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use
	Neutropenia	Grade 3 or 4:	• **Hold** dosing until improvement to baseline or Grade 2 or lower • **Consider** G-CSF prophylaxis for subsequent cycles
		Recurrent Grade 4 despite G-CSF prophylaxis:	• **Consider** discontinuation or dose reduction to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks
	Peripheral neuropathy	New or worsening Grade 2 or 3:	• **Hold** ADCETRIS dosing until improvement to baseline or Grade 1 • **Restart** at 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks
		Grade 4:	• **Discontinue**

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

Relapsed sALCL

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (any grade)†: 55%

Peripheral neuropathy (PN)[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• Peripheral sensory neuropathy (any grade): 53%

*Data from open-label, single-arm trial in 58 patients with relapsed sALCL treated with ADCETRIS.

†Derived from laboratory values and adverse reaction data.

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ADCETRIS® brentuximab vedotin | injection 50 mg

Relapsed sALCL

Dose delays and discontinuations*[1]

- Adverse reactions that led to dose delays in more than 5% of ADCETRIS-treated patients were neutropenia (12%) and peripheral sensory neuropathy (7%)
- Adverse reactions led to treatment discontinuation in 19% of ADCETRIS-treated patients
  - The adverse reaction that led to treatment discontinuation in 2 or more patients was peripheral sensory neuropathy (5%)

*Data from phase 2, open-label, single-arm trial in 58 patients with relapsed sALCL treated with ADCETRIS.

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ADCETRIS® brentuximab vedotin | injection 50 mg

FOR ADULTS

Relapsed pcALCL or CD30-expressing MF

Recommended dosage[1]

ADCETRIS 1.8 mg/kg up to a maximum of 180 mg*

Intravenous infusion over 30 minutes

Every 3 weeks until a maximum of 16 cycles, disease progression, or unacceptable toxicity

- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products[1]**

See next page for dosage modifications.

MF = mycosis fungoides; pcALCL = primary cutaneous anaplastic large cell lymphoma.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

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ADCETRIS® brentuximab vedotin | injection 50 mg

FOR ADULTS

Relapsed pcALCL or CD30-expressing MF

Dose modifications[1]

Renal impairment		• **No dosage adjustment is required for mild renal impairment (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min)** • **Severe (CrCL less than 30 mL/min):** Avoid use
Hepatic impairment		• **Mild (Child-Pugh A):** 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks • **Moderate (Child-Pugh B) or severe (Child-Pugh C):** Avoid use
Neutropenia	Grade 3 or 4:	• **Hold** dosing until improvement to baseline or Grade 2 or lower • **Consider** G-CSF prophylaxis for subsequent cycles
	Recurrent Grade 4 despite G-CSF prophylaxis:	• **Consider** discontinuation or dose reduction to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks
Peripheral neuropathy	New or worsening Grade 2 or 3:	• **Hold** ADCETRIS dosing until improvement to baseline or Grade 1 • **Restart** at 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks
	Grade 4:	• **Discontinue**

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

FOR ADULTS

Relapsed pcALCL or CD30-expressing MF

Monitoring for neutropenia and peripheral neuropathy

Neutropenia[1]

Monitoring	• Monitor complete blood counts prior to each dose of ADCETRIS • Monitor more frequently for patients with Grade 3 or 4 neutropenia • Monitor patients for fever
Rates*	• Neutropenia (any grade)†: 21% ADCETRIS vs 24% physician's choice‡

Peripheral neuropathy (PN)[1]

Monitoring	• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness • ADCETRIS-induced PN is cumulative and is predominantly sensory
Rates*	• Peripheral sensory neuropathy (any grade): 45% ADCETRIS vs 2% physician's choice‡

*Data from trial (ALCANZA) in 128 patients with relapsed pcALCL or CD30-expressing MF: 66 in the ADCETRIS arm and 62 in the physician's choice arm.

†Derived from laboratory values and adverse reaction data.

‡Physician's choice of either methotrexate or bexarotene.

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ADCETRIS® brentuximab vedotin | injection 50 mg

FOR ADULTS

Relapsed pcALCL or CD30-expressing MF

Dose delays and discontinuations*[1]

- Adverse reactions that led to dose delays in more than 5% of ADCETRIS-treated patients were peripheral sensory neuropathy (15%) and neutropenia (6%)
- Adverse reactions led to treatment discontinuation in 24% of ADCETRIS-treated patients
  - The most common adverse reaction that led to treatment discontinuation was peripheral neuropathy (12%)

*Data from phase 3 trial (ALCANZA) in 128 patients with relapsed pcALCL or CD30-expressing MF: 66 in the ADCETRIS arm and 62 in the physician's choice arm.

Preparation and administration

Administration[1]

- Administer only as an intravenous infusion over 30 minutes
- **Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products**

Reconstitution[1]

- Follow procedures for proper handling and disposal of anticancer drugs
- Use appropriate aseptic technique for reconstitution and preparation of dosing solutions
- Determine number of 50 mg vials based on the patient's weight and prescribed dose

Step	Instruction
1.	Reconstitute each 50 mg vial of ADCETRIS with 10.5 mL of Sterile Water for Injection, USP, to yield a single-dose solution containing 5 mg/mL brentuximab vedotin
2.	Direct stream toward wall of vial and not directly at cake or powder. Gently swirl vial to aid dissolution. **DO NOT SHAKE**
3.	Inspect reconstituted solution for particulates and discoloration. The reconstituted solution should be clear to slightly opalescent, colorless, and free of visible particulates
4.	Following reconstitution, dilute immediately into an infusion bag. If not diluted immediately, store at 2-8°C (36-46°F) and use within 24 hours of reconstitution. **DO NOT FREEZE**
5.	Discard any unused portion left in the vial

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ADCETRIS® brentuximab vedotin | injection 50 mg

Preparation and administration

Dilution and infusion[1]

Step	Instruction
1.	Calculate required volume of 5 mg/mL reconstituted ADCETRIS solution needed
2.	Withdraw amount from vial and immediately add to an infusion bag containing 0.9% Sodium Chloride Injection, USP, 5% Dextrose Injection, USP, or Lactated Ringer's Injection, USP to achieve a final concentration of 0.4 mg/mL to 1.8 mg/mL brentuximab vedotin
3.	Gently invert bag to mix solution
4.	Following dilution, infuse ADCETRIS solution immediately. If not used immediately, store at 2-8°C (36-46°F) and use within 24 hours of reconstitution. **DO NOT FREEZE**

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ADCETRIS® brentuximab vedotin | injection 50 mg

Supply and storage information

Dosage form and strengths[1]

- For injection: 50 mg of brentuximab vedotin as a sterile, white to off-white lyophilized, preservative-free cake or powder in a single-dose vial for reconstitution

How supplied[1]

- Sterile, white to off-white preservative-free lyophilized cake or powder in individually boxed single-dose vials: NDC (51144-050-01), 50 mg brentuximab vedotin

Storage[1]

- Store vial at 2-8°C (36-46°F) in the original carton to protect from light

Special handling[1]

- ADCETRIS is a hazardous product. Follow special handling and disposal procedures

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ADCETRIS® brentuximab vedotin | injection 50 mg

Patient counseling information

Peripheral neuropathy[1]

- Advise patients that ADCETRIS can cause peripheral neuropathy. They should be advised to report to their healthcare provider any numbness or tingling of the hands or feet or any muscle weakness

Fever/neutropenia[1]

- Advise patients to contact their healthcare provider if a fever of 100.5°F or greater or other evidence of potential infection such as chills, cough, or pain on urination develops

Infusion reactions[1]

- Advise patients to contact their healthcare provider if they experience signs and symptoms of infusion reactions including fever, chills, rash, or breathing problems within 24 hours of infusion

Hepatotoxicity[1]

- Advise patients to report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice

PML[1]

- Instruct patients receiving ADCETRIS to immediately report if they have any of the following neurological, cognitive, or behavioral signs and symptoms or if anyone close to them notices these signs and symptoms:
  - changes in mood or usual behavior
  - confusion, thinking problems, loss of memory
  - changes in vision, speech, or walking
  - decreased strength or weakness on one side of the body

Pulmonary toxicity[1]

- Instruct patients to report symptoms that may indicate pulmonary toxicity, including cough or shortness of breath

Acute pancreatitis[1]

- Advise patients to contact their healthcare provider if they develop severe abdominal pain

Gastrointestinal complications[1]

- Advise patients to contact their healthcare provider if they develop severe abdominal pain, chills, fever, nausea, vomiting, or diarrhea

Hyperglycemia[1]

- Educate patients about the risk of hyperglycemia and how to recognize associated symptoms

Females and males of reproductive potential[1]

- ADCETRIS can cause fetal harm. Advise women receiving ADCETRIS to avoid pregnancy during ADCETRIS treatment and for 2 months after the last dose of ADCETRIS
- Advise males with female sexual partners of reproductive potential to use effective contraception during ADCETRIS treatment and for 4 months after the last dose of ADCETRIS
- Advise patients to report pregnancy immediately

Lactation[1]

- Advise patients to avoid breastfeeding while receiving ADCETRIS

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ADCETRIS®
brentuximab vedotin | injection 50 mg

Seagen Secure® is a dynamic and comprehensive suite of solutions to help patients access prescribed Seagen therapies

ADCETRIS is covered for 9 out of 10 commercial and Medicare patients with previously untreated Stage III/IV cHL.*†

Coverage Support

- **Benefits investigation assistance** to evaluate insurance coverage
- **Prior authorization support** to help navigate the process
- **Assistance with appeals** to determine additional documentation that may be needed or track the status of appeals

Patient Assistance

- **Commercial Out-of-Pocket Assistance Program** allows eligible patients with commercial insurance to pay as little as $5 per prescription fill
- **Patient Assistance Program** provides the product for eligible patients for up to 1 year

Patient support beyond coverage and financial support

*Covered means reimbursement from a health plan with or without restrictions. Approximately 10% of national coverage is unknown, which is defined as not publicly available.

†Source: Coverage data are provided by MMIT and current as of April 2022. Coverage is subject to change. Individual coverage may vary, please confirm coverage with the individual health plan. Seagen does not endorse any individual health plan. Seagen does not guarantee that enrollment will result in patient assistance, coverage, and/or reimbursement. Seagen Secure is not intended to provide medical advice or replace medical advice from the patient's healthcare provider.

Seagen Secure®
Patient Assistance Program

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ADCETRIS®
brentuximab vedotin | injection 50 mg

Enrolling in Seagen Secure

Enroll by fax

Fax completed forms to
855-557-2480

Download the forms from
SeagenSecure.com

Enroll by phone

Call 855-4-SECURE

Monday–Friday,
8 AM–8 PM ET

Enroll online at

SeagenSecure.com

For more information on Seagen Secure, contact your field reimbursement manager.

Seagen Secure®
Patient Assistance Program

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ADCETRIS® brentuximab vedotin | injection 50 mg

Questions about ADCETRIS® (brentuximab vedotin) dosage, administration, or indications?

Contact your Seagen sales representative or visit adcetrispro.com

Reference: 1. ADCETRIS [Prescribing Information]. Bothell, WA: Seagen, Inc. June 2023.

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