ADCETRIS® (brentuximab vedotin)

DOSING AND ADMINISTRATION GUIDE

Important Safety Information

BOXED WARNING

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

Please see additional Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
ADCETRIS® (brentuximab vedotin)

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Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
Approved indications for CD30-expressing lymphomas

**Frontline indications**¹
ADCETRIS is indicated for the treatment of adult patients with:

**Previously untreated Stage III/IV cHL**
- Previously untreated Stage III/IV classical Hodgkin lymphoma (cHL) in combination with doxorubicin, vinblastine, and dacarbazine

**Previously untreated sALCL or other CD30-expressing PTCL**
- 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 and consolidation indications**¹
ADCETRIS is indicated for the treatment of adult patients with:

**Relapsed cHL**
- cHL after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates

**Relapsed sALCL**
- sALCL after failure of at least one prior multi-agent chemotherapy regimen

**Relapsed pcALCL or CD30-expressing MF**
- Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy

**cHL post-auto-HSCT consolidation**
- cHL at high risk of relapse or progression as post-auto-HSCT consolidation

**Important Safety Information**

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BOXED WARNING

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

Contraindication
ADCETRIS concomitant with 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. Institute dose modifications accordingly.

• 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 patients who receive ADCETRIS in combination with chemotherapy for previously untreated Stage III/IV cHL or previously untreated PTCL.

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 bacterial, fungal, or viral infections.

• Tumor lysis syndrome: Closely monitor patients with rapidly proliferating tumor and high tumor burden.

• 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 compared to patients with normal renal function. 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 compared to patients with normal hepatic function. 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 the potential risk to the fetus, and to avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

**Most Common (≥20% in any study) Adverse Reactions**

Peripheral neuropathy, fatigue, nausea, diarrhea, neutropenia, upper respiratory tract infection, pyrexia, constipation, vomiting, alopecia, decreased weight, abdominal pain, anemia, stomatitis, lymphopenia, and mucositis.

**Drug Interactions**

Concomitant use of strong CYP3A4 inhibitors or inducers has the potential to affect the exposure to monomethyl auristatin E (MMAE).

**Use in Specific Populations**

Moderate or severe hepatic impairment or severe renal impairment: MMAE exposure and adverse reactions are increased. Avoid use.

Advise males with female sexual partners of reproductive potential to use effective contraception during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

Advise patients to report pregnancy immediately and avoid breastfeeding while receiving ADCETRIS.
Recommended ADCETRIS dosage

- 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

Dose modifications

Renal impairment
- Mild (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min): 1.2 mg/kg up to a maximum of 120 mg* every 2 weeks
- 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

Peripheral neuropathy
- Grade 2: Reduce dose to 0.9 mg/kg up to a maximum of 90 mg* every 2 weeks
- 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

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

Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
Monitoring for neutropenia and peripheral neuropathy

Neutropenia¹

**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

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

A+AVD = ADCETRIS + doxorubicin, vinblastine, dacarbazine; ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine; cHL = classical Hodgkin lymphoma; CrCL = creatinine clearance; G-CSF = granulocyte-colony stimulating factor.

†Data from phase 3 trial (ECHELON-1) in 1334 previously untreated patients with Stage III or IV cHL: 664 in the A+AVD arm and 670 in the ABVD arm.
‡Derived from laboratory values and adverse reaction data; data are included for clinical relevance irrespective of rate between arms.
Recommended dosage

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 for 6 to 8 doses

G-CSF primary prophylaxis beginning with Cycle 1

Renal impairment

- Mild (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min): 1.8 mg/kg up to a maximum of 180 mg* every 3 weeks
- 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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Monitoring for neutropenia and peripheral neuropathy

**Neutropenia**

**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)**

**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, maximum grade was 34% Grade 1, 15% Grade 2, 3% Grade 3, <1% Grade 4
- PN was predominantly sensory with A+CHP (94% sensory, 16% motor)

**Dose delays, dose reduction, and discontinuations**

- 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)

A+CHP = ADCETRIS + cyclophosphamide, doxorubicin, prednisone; CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone; CrCL = creatinine clearance; G-CSF = granulocyte-colony stimulating factor; PTCL = peripheral T-cell lymphoma.

†Data from phase 3 trial (ECHELON-2) in 452 previously untreated patients with CD30-expressing PTCL: 226 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.

Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
Relapsed cHL

Recommended dosage

- 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

Dose modifications

- 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

- Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products

Recommended dosage

- 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

Renal impairment

- Mild (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min): 1.8 mg/kg up to a maximum of 180 mg every 3 weeks
- 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

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

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Monitoring for neutropenia and peripheral neuropathy

Neutropenia†

**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%

Peripheral neuropathy (PN)†

**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

Dose delays and discontinuations†

- 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%)

cHL = classical Hodgkin lymphoma; CrCL = creatinine clearance; G-CSF = granulocyte-colony stimulating factor.

†Data from phase 2, open-label, single-arm trial in 102 patients with cHL who relapsed after autologous hematopoietic stem cell transplantation and were treated with ADCETRIS.

‡Derived from laboratory values and adverse reaction data.
**Recommended dosage**

- **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***

### Dose modifications

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Mild (CrCl greater than 50-80 mL/min) or moderate (CrCl 30-50 mL/min): 1.8 mg/kg up to a maximum of 180 mg* every 3 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe (CrCl less than 30 mL/min): Avoid use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hepatic impairment</th>
<th>Mild (Child-Pugh A): 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate (Child-Pugh B) or severe (Child-Pugh C): Avoid use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neutropenia</th>
<th>Grade 3 or 4:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hold dosing until improvement to baseline or Grade 2 or lower</td>
</tr>
<tr>
<td></td>
<td>Consider G-CSF prophylaxis for subsequent cycles</td>
</tr>
</tbody>
</table>

**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**

<table>
<thead>
<tr>
<th>Peripheral neuropathy</th>
<th>New or worsening Grade 2 or 3:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hold ADCETRIS dosing until improvement to baseline or Grade 1</td>
</tr>
<tr>
<td></td>
<td>Restart at 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks</td>
</tr>
</tbody>
</table>

**Grade 4**

- **Discontinue**

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

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### Monitoring for neutropenia and peripheral neuropathy

#### Neutropenia

<table>
<thead>
<tr>
<th>Monitoring</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Monitor complete blood counts prior to each dose of ADCETRIS</td>
<td></td>
</tr>
<tr>
<td>• Monitor more frequently for patients with Grade 3 or 4 neutropenia</td>
<td></td>
</tr>
<tr>
<td>• Monitor patients for fever</td>
<td></td>
</tr>
</tbody>
</table>

| Rates†                          | Neutropenia (any grade)†: 55%                                      |

#### Peripheral neuropathy (PN)

<table>
<thead>
<tr>
<th>Monitoring</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesis, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness</td>
<td>ADCETRIS-induced PN is cumulative and is predominantly sensory</td>
</tr>
</tbody>
</table>

| Rates†                          | Peripheral sensory neuropathy (any grade): 53%                                 |

#### Dose delays and discontinuations††

- 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%)

CrCL = creatinine clearance; G-CSF = granulocyte-colony stimulating factor; sALCL = systemic anaplastic large cell lymphoma.

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

†††Derived from laboratory values and adverse reaction data.
**Recommended dosage**

| 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

**Dose modifications**

| Renal impairment | Mild (CrCL greater than 50–80 mL/min) or moderate (CrCL 30–50 mL/min): 1.8 mg/kg up to a maximum of 180 mg* every 3 weeks | 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.*

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Monitoring for neutropenia and peripheral neuropathy

Neutropenia†

**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)†

**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§

Dose delays and discontinuations††
- 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%)

CrCL = creatinine clearance; G-CSF = granulocyte-colony stimulating factor; MF = mycosis fungoides; pcALCL = primary cutaneous anaplastic large cell lymphoma.

†Data from phase 3 trial (ALCANZA) in 131 patients with relapsed pcALCL or CD30-expressing MF: 66 in the ADCETRIS arm and 65 in the physician’s choice arm.
‡Derived from laboratory values and adverse reaction data.
§Physician’s choice of either methotrexate or bexarotene.
### Recommended dosage

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

### Dose modifications

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Neutropenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (CrCL greater than 50-80 mL/min) or moderate (CrCL 30-50 mL/min): 1.8 mg/kg up to a maximum of 180 mg* every 3 weeks</td>
<td>Grade 3 or 4:</td>
</tr>
<tr>
<td>Severe (CrCL less than 30 mL/min): Avoid use</td>
<td>• Hold dosing until improvement to baseline or Grade 2 or lower</td>
</tr>
<tr>
<td></td>
<td>• Consider G-CSF prophylaxis for subsequent cycles</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hepatic impairment</th>
<th>Recurrent Grade 4 despite G-CSF prophylaxis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (Child-Pugh A): 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks</td>
<td>• Consider discontinuation or dose reduction to 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks</td>
</tr>
<tr>
<td>Moderate (Child-Pugh B) or severe (Child-Pugh C): Avoid use</td>
<td></td>
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</tbody>
</table>

### Peripheral neuropathy

<table>
<thead>
<tr>
<th>New or worsening Grade 2 or 3:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hold <strong>ADCETRIS</strong> dosing until improvement to baseline or Grade 1</td>
</tr>
<tr>
<td>• Restart at 1.2 mg/kg up to a maximum of 120 mg* every 3 weeks</td>
</tr>
</tbody>
</table>

* Grade 4 | • Discontinue

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

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Monitoring for neutropenia and peripheral neuropathy

**Neutropenia**

**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)**

**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

**Dose delays and discontinuations**
- 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%)

cHL = classical Hodgkin lymphoma; G-CSF = granulocyte-colony stimulating factor; HSCT = hematopoietic stem cell transplantation.

†Data from phase 3 trial (AETHERA) in 329 patients with cHL at high risk of relapse or disease progression post-auto-HSCT: 165 in the ADCETRIS arm and 164 in the placebo arm.

‡Derived from laboratory values and adverse reaction data.

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Preparation and administration

Administration

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

Reconstitution

- 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

<table>
<thead>
<tr>
<th>Step</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>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</td>
</tr>
<tr>
<td>2.</td>
<td>Direct stream toward wall of vial and not directly at cake or powder. Gently swirl vial to aid dissolution. DO NOT SHAKE</td>
</tr>
<tr>
<td>3.</td>
<td>Inspect reconstituted solution for particulates and discoloration. The reconstituted solution should be clear to slightly opalescent, colorless, and free of visible particulates</td>
</tr>
<tr>
<td>4.</td>
<td>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</td>
</tr>
<tr>
<td>5.</td>
<td>Discard any unused portion left in the vial</td>
</tr>
</tbody>
</table>

Dilution and infusion

<table>
<thead>
<tr>
<th>Step</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Calculate required volume of 5 mg/mL reconstituted ADCETRIS solution needed</td>
</tr>
<tr>
<td>2.</td>
<td>Withdraw amount from vial and immediately add to an infusion bag containing a minimum volume of 100 mL of 0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer’s Injection to achieve a final concentration of 0.4 mg/mL to 1.8 mg/mL brentuximab vedotin</td>
</tr>
<tr>
<td>3.</td>
<td>Gently invert bag to mix solution</td>
</tr>
<tr>
<td>4.</td>
<td>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</td>
</tr>
<tr>
<td>5.</td>
<td>Administer as 30-minute intravenous infusion only</td>
</tr>
</tbody>
</table>

Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
Supply and storage information

Dosage form and strengths

• 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

• 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

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

Special handling

• ADCETRIS is an antineoplastic product. Follow special handling and disposal procedures

Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
Peripheral neuropathy¹
• Advise patients that ADCETRIS can cause a 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/neutropenia¹
• 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 reactions¹
• 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

Hepatotoxicity¹
• Advise patients to report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice

Progressive multifocal leukoencephalopathy (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 toxicity¹
• Instruct patients to report symptoms that may indicate pulmonary toxicity, including cough or shortness of breath

Acute pancreatitis¹
• Advise patients to contact their healthcare provider if they develop severe abdominal pain

Gastrointestinal complications¹
• Advise patients to contact their healthcare provider if they develop severe abdominal pain, chills, fever, nausea, vomiting, or diarrhea

Hyperglycemia¹
• Educate patients about the risk of hyperglycemia and how to recognize associated symptoms

Females and males of reproductive potential¹
• ADCETRIS can cause fetal harm. Advise women receiving ADCETRIS to avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS
• Advise males with female sexual partners of reproductive potential to use effective contraception during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS
• Advise patients to report pregnancy immediately

Lactation¹
• Advise patients to avoid breastfeeding while receiving ADCETRIS
SeaGen Secure®: A comprehensive patient assistance program for ADCETRIS® (brentuximab vedotin)

Personalized services and helpful information for your patients

For your patients and caregivers

- Benefits investigation
- Claims assistance
- Reimbursement assistance
- Patient out-of-pocket cost assistance
- Ongoing support throughout treatment from an Oncology Nurse Advocate

- Referrals to:
  - Advocacy organizations for emotional support
  - Transportation assistance
  - Peer-to-peer connection programs

CALL SeaGen Secure at 855.4SECURE (855-473-2873) (Monday-Friday, 9 AM-8 PM ET)

ENROLL online at SeaGenSecure.com

Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com
Questions about ADCETRIS® (brentuximab vedotin) dosing, administration, or indications?

Contact your Seattle Genetics account manager, or visit adcetrispro.com

Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com

**Indication**

ADCETRIS® (brentuximab vedotin) is indicated for the treatment of adult patients with previously untreated sALCL or other CD30-expressing PTCL, including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone (CHP).

**ADCETRIS + CHP dosing**

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Components</th>
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<tbody>
<tr>
<td>Every 3 weeks for 6 to 8 cycles</td>
<td><strong>CHP</strong>:</td>
</tr>
<tr>
<td></td>
<td>• Cyclophosphamide: 750 mg/m² on Day 1 of each cycle intravenously</td>
</tr>
<tr>
<td></td>
<td>• Doxorubicin: 50 mg/m² on Day 1 of each cycle intravenously</td>
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<tr>
<td></td>
<td>• Prednisone: 100 mg daily on Days 1 to 5 of each cycle orally</td>
</tr>
<tr>
<td></td>
<td>+ <strong>ADCETRIS® (brentuximab vedotin)</strong>:</td>
</tr>
<tr>
<td></td>
<td>• 1.8 mg/kg up to a maximum of 180 mg intravenously over 30 minutes</td>
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<tr>
<td></td>
<td>• Sequence of ADCETRIS administration should be determined by provider</td>
</tr>
<tr>
<td></td>
<td>• For patients weighing &gt;100 kg, calculate dose based on a weight of 100 kg</td>
</tr>
</tbody>
</table>

Please see cyclophosphamide, doxorubicin, and prednisone full Prescribing Information for complete details.

**Recommended prophylactic medication**

| Myeloid growth factor: | • Administer G-CSF primary prophylaxis beginning with Cycle 1 of ADCETRIS + CHP |

See clinical practice guidelines for instructions on G-CSF use.

G-CSF = granulocyte-colony stimulating factor; sALCL = systemic anaplastic large cell lymphoma.

See pages 8 & 9 for complete dosing information and dose modifications for renal/hepatic impairment, neutropenia, and peripheral neuropathy.

**References:**


Please see Important Safety Information on pages 4-5 and full Prescribing Information, including BOXED WARNING, attached or at adcetrispro.com.