ADCETRIS® ▼ (brentuximab vedotin) PRESCRIBING INFORMATION

Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: 50 mg brentuximab vedotin powder for concentrate for solution for infusion. **Indication:** Treatment of adult patients with CD30+ HL at increased risk of relapse or progression following autologous stem cell transplantation (ASCT); relapsed or refractory (R/R) CD30+ HL following ASCT or following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option; R/R systemic anaplastic large cell lymphoma (sALCL); CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy. **Dosage & Administration:** Administration should be under the supervision of a physician experienced in the use of anti-cancer agents. HL at increased risk of relapse or progression: Recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. R/R HL and sALCL: Recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks; the same dose and schedule is recommended for retreatment of patients who previously responded to ADCETRIS or start at the last tolerated dose. Patients achieving stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year). Treatment should be continued until disease progression or unacceptable toxicity. CTCL: Recommended starting dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Patients should receive up to 16 cycles. General: If the patient's weight is more than 100 kg, the dose calculation should use 100 kg. Complete blood counts should be monitored prior to administration of each dose. Patients should be monitored during and after infusion. **Dose Adjustments:** If neutropenia develops during treatment it should be managed by dose delays. If peripheral sensory or motor neuropathy emerges or worsens during treatment patients may require delay and dose reduction or discontinuation of ADCETRIS. Refer to the SmPC for full dose modifications. Renal and hepatic impairment: *Monotherapy:* Recommended starting dose in patients with hepatic impairment or severe renal impairment is 1.2 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Elderly patients (≥65 yrs): Dose same as for adults. Paediatric patients (<18 yrs): *S*afety and efficacy has not yet been established. In nonclinical studies, thymus depletion has been observed. Method of administration: Infuse ADCETRIS over 30 minutes. ADCETRIS must not be administered as an intravenous push or bolus. ADCETRIS should be administered through a dedicated intravenous line and it must not be mixed with other medicinal products. **Contraindications:** Hypersensitivity to the active substance or excipients. Combined use of bleomycin and ADCETRIS causes pulmonary toxicity. **Warnings and Precautions:** Progressive multifocal leukoencephalopathy (PML) has been reported in patients who received ADCETRIS after receiving multiple prior chemotherapy regimens; patients should be closely monitored for new or worsening neurological, cognitive, or behavioural signs or symptoms, which may be suggestive of PML. ADCETRIS dosing should be held for any suspected case of PML and permanently discontinued if a diagnosis of PML is confirmed. Acute pancreatitis has been observed in patients treated with ADCETRIS. Patients should be monitored for abdominal pain suggestive of acute pancreatitis. ADCETRIS dosing should be held if acute pancreatitis is suspected and permanently discontinued if a diagnosis is confirmed. Pulmonary toxicity, including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome, some with fatal outcomes, have been reported in patients receiving ADCETRIS. In the event of new or worsening pulmonary symptoms, a prompt diagnostic evaluation is required and patients treated appropriately. Consider holding ADCETRIS dosing during evaluation and until symptomatic improvement. Serious infections such as pneumonia, staphylococcal bacteraemia, sepsis/septic shock (including fatal outcomes) and herpes zoster, cytomegalovirus (CMV) (reactivation) and opportunistic infections such as oral candidiasis and Pneumocystis jiroveci pneumonia have been reported in patients treated with ADCETRIS. Patients should be carefully monitored during treatment. Immediate and delayed infusion-related reactions (IRR), as well as anaphylactic reactions, have been reported. Monitor patients during and after infusion. ADCETRIS should be immediately and permanently discontinued if anaphylactic reaction occurs. Infusion should be interrupted if IRR occurs and appropriate management instituted. Infusion may be restarted at slower rate after resolution. Use premedication for subsequent infusions in instances of prior IRR. Patients with rapidly proliferating tumour and high tumour burden are at risk of tumour lysis syndrome; these patients should be monitored and managed according to best medical practice. ADCETRIS may cause peripheral neuropathy which is reversible in most cases. Patients should be monitored for symptoms of neuropathy. Patients experiencing new or worsening peripheral neuropathy may require delay and dose reduction or discontinuation of ADCETRIS. Refer to SmPC for dose adjustments if peripheral neuropathy develops. Grade 3 or 4 anaemia, thrombocytopenia and neutropenia can occur with ADCETRIS. Refer to SmPC for dose adjustments if neutropenia develops. Patients should be monitored for fever and managed according to best medical practice if febrile neutropenia develops. Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with ADCETRIS with fatal outcomes. If SJS or TEN occurs, treatment with ADCETRIS should be discontinued and appropriate medical therapy administered. Gastrointestinal (GI) complications including intestinal obstruction, ileus, enterocolitis, neutropenic colitis, erosion, ulcer, perforation and haemorrhage, some with fatal outcomes, have been reported. In the event of new or worsening GI symptoms, perform a prompt diagnostic evaluation and treat appropriately. Elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST), in the form of hepatotoxicity, has been reported. Serious cases of hepatotoxicity, including fatal outcomes, have also occurred. Liver function should be tested before initiating the treatment and routinely monitored in patients receiving ADCETRIS. Patients experiencing hepatotoxicity may require a delay, change in dose or discontinuation of ADCETRIS. Any patient who experiences an event of hyperglycaemia should have their serum glucose closely monitored and managed appropriately. Monomethyl auristatin E (MMAE) clearance might be affected by severe renal impairment, hepatic impairment, and by low serum albumin concentrations. The size of the treatment effect in CD30+ CTCL subtypes other than mycosis fungoides and primary cutaneous anaplastic large cell lymphoma is not clear due to lack of high level evidence. ADCETRIS should be used with caution in other CD30+ CTCL patients after consideration of the potential benefit-risk. ADCETRIS contains 13.2 mg sodium per vial. **Drug Interactions:** Co-administration of ADCETRIS: with strong CYP3A4 and P-gp inhibitors, such as ketoconazole, may increase the incidence of neutropenia; with rifampicin, a strong CYP3A4 inducer did not alter the plasma exposure to ADCETRIS, however, it appeared to reduce plasma concentrations of MMAE metabolites. ADCETRIS is not expected to alter the exposure to medicines that are metabolized by CYP3A4 enzymes e.g. midazolam. - administration of ADCETRIS with bleomycin is contraindicated. **Pregnancy & lactation:** Women of childbearing potential should be using two methods of effective contraception during treatment with ADCETRIS and until 6 months after treatment. There are no data from the use of ADCETRIS in pregnant women. Animal studies have shown reproductive toxicity. There are no data as to whether ADCETRIS or its metabolites are excreted in human milk. **Fertility:** In non-clinical studies, ADCETRIS treatment has resulted in testicular toxicity, and may alter male fertility. Men being treated with ADCETRIS are advised not to father a child during treatment and for up to 6 months following the last dose. **Adverse Effects (monotherapy):** *Very common (⩾10%):* Infection, upper respiratory tract infection, neutropenia, peripheral sensory neuropathy, peripheral motor neuropathy, cough, dyspnoea, nausea, diarrhoea, vomiting, constipation, abdominal pain, rash, pruritus, arthralgia, myalgia, fatigue,

pyrexia, infusion-related reactions, weight decreased. *Common (≥1/100 to <1/10):* Herpes zoster, pneumonia, herpes simplex, oral candidiasis, anaemia, thrombocytopenia, hyperglycaemia, dizziness, ALT/AST increased, alopecia, back pain, chills. Refer to the SmPC for details on full side effect profile and interactions. **Pharmaceutical Precautions:** Store vial in a refrigerator (2°C-8°C), protected from light. After reconstitution/dilution, chemical and physical in-use stability has been demonstrated for 24 hours at 2°C-8°C. **PI Date of Preparation:** March 2019. **PI approval code:** UK/ADC/1902/0010 **Legal category:** POM **Basic NHS Price & Marketing Authorisation:** £2,500 for each ADCETRIS 50mg vial (EU/1/12/794/001). **Additional information is available on request from:** Takeda UK Ltd. Building 3, Glory Park, Glory Park Avenue, Wooburn Green, Buckinghamshire, HP10 0DF. Tel: 01628 537900 Fax: 01628 526617. Takeda Products Ireland Ltd. 3013 Lake Drive, Citywest Business Campus, Dublin 24. Tel: +353 (0)1 642 0021 Fax: +353 (0)1 642 0020 are responsible for the sale of ADCETRIS in Ireland. ADCETRIS® is a registered trademark.

ADCETRIS has received a conditional marketing authorisation in Europe. A conditional marketing authorisation is granted to a medicinal product that fulfils an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact additional data are still required. The European regulatory agency will review new information on ADCETRIS at least every year and the summary of product characteristics will be updated as necessary.

UK: Adverse events should be reported to the Medicines and Healthcare products Regulatory Agency. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/. Adverse events should also be reported to Takeda UK Ltd 01628 537900

Ireland: Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (medsafety@hpra.ie). Information about Adverse Event reporting can be found on the HPRA website (www.hpra.ie). Adverse events should also be reported to Takeda UK Ltd 1800 937 970