ADCETRIS® ▼ (brentuximab vedotin) PRESCRIBING INFORMATION FOR NORTHERN IRELAND

Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: Each vial contains 50 mg brentuximab vedotin powder for concentrate for solution for infusion. **Indications:** Treatment of adult patients as follows: ***Monotherapy:*** CD30+ Hodgkin lymphoma (HL) at increased risk of relapse or progression following autologous stem cell transplant (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. ***Combination therapy:*** ADCETRIS in combination with doxorubicin, vinblastine and dacarbazine (AVD) in previously untreated CD30+ Stage IV HL; ADCETRIS in combination with cyclophosphamide, doxorubicin and prednisone (CHP) in previously untreated sALCL. Refer to the SmPCs of chemotherapy agents given in combination. **Dosage and administration:** Administration should be under supervision of a physician experienced in the use of anti-cancer agents. Administer as an intravenous infusion over 30 minutes. Recommended doses are as follows: ***Monotherapy:*** *HL at increased risk of relapse or progression:* 1.8 mg/kg every 3 weeks for up to 16 cycles following recovery from ASCT; *R/R HL and R/R sALCL:* 1.8 mg/kg every 3 weeks; 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). Treat until disease progression or unacceptable toxicity; *CTCL:* 1.8 mg/kg every 3 weeks up to 16 cycles. ***Combination therapy:*** Primary prophylaxis with growth factor support (G-CSF) beginning with the first dose is recommended for all adult patients. *Previously untreated HL:* ADCETRIS dose with AVD is 1.2 mg/kg on days 1 and 15 of each 28 day cycle for 6 cycles; *Previously untreated sALCL:* ADCETRIS dose with CHP is 1.8 mg/kg every 3 weeks for 6 to 8 cycles. **General:** If patient's weight is more than 100 kg, dose calculation should use 100 kg. Monitor complete blood counts prior to administration of each dose and monitor patients during and after infusion. **Dose adjustments:** Refer to SmPC for full dose modifications. If peripheral sensory or motor neuropathy emerges or worsens during treatment, patients may require dose delay and reduction or discontinuation of ADCETRIS (≥Grade 2). ***Monotherapy:*** If Grade 3 or 4 neutropenia develops, manage by dose delays and consider use of G-CSF. Continue with same dose and schedule for Grade 1 or 2 neutropenia. ***Combination therapy:*** For all Grades, if neutropenia develops, continue with same dose and schedule. **Renal and hepatic impairment:** Closely monitor patients for adverse events. Recommended starting doses are as follows: ***Monotherapy:*** 1.2 mg/kg every 3 weeks in patients with hepatic impairment or severe renal impairment. ***Combination therapy:*** Avoid use in patients with moderate and severe hepatic impairment or severe renal impairment. Mild hepatic impairment: *Previously untreated HL:* 0.9 mg/kg every 2 weeks in combination with AVD; *Previously untreated sALCL:* 1.2 mg/kg every 3 weeks in combination with CHP. **Elderly patients (≥65 years):** Dose same as for adults. ***Monotherapy:*** May be more susceptible to events such as pneumonia, neutropenia and febrile neutropenia. ***Combination therapy:*** More serious adverse events and dose modifications were reported in older patients compared with overall study population. Advanced age was a risk factor for febrile neutropenia. **Paediatric patients (<18 years):** Safety and efficacy has not been established. **Method of administration:** Requires reconstitution and dilution before administration – refer to SmPC. Infuse ADCETRIS over 30 minutes. Must not be administered as an intravenous push or bolus. Administer ADCETRIS through a dedicated intravenous line and do not mix with other medicinal products. **Contraindications:** Hypersensitivity to active substance or excipients. Combined use of bleomycin and ADCETRIS causes pulmonary toxicity. **Warnings and precautions:** Progressive multifocal leukoencephalopathy (PML): John Cunningham virus reactivation resulting in PML and death can occur in ADCETRIS-treated patients. PML has been reported in patients who received ADCETRIS after receiving multiple prior chemotherapy regimens. Monitor patients closely for new or worsening neurological, cognitive, or behavioural signs or symptoms, which may be suggestive of PML. Withhold ADCETRIS dosing for any suspected case of PML and permanently discontinue if diagnosis of PML is confirmed. Pancreatitis: Acute pancreatitis has been observed and fatal outcomes reported. Monitor patients for abdominal pain suggestive of acute pancreatitis. Withhold dosing if acute pancreatitis is suspected and permanently discontinue if a diagnosis is confirmed. Pulmonary toxicity: Cases of pulmonary toxicity including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome, some with fatal outcomes, have been reported. In 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 and opportunistic infections: Serious infections such as pneumonia, staphylococcal bacteraemia, sepsis/septic shock (including fatal outcomes) and herpes zoster, cytomegalovirus (CMV) (reactivation) and opportunistic infections such as Pneumocystis jiroveci pneumonia (PJP) and oral candidiasis have been reported in patients treated with ADCETRIS. Monitor patients carefully during treatment. Infusion-related reactions (IRR): Immediate and delayed IRRs, as well as anaphylactic reactions, have been reported (more frequently and severely in patients with antibodies to ADCETRIS). 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. Tumour lysis syndrome (TLS): Patients with rapidly proliferating tumour and high tumour burden are at risk of TLS; monitor these patients and manage according to best medical practice. Peripheral neuropathy: May cause peripheral neuropathy which is reversible in most cases. Monitor patients 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. Haematological toxicities: Grade 3 or 4 anaemia, thrombocytopenia and prolonged (≥1 week) Grade 3 or 4 neutropenia can occur with ADCETRIS. Refer to SmPC for dose adjustments if neutropenia develops. Febrile neutropenia: Has been reported with ADCETRIS. Monitor patients for fever and manage according to best medical practice if febrile neutropenia develops. When ADCETRIS was administered in combination with AVD or CHP, advanced age was a risk factor for febrile neutropenia; primary prophylaxis with G-CSF beginning with the first dose is recommended for all adult patients regardless of age. Severe cutaneous adverse reactions (SCARs): Cases of SCARs, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with ADCETRIS. Fatal outcomes have been reported for SJS and TEN. If SJS, TEN or DRESS occur, discontinue ADCETRIS treatment and administer appropriate medical therapy. Gastrointestinal (GI) complications: GI complications including intestinal obstruction, ileus, enterocolitis, neutropenic colitis, erosion, ulcer, perforation and haemorrhage, some with

fatal outcomes, have been reported. In event of new or worsening GI symptoms, perform a prompt diagnostic evaluation and treat appropriately. Hepatotoxicity: Elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been reported. Serious cases of hepatotoxicity, including fatal outcomes, have also occurred. Test liver function before initiating treatment and routinely monitor in patients receiving ADCETRIS. Patients experiencing hepatotoxicity may require a delay, change in dose or discontinuation of ADCETRIS. Hyperglycaemia: Any patient who experiences an event of hyperglycaemia should have their serum glucose closely monitored and anti-diabetic treatment administered as appropriate. Infusion site extravasation: Extravasation during intravenous infusion has occurred therefore it is recommended to closely monitor the infusion site for possible infiltration during drug administration. Renal and hepatic impairment: Monomethyl auristatin E (MMAE) clearance might be affected by severe renal impairment, hepatic impairment, and by low serum albumin concentrations. CD30+ CTCL: Size of 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. Use ADCETRIS with caution in other CD30+ CTCL subtypes after consideration of the potential benefit-risk. Sodium content in excipients: Contains 13.2 mg sodium per vial. **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 metabolised by CYP3A4 enzymes e.g. midazolam. Co-administration of ADCETRIS is not expected to affect the exposure of AVD or CHP. Co-administration of ADCETRIS with bleomycin is contraindicated. **Fertility, pregnancy and lactation:** Women of childbearing potential should use two methods of effective contraception during treatment with ADCETRIS and until 6 months after treatment. There are no data in pregnant women. Animal studies have shown reproductive toxicity. ADCETRIS should not be used during pregnancy unless benefit to mother outweighs potential risks to foetus. There are no data as to whether ADCETRIS or its metabolites are excreted in human milk. A risk to the newborn/infant cannot be excluded. 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. **Undesirable effects: Very common (≥1/10): *Monotherapy:*** 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. ***Combination therapy:*** Infection, upper respiratory tract infection, neutropenia, anaemia, febrile neutropenia, decreased appetite, insomnia, peripheral sensory neuropathy, peripheral motor neuropathy, dizziness, cough, dyspnoea, nausea, constipation, vomiting, diarrhoea, abdominal pain, stomatitis, alopecia, rash, bone pain, arthralgia, myalgia, back pain, fatigue, pyrexia, weight decreased. **Common (≥1/100 to <1/10): *Monotherapy:*** Herpes zoster, pneumonia, herpes simplex, oral candidiasis, anaemia, thrombocytopenia, hyperglycaemia, dizziness, ALT/AST increased, alopecia, back pain, chills. ***Combination therapy:*** Pneumonia, oral candidiasis, sepsis/septic shock, herpes zoster, thrombocytopenia, hyperglycaemia, ALT/AST increased, pruritus, infusion-related reactions, chills. **Other serious undesirable effects: Uncommon (≥1/1000 to <1/100): *Monotherapy:*** PJP, staphylococcal bacteraemia, cytomegalovirus infection or reactivation, sepsis/septic shock, febrile neutropenia, anaphylactic reaction, TLS, demyelinating polyneuropathy, pancreatitis acute, SJS/TEN. ***Combination therapy:*** Herpes simplex, PJP, anaphylactic reaction, TLS, pancreatitis acute, SJS. **Frequency not known: *Monotherapy:*** PML, DRESS. **Refer to the SmPC for details on full side effect profile and interactions. UK basic NHS price:** £2,500 for each ADCETRIS 50 mg vial. **Legal classification:** POM. **Marketing authorisation (MA) number:** EU/1/12/794/001. **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-01824. **Date of preparation:** December 2021.

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.

▼ This medicinal product is subject to additional monitoring. Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com