Adcetris® ▼ (Brentuximab vedotin 50mg Powder for concentrate for solution for infusion in vial**)** This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions**.**

ABBREVIATED PRESCRIBING INFORMATION

Please refer India Package Insert, before prescribing.

Product Name: Brentuximab vedotin 50mg
Active Ingredient: Each vial contains 50 mg of Brentuximab vedotin. After reconstitution, each mL contains 5mg of Brentuximab vedotin.
Pharmaceutical Form: Powder for concentrate for solution for infusion in vial. White to off-white cake or powder. **Indication:** Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy: Adult patients with previously untreated Stage III or IV cHL, in combination with doxorubicin, vinblastine, and dacarbazine. Classical Hodgkin lymphoma (cHL) consolidation: Adult patients with cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation. Relapsed classical Hodgkin lymphoma (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 systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), in combination with chemotherapy: 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. Relapsed systemic anaplastic large cell lymphoma (sALCL): Adult patients with sALCL after failure of at least one prior multi-agent chemotherapy regimen. Relapsed primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30- expressing mycosis fungoides (MF): Adult patients with pcALCL or CD30-expressing MF who have received prior systemic therapy. **Dosage & Administration:** For the use of registered medical practitioner, hospital and laboratory only. Administer ADCETRIS as a 30-minute intravenous infusion. Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL): 1.2 mg/kg up to a maximum of 120 mg in combination with chemotherapy administered every 2 weeks until a maximum of 12 doses, disease progression or unacceptable toxicity. Classical Hodgkin Lymphoma Consolidation: 1.8 mg/kg up to a maximum of 180 mg administered 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. Relapsed Classical Hodgkin Lymphoma: 1.8 mg/kg up to a maximum of 180 mg administered every 3 weeks until disease progression or unacceptable toxicity. Previously Untreated Systemic ALCL or Other CD30-expressing Peripheral T-Cell Lymphomas: 1.8 mg/kg up to a maximum of 180 mg in combination with chemotherapy administered every 3 weeks with each cycle of chemotherapy for 6 to 8 doses. Relapsed Systemic ALCL: 1.8 mg/kg up to a maximum of 180 mg administered every 3 weeks until disease progression or unacceptable toxicity. Relapsed Primary Cutaneous ALCL or CD30-expressing Mycosis Fungoides: 1.8 mg/kg up to a maximum of 180 mg administered every 3 weeks until a maximum of 16 cycles, disease progression or unacceptable toxicity. The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg. Paediatric populations: Safety and effectiveness of ADCETRIS has not been established in pediatric patients. Elderly patients: No dosage adjustment required. Renal impairment: Avoid the use of ADCETRIS in patients with severe renal impairment (CrCL <30 mL/min). No dosage adjustment is required for mild (CrCL >50–80 mL/min) or moderate (CrCL 30–50 mL/min) renal impairment. Hepatic Impairment: Avoid the use of ADCETRIS in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment. Dosage reduction is required in patients with mild (Child-Pugh A) hepatic impairment. **Contraindications:** ADCETRIS is contraindicated with concomitant bleomycin due to pulmonary toxicity (e.g., interstitial infiltration and/or inflammation). **Special Warnings and Precautions for use:** Peripheral Neuropathy: ADCETRIS treatment causes a peripheral neuropathy that is predominantly sensory. Cases of peripheral motor neuropathy have also been reported. ADCETRIS-induced peripheral neuropathy is cumulative. Patients experiencing new or worsening peripheral neuropathy may require a delay, change in dose, or discontinuation of ADCETRIS. Anaphylaxis and Infusion Reactions: Infusion-related reactions, including anaphylaxis, have occurred with ADCETRIS. Monitor patients during infusion. If anaphylaxis occurs, immediately and permanently discontinue administration of ADCETRIS and administer appropriate medical therapy. If an infusion-related reaction occurs, interrupt the infusion and institute appropriate medical management. Patients who have experienced a prior infusion-related reaction should be premedicated for subsequent infusions. Premedication may include acetaminophen, an antihistamine, and a corticosteroid. Hematological Toxicities: Fatal and serious cases of febrile neutropenia have been reported with ADCETRIS. Prolonged (≥1 week) severe neutropenia and Grade 3 or Grade 4 thrombocytopenia or anemia can occur with ADCETRIS. Start primary prophylaxis with G-CSF beginning with Cycle 1 for patients who receive ADCETRIS in combination with chemotherapy. 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. If Grade 3 or 4 neutropenia develops, consider dose delays, reductions, discontinuation, or G-CSF prophylaxis with subsequent ADCETRIS doses. Serious Infections and Opportunistic Infections: Serious infections and opportunistic infections such as pneumonia, bacteremia, and sepsis or septic shock (including fatal outcomes) have been reported in patients treated with ADCETRIS. Monitor patients closely during treatment for the emergence of possible bacterial, fungal, or viral infections. Tumor Lysis Syndrome: Patients with rapidly proliferating tumor and high tumor burden may be at increased risk of tumor lysis syndrome. 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 compared to patients with normal renal function. Avoid the use of ADCETRIS in patients with severe renal impairment [creatinine clearance (CrCL) <30 mL/min]. 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 and severe hepatic impairment compared to patients with normal hepatic function. Avoid the use of ADCETRIS in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment. Hepatotoxicity: Fatal and serious cases of hepatotoxicity have occurred in patients receiving ADCETRIS. Cases were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin. Cases have occurred after the first dose of ADCETRIS or after ADCETRIS rechallenge. Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may also increase the risk. Monitor liver enzymes and bilirubin. Patients experiencing new, worsening, or recurrent hepatotoxicity may require a delay, change in dose, or discontinuation of ADCETRIS. Progressive Multifocal Leukoencephalopathy: Fatal cases of JC virus infection resulting in PML have been reported in ADCETRIS-treated patients. In addition to ADCETRIS therapy, other possible contributory factors include prior therapies and underlying disease that may cause immunosuppression. Consider the diagnosis of PML in any patient presenting with new-onset signs and symptoms of central nervous system abnormalities. Hold ADCETRIS dosing for any suspected case of PML and discontinue ADCETRIS dosing if a diagnosis of PML is confirmed. Pulmonary Toxicity: Fatal and serious events of noninfectious pulmonary toxicity including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome (ARDS), have been reported. Monitor patients for signs and symptoms of pulmonary toxicity, 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 Complications: Fatal and serious events of acute pancreatitis have been reported. Other fatal and serious gastrointestinal (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 events of hyperglycemia, such as new-onset hyperglycemia, exacerbation of preexisting diabetes mellitus, and ketoacidosis (including fatal outcomes) have been reported in ADCETRIS-treated patients. 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. Embryofetal Toxicities: Based on the mechanism of action and findings in animals, ADCETRIS can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of ADCETRIS in pregnant women. Advise females of reproductive potential to avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS. Advise a pregnant woman of the potential risk to the fetus. **Interactions:** Co-administration of ADCETRIS with ketoconazole, a potent CYP3A4 inhibitor, increased exposure to MMAE, which may increase the risk of adverse reaction. Closely monitor adverse reactions when ADCETRIS is given concomitantly with strong CYP3A4 inhibitors. **Elimination:** ADC elimination exhibited a multi-exponential decline with a t1/2 of approximately 4 to 6 days. MMAE elimination exhibited a mono-exponential decline with a t1/2 of approximately 3 to 4 days. Elimination of MMAE appeared to be limited by its rate of release from ADC. **Fertility, pregnancy and lactation:** ADCETRIS may damage spermatozoa and testicular tissue, resulting in possible genetic abnormalities. Males with female sexual partners of reproductive potential should use effective contraception during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS. Based on findings in rats, male fertility may be compromised by treatment with ADCETRIS. Advise females of reproductive potential to avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS. Advise females to immediately report pregnancy. ADCETRIS can cause fetal harm based on the findings from animal studies and the drug's mechanism of action. The available data from case reports on ADCETRIS use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. There is no information regarding the presence of brentuximab vedotin in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child from ADCETRIS, including cytopenias and neurologic or gastrointestinal toxicities, advise patients that breastfeeding is not recommended during ADCETRIS treatment. **Effects on ability to drive and use machines:** ADCETRIS may have a moderate influence on the ability to drive and use machines (e.g., dizziness). **Special population data:** Safety and effectiveness of ADCETRIS has not been established in pediatric patients. In the clinical trial of ADCETRIS in pcALCL or CD30-expressing MF (Study 4: ALCANZA), 42% of ADCETRIS-treated patients were age 65 or older. No meaningful differences in safety or efficacy were observed between geriatric patients and younger patients. **Undesirable Effects:** Previously

untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy: Adverse Reactions Reported in ≥10% of ADCETRIS + AVD-Treated: Anemia, neutropenia, febrile neutropenia, constipation, vomiting, diarrhea, stomatitis, abdominal pain, peripheral sensory neuropathy, peripheral motor neuropathy, pyrexia, bone pain, back pain, rashes, eruptions and exanthems, dyspnea, decreased weight, increased alanine aminotransferase, decreased appetite, insomnia. Adverse Reactions Reported in ≥10% in ADCETRIS-Treated Patients with Classical Hodgkin Lymphoma Post-Auto-HSCT Consolidation: Adverse Reactions Reported in ≥10% of ADCETRIS treated patients: neutropenia, thrombocytopenia, anemia, peripheral sensory neuropathy, peripheral motor neuropathy, headache, upper respiratory tract infection, fatigue, pyrexia, chills, nausea, diarrhea, vomiting, abdominal pain, constipation, cough, dyspnea, weight decreased, arthralgia, muscle spasms, myalgia, pruritus, decreased appetite. Adverse Reactions Reported in ≥10% of Patients with Relapsed Classical Hodgkin Lymphoma: Neutropenia, anemia, thrombocytopenia, lymphadenopathy, peripheral sensory neuropathy, peripheral motor neuropathy, headache, dizziness, fatigue, pyrexia, chills, upper respiratory tract infection, nausea, diarrhea, abdominal pain, vomiting, constipation, rash, pruritus, alopecia, night sweats, cough, dyspnea, oropharyngeal pain, arthralgia, myalgia, back pain, pain in extremity, insomnia, anxiety, decreased appetite. Adverse Reactions Reported in ≥10% of ADCETRIS + CHP-treated Patients with Previously Untreated, CD30-Expressing PTCL: Anemia, neutropenia, lymphopenia, febrile neutropenia, thrombocytopenia, nausea, diarrhea, mucositis, constipation, vomiting, abdominal pain, peripheral neuropathy, headache, dizziness, fatigue or asthenia, pyrexia, edema, upper respiratory tract infection, alopecia, rash, myalgia, dyspnea, cough, decreased appetite, hypokalemia, weight decreased, insomnia. Adverse Reactions Reported in ≥10% of Patients with Relapsed Systemic Anaplastic Large Cell Lymphoma: Neutropenia, anemia, thrombocytopenia, lymphadenopathy, peripheral sensory neuropathy, headache, dizziness, fatigue, pyrexia, chills, pain, edema peripheral, upper respiratory tract infection, nausea, diarrhea, vomiting, constipation, rash, pruritus, alopecia, dry skin, cough, dyspnea, myalgia, back pain, pain in extremity, muscle spasms, psychiatric disorders, insomnia, decreased appetite, weight decreased. Adverse Reactions Reported in ≥10% ADCETRIS-Treated Patients with pcALCL or CD30-Expressing MF: anemia, neutropenia, thrombocytopenia, peripheral sensory neuropathy, nausea, diarrhea, vomiting, fatigue, pyrexia, edema peripheral, asthenia, pruritus, alopecia, rash maculo-papular, pruritus generalized, decreased appetite, arthralgia, myalgia, dyspnea. **Overdosage/Overdose:** There is no known antidote for overdosage of ADCETRIS. In case of overdosage, the patient should be closely monitored for adverse reactions, particularly neutropenia, and supportive treatment should be administered. **Refer to the PI for details on full side effect profile and interactions. Pharmacotherapeutic Classification:** Immunosuppressive, Selective Immunosuppressive, ATC-Code: L04AA33.
Marketing Authorisation Holder: Takeda Pharmaceuticals India Pvt. Ltd. BLD B-4, Vadapa Village, Citylink Warehousing Complex, Mumbai Nashik Highway, Bhiwandi, Thane 421302, Maharashtra, India.

Adverse events should be reported to the authorities as required by local law. Adverse events should be reported to Takeda at AE.India@takeda.com

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