▼ 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. See section "Undesirable Effects" for how to report adverse reactions. NAME OF THE MEDICINAL PRODUCT ADCETRIS 50 mg powder for concentrate for solution for infusion. QUALITATIVE AND QUANTITATIVE COMPOSITION Each vial contains 50 mg of brentuximab vedotin. After reconstitution, each mL contains 5 mg of brentuximab vedotin. ADCETRIS is an antibody-drug conjugate composed of a CD30-directed monoclonal antibody (recombinant chimeric immunoglobulin G1 [IgG1], produced by recombinant DNA technology in Chinese Hamster ovary cells) that is covalently linked to the antimicrotubule agent monomethyl auristatin E (MMAE). Excipient with known effect Each vial contains approximately 13.2 mg of sodium. PHARMACEUTICAL form Powder for concentrate for solution for infusion. White to off-white cake or powder. THERAPEUTIC INDICATIONS ADCETRIS is indicated for adult patients with previously untreated CD30+ Stage IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD). ADCETRIS is indicated for the treatment of adult patients with CD30+ HL at increased risk of relapse or progression following autologous stem cell transplant (ASCT). ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL): following ASCT, or following at least two prior therapies when ASCT or multi -agent chemotherapy is not a treatment option. ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL). ADCETRIS is indicated for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy. POSOLOGY AND METHOD OF ADMINISTRATION ADCETRIS should be administered under the supervision of a physician experienced in the use of anti-cancer agents. Posology *Previously Untreated HL* The recommended dose in combination with chemotherapy (doxorubicin [A], vinblastine [V] and dacarbazine [D] [AVD]) is 1.2 mg/kg administered as an intravenous infusion over 30 minutes on days 1 and 15 of each 28-day cycle for 6 cycles. Primary prophylaxis with growth factor support (G-CSF) is recommended for all patients with previously untreated HL receiving combination therapy beginning with the first dose. Refer to the summary of product characteristics (SmPC) of chemotherapy agents given in combination with ADCETRIS for patients with previously untreated HL. *HL at increased risk of relapse or progression* The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. ADCETRIS treatment should start following recovery from ASCT based on clinical judgment. These patients should receive up to 16 cycles. *Relapsed or refractory HL* The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. The recommended starting dose for the retreatment of patients who have previously responded to treatment with ADCETRIS is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Alternatively, treatment may be started at the last tolerated dose. Treatment should be continued until disease progression or unacceptable toxicity. Patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year). *sALCL* The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. The recommended starting dose for the retreatment of patients who have previously responded to treatment with ADCETRIS is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Alternatively, treatment may be started at the last tolerated dose. Treatment should be continued until disease progression or unacceptable toxicity. Patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year). *CTCL* The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Patients with CTCL 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 of this treatment. Patients should be monitored during and after infusion. Dose adjustments *Neutropenia* If neutropenia develops during treatment it should be managed by dose delays. See Table 1 below for appropriate dosing recommendations. **Table 1: Dosing recommendations for neutropenia. Severity grade of neutropenia (signs and symptoms** [abbreviated description of CTCAE[a]). **Grade 1** (< LLN-1500/mm^3 < LLN-1.5 x 10^9/L) or **Grade 2** (< 1500-1000/mm^3 < 1.5-1.0 x 10^9/L). **Monotherapy. Modification of dosing schedule:** Continue with the same dose and schedule. **Combination therapy** Note: Primary prophylaxis with G-CSF is recommended for all patients receiving combination therapy beginning with the first dose. **Modification of dosing schedule:** Continue with the same dose and schedule. **Severity grade of neutropenia (signs and symptoms** [abbreviated description of CTCAE[a]). **Grade 3** (< 1,000-500/ mm^3 < 1.0-0.5 x 10^9/L) or **Grade 4** (< 500/mm^3 < 0.5 x 10^9/L). **Monotherapy. Modification of dosing schedule:** Withhold dose until toxicity returns to ≤ Grade 2 or baseline then resume treatment at the same dose and schedule [b]. Consider G-CSF or GM-CSF in subsequent cycles for patients who develop Grade 3 or Grade 4 neutropenia. **Combination therapy** Note: Primary prophylaxis with G-CSF is recommended for all patients receiving combination therapy beginning with the first dose. **Modification of dosing schedule:** Consider G-CSF or GM-CSF in subsequent cycles for patients who develop Grade 3 or Grade 4 neutropenia. Grading based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v3.0; see Neutrophils/ granulocytes; LLN = lower limit of normal Patients who develop Grade 3 or Grade 4 lymphopenia may continue treatment without interruption. *Peripheral neuropathy* If peripheral sensory or motor neuropathy emerges or worsens during treatment see Table 2 below for appropriate dosing recommendations. **Table 2: Dosing recommendations for new or worsening peripheral sensory or motor neuropathy Severity of peripheral sensory or motor neuropathy (signs and symptoms** [abbreviated description of CTCAE[a]). **Grade 1** (paraesthesia and/or loss of reflexes, with no loss of function). **Monotherapy. Modification of dose and schedule:** Continue with the same dose and schedule. **Combination therapy. Modification of dose and schedule:** Continue with the same dose and schedule. **Severity of peripheral sensory or motor neuropathy (signs and symptoms** [abbreviated description of CTCAE[a]). **Grade 2** (interfering with function but not with activities of daily living). **Monotherapy. Modification of dose and schedule:** Withhold dose until toxicity returns to ≤ Grade 1 or baseline, then restart treatment at a reduced dose of 1.2 mg/kg up to a maximum of 120 mg every 3 weeks. **Combination therapy. Modification of dose and schedule:** Reduce dose to 0.9 mg/kg up to a maximum of 90 mg every 2 weeks. **Severity of peripheral sensory or motor neuropathy (signs and symptoms** [abbreviated description of CTCAE[a]). Grade 3 (interfering with activities of daily living). **Monotherapy. Modification of dose and schedule:** Withhold dose until toxicity returns to ≤ Grade 1 or baseline, then restart treatment at a reduced dose of 1.2 mg/kg every 3 weeks. **Combination therapy. Modification of dose and schedule:** Withhold treatment with ADCETRIS until toxicity is ≤ Grade 2, then restart treatment at a reduced dose to 0.9 mg/kg every 2 weeks. **Severity of peripheral sensory or motor neuropathy (signs and symptoms** [abbreviated description of CTCAE[a]). **Grade 4** (sensory neuropathy which is disabling or motor neuropathy that is life threatening or leads to paralysis). **Monotherapy. Modification of dose and schedule:** Discontinue treatment. **Combination therapy. Modification of dose and schedule:** Discontinue treatment. Grading based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v3.0; see neuropathy: motor; neuropathy: sensory; and neuropathic pain. Special patient populations Renal and hepatic impairment Combination therapy Patients with renal impairment should be closely monitored for adverse events. There is no clinical trial experience using ADCETRIS in combination with chemotherapy in patients with renal impairment, where serum creatinine is ≥ 2.0 mg/dL and/or creatinine clearance or calculated creatinine clearance is ≤ 40 mL/minute. Use of ADCETRIS in combination with chemotherapy should be avoided in patients with severe renal impairment. Patients with hepatic impairment should be closely monitored for adverse events. The recommended starting dose in patients with mild hepatic impairment is 0.9 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. There is no clinical trial experience using ADCETRIS in combination with chemotherapy in patients with hepatic impairment, where total bilirubin is > 1.5 times the upper limit of normal (ULN) (unless due to Gilbert syndrome), or aspartate aminotransferase (AST) or alanine aminotransferase (ALT) are > 3 times the ULN, or > 5 times the ULN if their elevation may be reasonably ascribed to the presence of HL in the liver. Use of ADCETRIS in combination with chemotherapy should be avoided in patients with moderate and severe hepatic impairment. Monotherapy The recommended starting dose in patients with severe renal impairment is 1.2 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Patients with renal impairment should be closely monitored for adverse events. The recommended starting dose in patients with hepatic impairment is 1.2 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Patients with hepatic impairment should be closely monitored for adverse events. Elderly The dosing recommendations for patients aged 65 and older are the same as for adults. Currently available data are described in section "Undesirable Effects" (and 5.1 and 5.2 in full SmPC). Paediatric population The safety and efficacy of ADCETRIS in children less than 18 years have not yet been established. Currently available data are described in section "Undesirable Effects" (and 5.1 and 5.2 in full SmPC) but no recommendation on a posology can be made. In nonclinical studies, thymus depletion has been observed. Method of administration The recommended dose of ADCETRIS is infused over 30 minutes. For instructions on reconstitution and dilution of the medicinal product before administration (see section 6.6 in full SmPC). 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 to any of the excipients. Combined use of bleomycin and ADCETRIS causes pulmonary toxicity. UNDESIRABLE EFFECTS Summary of the safety profile The safety profile of ADCETRIS is based on available clinical trial data, the Named Patient Program (NPP), and post-marketing experience to date. Frequencies of adverse reactions described below and in Table 3 have been determined based on data generated from clinical studies. *Monotherapy* In the pooled dataset of ADCETRIS as monotherapy across HL, sALCL and CTCL studies (SG035-0003, SG035-0004, SGN35-005, SGN35-006, C25001 and C25007) the most frequent adverse reactions (≥ 10%) were infections, peripheral sensory neuropathy, nausea, fatigue, diarrhoea, pyrexia, upper respiratory tract infection, neutropenia, rash, cough, vomiting, arthralgia, peripheral motor neuropathy, infusion-related reactions, pruritus, constipation, dyspnoea, weight decreased, myalgia and abdominal pain. Serious adverse drug reactions occurred in 12% of patients. The frequency of unique serious adverse drug reactions was ≤ 1%. Adverse events led to treatment discontinuation in 24% of patients receiving ADCETRIS. The safety data in patients retreated with ADCETRIS (SGN35-006) were consistent with those observed in the combined pivotal phase 2 studies, with the exception of peripheral motor neuropathy, which had a higher incidence (28% vs. 9% in the pivotal phase 2 studies) and was primarily Grade 2. Patients also had a higher incidence of arthralgia, Grade 3 anaemia, and back pain compared to patients observed in the combined pivotal phase 2 studies. The safety data in patients with relapsed or refractory HL who had not received an autologous stem cell transplant and were treated with the recommended dose of 1.8 mg/kg every three weeks in a single-arm phase 4 study (n = 60), the phase 1 dose escalation and clinical pharmacology studies (n = 15 patients) and in the NPP (n = 26 patients) were consistent with the safety profile of the pivotal clinical studies. *Combination therapy* For safety information of chemotherapy agents given in combination with ADCETRIS (doxorubicin, vinblastine and dacarbazine) for newly diagnosed patients with HL, refer to their summary of product characteristics. In the study of ADCETRIS as combination therapy with AVD in 662 patients with previously untreated advanced HL (C25003), the most common adverse reactions (≥ 10%) were: neutropenia, nausea, constipation, vomiting, fatigue, peripheral sensory neuropathy, diarrhoea, pyrexia, alopecia, peripheral motor neuropathy, decreased weight, abdominal pain, anaemia, stomatitis, febrile neutropenia, bone pain, insomnia, decreased appetite, cough, headache, arthralgia, back pain, dyspnoea, myalgia, upper respiratory tract infection, alanine aminotransferase increased. In patients receiving ADCETRIS combination therapy, serious adverse reactions occurred in 36% of patients. Serious adverse reactions occurring in ≥ 3% of patients included febrile neutropenia (17%), pyrexia (6%), and neutropenia (3%). Adverse events led to treatment discontinuation in 13% of patients. Adverse events that led to treatment discontinuation in ≥ 2% of patients included peripheral sensory neuropathy, peripheral neuropathy, and peripheral motor neuropathy. Tabulated list of adverse reactions Adverse reactions for ADCETRIS are listed by MedDRA System Organ Class and Preferred Term (see Table 3). Within each System Organ Class, adverse reactions are listed under frequency categories of: Very common (≥ 1/10); Common (≥ 1/100 to < 1/10); Uncommon (≥ 1/1,000 to < 1/100); Rare (≥ 1/10,000 to < 1/1,000); Very rare (< 1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. **Table 3: Adverse reactions to ADCETRIS System organ class. Infections and infestations:** Very common. **Adverse reactions (monotherapy):** Infection[a], upper respiratory tract infection. **Adverse reactions (combination therapy):** Infection[a], upper respiratory tract infection. **System organ class. Infections and infestations:** Common. **Adverse reactions (monotherapy):** Herpes zoster, pneumonia, herpes simplex, oral candidiasis. **Adverse reactions (combination therapy):** Pneumonia, oral candidiasis, sepsis/septic shock, herpes simplex. **System organ class. Infections and infestations:** Uncommon. **Adverse reactions (monotherapy):** Pneumocystis jiroveci pneumonia, staphylococcal bacteraemia, cytomegalovirus infection or reactivation, sepsis/ septic shock. **Adverse reactions (combination therapy):** Herpes zoster, Pneumocystis jiroveci pneumonia. **System organ class. Infections and infestations:** Frequency not known. **Adverse reactions (monotherapy):** Progressive multifocal leukoencephalopathy. **System organ class. Blood and lymphatic system disorders:** Very common. **Adverse reactions (monotherapy):** Neutropenia. **Adverse reactions (combination therapy):** Neutropenia[a], anaemia, febrile neutropenia. **System organ class. Blood and lymphatic system disorders:** Common. **Adverse reactions (monotherapy):** Anaemia, thrombocytopenia. **Adverse reactions (combination therapy):** Thrombocytopenia. **System organ class. Blood and lymphatic system disorders:** Uncommon. **Adverse reactions (monotherapy):** Febrile neutropenia. **System organ class. Immune system disorders:** Uncommon. **Adverse reactions (monotherapy):** Anaphylactic reaction. **Adverse reactions (combination therapy):** Anaphylactic reaction. **System organ class. Metabolism and nutrition disorders:** Very common. **Adverse reactions (combination therapy):** Decreased appetite. **System organ class. Metabolism and nutrition disorders:** Common. **Adverse reactions (monotherapy):** Hyperglycaemia. **Adverse reactions (combination therapy):** Decreased appetite. **System organ class. Metabolism and nutrition disorders:** Uncommon. **Adverse reactions (combination therapy):** Tumour lysis syndrome. **Adverse reactions (combination therapy):** Tumour lysis syndrome. **System organ class. Nervous system disorders:** Very common. **Adverse reactions (monotherapy):** Peripheral sensory neuropathy, peripheral motor neuropathy. **Adverse reactions (combination therapy):** Peripheral sensory neuropathy, peripheral motor neuropathy[a], dizziness. **System organ class. Nervous system disorders:** Common. **Adverse reactions (monotherapy):** Dizziness. **System organ class. Nervous system disorders:** Uncommon. **Adverse reactions (monotherapy):** Demyelinating polyneuropathy. **System organ class. Respiratory, thoracic and mediastinal disorders:** Very common. **Adverse reactions (monotherapy):** Cough, dyspnoea. **Adverse reactions (combination therapy):** Cough, dyspnoea. **System organ class. Gastro-intestinal disorders:** Very common. **Adverse reactions (monotherapy):** Nausea, diarrhoea vomiting, constipation, abdominal pain. **Adverse reactions (combination therapy):** Nausea, constipation, vomiting, diarrhoea, abdominal pain, stomatitis. **System organ class. Gastro-intestinal disorders:** Uncommon. **Adverse reactions (monotherapy):** Pancreatitis acute. **Adverse reactions (combination therapy):** Pancreatitis acute. **System organ class. Hepatobiliary disorders:** Very common. **Adverse reactions (combination therapy):** Ianine aminotransferase (ALT) increased. **System organ class. Hepatobiliary disorders:** Common. **Adverse reactions (monotherapy):** Alanine aminotransferase/aspartate, aminotransferase (ALT/AST) increased. **Adverse reactions (combination therapy):** Alanine aminotransferase/ aspartate, aminotransferase (ALT/AST) increased. **System organ class. Skin and subcutaneous tissue disorders:** Very common. **Adverse reactions (monotherapy):** Rash[a], pruritus. **Adverse reactions (combination therapy):** Alopecia, rash[a]. **System organ class. Skin and subcutaneous tissue disorders:** Common. **Adverse reactions (monotherapy):** Alopecia. **Adverse reactions (combination therapy):** Pruritus. **System organ class. Skin and subcutaneous tissue disorders:** Uncommon. **Adverse reactions (monotherapy):** Stevens-Johnson syndrome/toxic epidermal necrolysis. **Adverse reactions (combination therapy):** Stevens-Johnson syndrome[b]. **System organ class. Musculoskeletal and connective tissue disorders:** Very common. **Adverse reactions (monotherapy):** Arthralgia, myalgia. **Adverse reactions (combination therapy):** Bone pain, arthralgia, back pain, myalgia. **System organ class. Musculoskeletal and connective tissue disorders:** Common. **Adverse reactions (monotherapy):** Back pain. **System organ class. General disorders and administration site conditions:** Very common. **Adverse reactions (monotherapy):** Fatigue, pyrexia, infusion-related reactions[a]. **Adverse reactions (combination therapy):** Fatigue, pyrexia. **System organ class. General disorders and administration site conditions:** Common. **Adverse reactions (monotherapy):** Chills. **Adverse reactions (combination therapy):** Infusion-related reactions[a], chills. **System organ class. Investigations:** Very common. **Adverse reactions (monotherapy):** Weight decreased. **Adverse reactions (combination therapy):** Weight decreased. **System organ class. Investigations:** Very common. **Adverse reactions (combination therapy):** Insomnia. Represents pooling of preferred terms. Toxic epidermal necrolysis was not reported in the combination therapy setting. Description of selected adverse reactions *Neutropenia and febrile neutropenia* Monotherapy In clinical trials, neutropenia led to dose delays in 14% of patients. Grade 3 neutropenia was reported in 13% and Grade 4 neutropenia was reported in 5% of patients. No patients required dose reduction or discontinued treatment for neutropenia. Severe and prolonged (≥ 1 week) neutropenia can occur with this treatment which may increase the risk of patients developing serious infections. Febrile neutropenia reported in < 1% of the patients. In the pivotal phase 2 population (SG035-0003 and SG035-0004), the median duration of Grade 3 or Grade 4 neutropenia was limited (1 week); 2% of patients had Grade 4 neutropenia that lasted ≥ 7 days. Less than half of the patients in the pivotal phase 2 population with Grade 3 or Grade 4 neutropenia had temporally associated infections, and the majority of temporally associated infections were Grade 1 or Grade 2. Combination therapy In the clinical trial of ADCETRIS as combination therapy, neutropenia led to dose delays in 24% of patients. Grade 3 neutropenia was reported in 18% and Grade 4 neutropenia was reported in 47% of patients. Two percent of patients required dose reduction and < 1% discontinued one of more of the study drugs due to neutropenia. Febrile neutropenia was reported in 21% of the patients who did not receive primary prophylaxis with G-CSF. The frequency of febrile neutropenia was 11% in patients who received primary prophylaxis with G-CSF. *Serious infections and opportunistic infections* Monotherapy In clinical trials, serious infections and opportunistic infections occurred in 10% of patients, sepsis or septic shock occurred in < 1% of the patients. The most commonly reported opportunistic infections were herpes zoster and herpes simplex. Combination therapy In the clinical trial of ADCETRIS as combination therapy, serious infections including opportunistic infections occurred in 15% of patients; sepsis, neutropenic sepsis, septic shock or bacteraemia occurred in 4% of the patients. The most commonly reported opportunistic infections were herpes viral infections. *Peripheral neuropathy* Monotherapy In clinical trials treatment emergent neuropathy occurred in 59% of the population, peripheral motor neuropathy occurred in 14% of patients. Peripheral neuropathy led to treatment discontinuation in 15%, dose reductions in 15%, and dose delays in 17% of patients. For patients who experienced peripheral neuropathy the median time of onset of peripheral neuropathy was 12 weeks. The median duration of treatment for patients who discontinued due to peripheral neuropathy was 12 cycles. Among patients who experienced peripheral neuropathy in the pivotal phase 2 studies (SG035-0003 and SG035-0004) and randomised phase 3 monotherapy studies (SGN35-005 and C25001), the median follow up time from end of treatment until last evaluation ranged from 48.9 to 98 weeks. At the time of last evaluation, most of the patients (82-85%) who experienced peripheral neuropathy had resolution or improvement of their peripheral neuropathy symptoms. The median time from onset to resolution or improvement for all events ranged from 16 to 23.4 weeks. In patients with relapsed or refractory HL or sALCL who were retreated with ADCETRIS (SGN35-006), the majority of patients (80%) also had improvement or resolution of their peripheral neuropathy symptoms at the time of last evaluation. Combination therapy In the clinical trial of ADCETRIS as combination therapy, treatment emergent neuropathy occurred in 67% of the population; peripheral motor neuropathy occurred in 11% of patients. Peripheral neuropathy led to treatment discontinuation in 7%, dose reductions in 21%, and dose delays in 1% of patients. For patients who experienced peripheral neuropathy the median time of onset of peripheral neuropathy was 8 weeks. Patients who discontinued due to peripheral neuropathy received a median of 8 doses of ADCETRIS+AVD (A+AVD) before discontinuation of one or more agents. Among patients who experienced peripheral neuropathy, the median follow up time from end of treatment until last evaluation was approximately 91 weeks. At the time of last evaluation, most of the patients (76%) who experienced peripheral neuropathy had resolution or improvement of their peripheral neuropathy symptoms. The median time from onset to resolution or improvement of peripheral neuropathy events was 10 weeks (ranged from 0 weeks to 139 weeks). *Infusion-related reactions* Monotherapy IRRs, such as headache, rash, back pain, vomiting, chills, nausea, dyspnoea, pruritus and cough were reported in 13% of patients. Anaphylactic reactions have been reported. Symptoms of an anaphylactic reaction may include, but are not limited to, urticaria, angioedema, hypotension and bronchospasm. Combination therapy IRRs, such as headache, rash, back pain, vomiting, chills, nausea, dyspnoea, pruritus, cough, infusion site pain and pyrexia were reported in 9% of patients. Anaphylactic reactions have been reported. Symptoms of an anaphylactic reaction may include, but are not limited to, urticaria, angioedema, hypotension and bronchospasm. *Immunogenicity* In clinical trials, patients were periodically tested for antibodies to brentuximab vedotin using a sensitive electrochemiluminescent immunoassay. There was a higher incidence of infusion-related reactions observed in patients with antibodies to brentuximab vedotin relative to patients who tested transiently positive or negative. The presence of antibodies to brentuximab vedotin did not correlate with a clinically meaningful reduction in serum brentuximab vedotin levels and did not result in a decrease in the efficacy of brentuximab vedotin. While the presence of antibodies to brentuximab vedotin does not necessarily predict the development of an IRR, there was a higher incidence of IRRs observed in patients with persistently positive anti-drug antibodies (ADA) relative to patients with transiently positive ADA and never positive ADA. There was a trend of increased clearance of brentuximab vedotin in paediatric patients confirmed positive for ADAs. No patients aged < 12 years (0 of 11) and 2 patients aged ≥ 12 years (2 of 23) became persistently ADA positive. Paediatric population Safety was evaluated in a phase 1/2 study in paediatric patients aged 7-17 years of age (n = 36) with relapsed or refractory (r/r) HL and sALCL. In this study in 36 patients, no new safety concerns were reported. Elderly *Monotherapy* The safety profile in elderly patients was consistent with that of adult patients. *Combination therapy* In older patients (≥ 60 years of age; n = 83 [13%]), the incidence of adverse events was similar across treatment arms. More serious adverse events and dose modifications (including dose delays, reductions, and discontinuations) were reported in the older patients compared with the overall study population. Advanced age was a risk factor for febrile neutropenia in patients in both arms. Older patients who received G-CSF primary prophylaxis had lower incidence of neutropenia and febrile neutropenia than those who did not receive G-CSF primary prophylaxis. Reporting of suspected adverse reactions Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system: **Belgium** Federal Agency for Medicines and Health Products Vigilance of medicines for human use EUROSTATION II Victor Hortaplein, 40/40 B-1060 Brussels Website : www.fagg.be e-mail : adversedrugreactions@fagg-afmps.be **Luxembourg** Direction de la Santé – Division de la Pharmacie et des Médicaments Villa Louvigny – Allée Marconi L-2120 Luxembourg Website: http://www.ms.public.lu/fr/ activites/pharmacie-medicament/index.html NATURE AND CONTENTS OF CONTAINER Type I glass vial with a butyl rubber stopper and an aluminium/plastic flip-off seal, containing 50 mg powder. Pack of 1 vial. MARKETING AUTHORISATION HOLDER Takeda Pharma A/S Dybendal Alle 10 2630 Taastrup Denmark MARKETING AUTHORISATION NUMBER EU/1/12/794/001 LEGAL STATUS Medicinal product subject to medical prescription DATE OF REVISION OF THE TEXT 06/02/2019 Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

(*) hospital use only - (**) incl. IFN-alpha, methotrexate or bexarotene or a combination of those - CTCL : cutaneous T-Cell lymphoma – MF: Mycosis Fungoides – pcALCL: primary cutaneous Anaplasic Large cell Lymhoma.
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Takeda