	Hospital Price
0.2 to 5 x 10^6 CAR positive viable T cells/kg body weight	€ 320.000
0.1 to 2.5 x 10^8 CAR positive viable T cells	€ 320.000
0.6 to 6 x 10^8 CAR positive viable T cells	€ 320.000

▼ 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 4.8 of the full leafletfor how to report adverse reactions. **Name:** Kymriah 1.2 x 10^6 – 6 x 10^8 cells dispersion for infusion **Composition:** Kymriah is an immunocellular therapy containing tisagenlecleucel, autologous T cells genetically modified *ex vivo* using a lentiviral vector encoding an anti-CD19 chimeric antigen receptor (CAR). Each ethylene vinyl acetate (EVA) infusion bag of Kymriah contains tisagenlecleucel cell dispersion at a batch-dependent concentration of autologous T cells genetically modified to express an anti-CD19 chimeric antigen receptor (CAR-positive viable T cells) (see full leaflet). The concentration of CAR-positive viable T cells is dependent on indication and patient body weight (for B-cell acute lymphoblastic leukaemia [ALL]). The cellular composition and the final cell number varies between individual patient batches. In addition to T cells, NK cells may be present. The quantitative information regarding CAR-positive viable T cells/mL and total cells in the product is presented in the batch-specific documentation accompanying Kymriah. 1 or more infusion bags containing a total of 1.2 x 10^6 to 6 x 10^8 CAR-positive viable T cells. Excipient with known effect: This medicinal product contains 2.43 mg sodium per mL and 24.3 to 121.5 mg sodium per dose. For the full list of excipients, see full leaflet. **Pharmaceutical form:** Dispersion for infusion. A colourless to slightly yellow dispersion. **Therapeutic indications:** Kymriah is indicated for the treatment of (i) Paediatric and young adult patients up to and including 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse. (ii) Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. **Posology:** Kymriah must be administered in a qualified treatment centre. Therapy should be initiated under the direction of and supervised by a healthcare professional experienced in the treatment of haematological malignancies and trained for administration and management of patients treated with Kymriah. Tocilizumab for use in the event of cytokine release syndrome and emergency equipment must be available per patient prior to infusion. The treatment centre must have access to additional doses of tocilizumab within 8 hours. Kymriah is intended for autologous use only (see full leaflet). Manufacture and release of Kymriah usually takes about 3-4 weeks. *Dosage in paediatric and young adult B-cell ALL patients*: For patients 50 kg and below: 0.2 to 5 x 10^6 CAR-positive viable T cells/kg body weight. For patients above 50 kg: 0.1 to 2.5 x 10^8 CAR-positive viable T cells (non-weight based). *Dosage in adult DLBCL patients*: 0.6 to 6 x 10^8 CAR-positive viable T cells (non-weight based). Pre-treatment conditioning (lymphodepleting chemotherapy): Lymphodepleting chemotherapy is recommended to be administered before Kymriah infusion unless the white blood cell (WBC) count within one week prior to infusion is ≤1,000 cells/µL. Kymriah is recommended to be infused 2 to 14 days after completion of the lymphodepleting chemotherapy. The availability of Kymriah must be confirmed prior to starting the lymphodepleting regimen. If there is a delay of more than 4 weeks between completing lymphodepleting chemotherapy and the infusion and the WBC count is >1,000 cells/µL, then the patient should be re-treated with lymphodepleting chemotherapy prior to receiving Kymriah. *B-cell ALL:* The recommended lymphodepleting chemotherapy regimen is: Fludarabine (30 mg/m^2 intravenous daily for 4 days) and cyclophosphamide (500 mg/m^2 intravenous daily for 2 days starting with the first dose of fludarabine). If the patient experienced a previous Grade 4 haemorrhagic cystitis with cyclophosphamide, or demonstrated a chemorefractory state to a cyclophosphamide-containing regimen administered shortly before lymphodepleting chemotherapy, then the following should be used: Cytarabine (500 mg/m^2 intravenous daily for 2 days) and etoposide (150 mg/m^2 intravenous daily for 3 days starting with the first dose of cytarabine). *DLBCL:* The recommended lymphodepleting chemotherapy regimen is: Fludarabine (25 mg/m^2 intravenous daily for 3 days) and cyclophosphamide (250 mg/m^2 intravenous daily for 3 days starting with the first dose of fludarabine). If the patient experienced a previous Grade 4 haemorrhagic cystitis with cyclophosphamide, or demonstrated a chemorefractory state to a cyclophosphamide-containing regimen administered shortly before lymphodepleting chemotherapy, then the following should be used: Bendamustine (90 mg/m^2 intravenous daily for 2 days). Lymphodepleting chemotherapy may be omitted if a patient's white blood cell (WBC) count is ≤1,000 cells/µL within 1 week prior to Kymriah infusion. *Pre-medication:* To minimise potential acute infusion reactions, it is recommended that patients be pre-medicated with paracetamol and diphenhydramine or another H1 antihistamine within approximately 30 to 60 minutes prior to Kymriah infusion. Corticosteroids should not be used at any time except in the case of a life-threatening emergency (see full leaflet). Clinical assessment prior to infusion: Kymriah treatment should be delayed in some patient groups at risk (see full leaflet). *Monitoring after infusion:* Patients should be monitored daily for the first 10 days following infusion for signs and symptoms of potential cytokine release syndrome, neurological events and other toxicities. Physicians should consider hospitalisation for the first 10 days post infusion or at the first signs/symptoms of cytokine release syndrome and/or neurological events. After the first 10 days following the infusion, the patient should be monitored at the physician's discretion. Patients should be instructed to remain within proximity (within 2 hours of travel) of a qualified clinical facility for at least 4 weeks following infusion. Special populations: *Paediatric population: B-cell ALL*: No formal studies have been performed in paediatric patients below 3 years of age. *DLBCL*: The safety and efficacy of Kymriah in children and adolescents below 18 years of age have not yet been established. No data are available. *Elderly: B-cell ALL*: The safety and efficacy of Kymriah in this population have not been established. *DLBCL*: No dose adjustment is required in patients over 65 years of age. *Patients seropositive for hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV):* There is no experience with manufacturing Kymriah for patients with a positive test for HIV, active HBV, or active HCV infection. Leukapheresis material from these patients will not be accepted for Kymriah manufacturing. Screening for HBV, HCV, and HIV must be performed in accordance with clinical guidelines before collection of cells for manufacturing. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the full leaflet. Contraindications of the lymphodepleting chemotherapy must be considered. **Undesirable effects:** Summary of the safety profile: Safety assessment was based on a total of 194 patients (with paediatric and young adult B-cell ALL and DLBCL) who received Kymriah in two multi-centre pivotal clinical studies. *B-cell ALL:* The adverse reactions described in this section were characterised in 79 patients infused with Kymriah in the multi-centre, pivotal clinical study CCTL019B2202. The most common non-haematological adverse reactions were cytokine release syndrome (77%), infections (73%), hypogammaglobulinaemia (53%), pyrexia (42%) and decreased appetite (38%). The most common haematological adverse reactions were decreased white blood cells (100%), decreased haemoglobin (100%), decreased neutrophils (100%), decreased lymphocytes (100%) and decreased platelets (97%). Grade 3 and 4 adverse reactions were reported in 89% of patients. The most common Grade 3 and 4 non-haematological adverse reaction was cytokine release syndrome (48%). The most common Grade 3 and 4 haematological laboratory abnormalities were white blood cells decreased (97%), lymphocytes decreased (96%), neutrophils decreased (95%), platelets decreased (77%) and haemoglobin decreased (48%). Grade 3 and 4 adverse reactions were more often observed within the initial 8 weeks post-infusion (82% of patients) compared to after 8 weeks post-infusion (51% of patients). *DLBCL:* The adverse reactions described in this section were characterised in 115 patients infused with Kymriah in one global multicentre international study, i.e. the ongoing pivotal clinical study CCTL019C2201. The most common non-haematological adverse reactions were cytokine release syndrome (57%), infections (58%), pyrexia (35%), diarrhoea (31%), nausea (29%), fatigue (27%) and hypotension (25%). The most common haematological adverse reactions were decreased lymphocytes (100%), decreased white blood cells (99%), decreased haemoglobin (99%), decreased neutrophils (97%), and decreased platelets (95%). Grade 3 and 4 adverse reactions were reported in 88% of patients. The most common Grade 3 and 4 non-haematological adverse reactions were infections (34%) and cytokine release syndrome (23%). The most common (>25%) Grade 3 and 4 haematological laboratory abnormalities were lymphocyte count decreased (95%), neutrophil count decreased (82%), white blood cell count decreased (78%), haemoglobin decreased (59%) and platelet count decreased (56%). Grade 3 and 4 adverse reactions were more often observed within the initial 8 weeks post-infusion (82%) compared to after 8 weeks post-infusion (48%). Tabulated list of adverse drug reactions and Description of selected adverse drug reactions: Cytokine release syndrome, Infections and febrile neutropenia, Prolonged cytopenias, Neurological adverse reactions, Hypogammaglobulinaemia, Immunogenicity: see full leaflet. 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. **Marketing authorisation holder and number:** Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Ireland; EU/1/18/1297/001. **Date of revision of the text:** 17.07.2020. Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

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