Tisagenlecleucel (Kymriah®) in the treatment of B-cell acute lymphoblastic leukaemia
Approved at the Council for Choices in Health Care in Finland's meeting on 13 March 2019

Council for Choices in Health Care in Finland recommendation		Tisagenlecleucel is included in Finland's national range of services in the treatment of B-cell acute lymphoblastic leukaemia (ALL) in paediatric patients and young adult patients up to 25 years of age when the disease has not responded to the previous treatment (refractory disease), has come back two or more times, or has come back after a transplant of stem cells. A precondition for this recommendation is that the marketing authorisation holder and the buyer agree on a price for the product that is lower than the wholesale price. Treatments must be centralised because of the advanced nature of the therapy and the small size of the target group. Information about the effects of the therapy should be collected in a systematic and consistent manner. The position of the therapy in Finland's national range of services will be re-assessed in 2023 at the latest.
Areas of assessment	Severity and prevalence of the health issue	In children and young adults, the prognosis of ALL is good. With present therapies, about 85–90% are cured permanently. For a relapsed disease, the prognosis is poorer and there are fewer treatment alternatives available. The prognosis is markedly poor if the disease is refractory or has come back after a transplant of stem cells or after two or more previous treatment cycles. The number of patients in Finland who are eligible for tisagenlecleucel therapy is not more than 4–8 per year.
	Treatment alternatives	The only potentially curing treatment alternative for patients who are eligible for tisagenlecleucel therapy is allogeneic transplantation of stem cells. However, for a significant part of patients, the transplantation of stem cells is not possible. In the previous studies where different treatment alternatives were used in the treatment of refractory or relapsed ALL, half of the patients died in 3–11 months after their admission to the study or commencement of therapy.
	Effectiveness	Based on research evidence, the results of tisagenlecleucel therapy are better than those reported for the other treatment alternatives for refractory or relapsed ALL. According to the published data, about four-fifths of the patients achieved a complete or partial response. However, the clinical evidence involves significant limitations, such as the single-arm study setting without a control group and the short follow-up period. For this reason, there is no evidence available on the long-term effects of tisagenlecleucel therapy and the prognosis of the treated patients.
	Safety	The tisagenlecleucel therapy causes severe adverse reactions in most patients. Some of the adverse reactions are life-threatening, and the effects of the therapy may also result in permanent incapacity.
	Costs and budget impacts	The wholesale price of the tisagenlecleucel preparation is €320,000. In addition to the price of the medicine, the treatment of a single patient involves other costs in the amount of approximately €130,000 during the first year of treatment. If 4–8 patients receive treatment, the annual costs will amount to EUR 1.8–3.6 million. With the alternative treatment taken into account, the additional costs (budget effect) of tisagenlecleucel therapy are about EUR 1.0–2.1 million.
	Ethical and financial aspects as a whole	Tisagenlecleucel therapy is extremely expensive. The clinical effects and cost-effectiveness of the therapy involve considerable uncertainties. A treatment decision requires that the patient understands the uncertainties and risks involved with the therapy. The uptake of the therapy could be justified with a lowered price under a managed entry agreement, for example. Ethical considerations support the inclusion of the therapy in the range of services.
Collection of supplementary evidence		When the recommendations related to the therapy are re-assessed, information will be needed about factors such as the number and characteristics of the patients treated, implementation of the therapy and treatment outcomes in the short and longer term (for example, mortality, permanent incapacity, transplant of stem cells carried out after the therapy and need for additional treatment). The position of the therapy in Finland's national range of services will be re-assessed in 2023 at the latest when the follow-up data required in the EMA's marketing authorisation decision is available.
Diagnosis (ICD-10) codes		C91.0 Acute lymphoblastic leukaemia (ALL)
Background information and references		Background memorandum by COHERE Finland (in Finnish), Fimea's assessment report (in Finnish with English summary)