Product Name	BLINCYTO®
Active substance	blinatumomab
Indication and conditions of use	Indication: Treatment of adults with Philadelphia chromosome negative (Ph-) relapsed or refractory B-precursor acute lymphoblastic leukemia (ALL). Conditions of use: Blinatumomab is administered as a continuous intravenous infusion delivered at a constant flow rate using an infusion pump, over a period of up to 96 hours. Patients should receive up to 2 initial cycles of treatment. A single cycle of treatment is 4 weeks of continuous infusion. Each cycle of treatment is separated by a 2 week treatment-free interval. The treatment consists of a maximum of 5 cycles. Patients who have achieved complete remission (CR/CRh) after 2 treatment cycles may receive up to 3 additional cycles of blinatumomab consolidation treatment, based on an individual benefits-risks assessment. The recommended dose of blinatumomab is 9 µg/day during the first week of the first cycle and 28 µg/day for the subsequent weeks of the first cycle and during all other cycles.
Conditions, delays and further rules for participation of patients	Inclusion criteria: 1. Subjects with Philadelphia negative B-precursor ALL, with any of the following characteristics: a. refractory to treatment b. in untreated relapse (first, second of greater relapse) c. or relapse at any time after allogeneic HSCT 2. Subject has received intensive combination chemotherapy for the treatment of ALL for initial treatment or subsequent salvage therapy 3. Age ≥ 18 years 4. Patients cannot be satisfactorily treated with the approved and commercially available alternative treatments, in accordance with clinical guidelines, because of efficacy and/or safety issues 5. Ability to understand and willingness to sign a written informed consent 6. Signed and dated written informed consent is available Exclusion criteria: 1. Active ALL in the CNS or testes 2. Isolated extra-medullary disease 3. History of relevant CNS pathology or current relevant CNS pathology 4. Current autoimmune disease or history of autoimmune disease with potential CNS involvement 5. Known hypersensitivity to immunoglobulins or to any other component of the study drug formulation 6. Breast-feeding

	7. The patient is eligible for a clinical trial running with blinatumomab and/or a clinical trial running in the envisaged indication of this program Treatment with blinatumomab should be carefully considered based on individual patient benefit/risk ratio (e.g taking into account age, comorbidity, toxicity, bone marrow function, etc.). <u>Process to include patients</u>: 1. Completed and signed ICF 2. Written request of the treating physician 3. Positive advice by the responsible physician 4. Confirmation of enrolment by the responsible of the program Taken into account the urgency of the disease, all requests will be treated as soon as possible, and at the latest within 1 week after the request. Blinatumomab will be provided for 2 treatment cycles. The need for up to 3 additional treatment cycles is patient-dependent and will be determined by the treating physician.
Duration of the program	This program will start at the submission of the cohort proposition to RIZIV/INAMI end 2015 and its execution will be in line with the legal requirements. Blinatumomab will be provided free of charge by Amgen on an individual patient basis following the criteria stated in this program until, in the clinical judgement of the treating physician, the patient is no longer benefiting from continuation of the treatment. Or, until one of the following stopping criteria for ending the CU is met (whichever comes first): • Blinatumomab is reimbursed in the indication of R/R Ph(-) B-precursor ALL in Belgium • EMA ultimately decides that the benefit/risk assessment is not supportive of registration of blinatumomab in this indication • Amgen decides to withdraw the registration dossier following an unfavorable benefit/risk profile of blinatumomab in the treatment of R/R Ph(-) B-precursor ALL • Amgen decides to stop the development of blinatumomab in this indication Or at the latest until December 2017. The program will be reviewed regularly by Amgen, who has the right to stop the program at any time. Patients that were already included in the program will be supported until the end of their treatment.

Conditions of distribution	Blinatumomab will be requested by the treating physician. The responsible of the program only makes available the medicinal product to the treating physician if the advice of the responsible physician is positive. After approval of the request, a written confirmation will be sent to the treating physician and blinatumomab will be sent to the hospital pharmacy. Treatment should be initiated under the direction of and supervised by the treating physician.
Responsible of the program	Responsible of the program: Amgen n.v. Arianelaan 5 1200 Brussel +32 2 775 27 11 Responsible physician: Dr Jo Van der Veken Arianelaan 5 1200 Brussel Point of contact for this program: Dr Anke Van den broeck Arianelaan 5 1200 Brussel Tel: +32 2 775 27 81 Email: anke.van.den.broeck@amgen.com
Modalities for the disposal	Any unused medication needs to be returned to Amgen or destroyed in an appropriate facility as soon as possible after the patient's discontinuation from the compassionate use program. The medication delivered for an individual patient request in the context of a compassionate use program can only be used for that particular patient.
The information for registration of suspected unexpected serious adverse reactions	Physicians are requested to report all adverse events (non-serious and serious) and other safety findings by OR faxing a completed, signed and dated Safety Report Form to the Amgen – Belgian Safety Department (Safety fax nr: 0800 80 877) within one working day OR mailing a completed, signed and dated Safety Report Form to the email svc-ags-in-be@amgen.com within one working day. The physician may be asked to provide follow-up information on the reported event. In case of an adverse event, the treating physician will decide on the further treatment with blinatumomab, and on the actions needed to take. The most common adverse reactions were: infusion-related reactions (67.2%), infections (63.0%), pyrexia (59.8%), headache (34.4%), febrile neutropenia (28%), peripheral oedema (25.9%), nausea (24.3%), hypokalaemia (23.8%), constipation (20.6%), anaemia (20.1%), cough (18.5%), diarrhoea (18.0%), tremor (17.5%), neutropenia (17.5%), abdominal pain (16.9%), insomnia (15.3%), fatigue (15.3%) and chills (15.3%).

	The most serious adverse reactions that may occur during blinatumomab treatment include: neurologic events (16.4%), infections (31.7%), cytokine release syndrome (0.5%), tumour lysis syndrome (0.5%), and neutropenia/febrile neutropenia (15.3%).