

Title of the program	A Medical Need Program of Blinatumomab for the Treatment of Relapsed / Refractory B-precursor Acute Lymphoblastic Leukemia (ALL).
Product Name	BLINCYTO®
Active substance	Blinatumomab
Indication	<p><u>Intended indication for the Medical Need Program</u> Blinatumomab for the treatment of patients with a Philadelphia chromosome negative (Ph-) B-precursor acute lymphoblastic leukemia (ALL) who have received at least one previous treatment line.</p> <p><u>Authorized Indication</u> Treatment of adults with Philadelphia chromosome negative (Ph-) relapsed or refractory B-precursor acute lymphoblastic leukemia (ALL).</p>
In- and exclusion criteria	<p><u>Inclusion Criteria:</u></p> <ul style="list-style-type: none"> - Subjects with Philadelphia negative B-precursor ALL, with any of the following characteristics: <ul style="list-style-type: none"> • refractory to treatment • in untreated relapse (first, second of greater relapse) • or relapse at any time after allogeneic HSCT - Subject has received intensive combination chemotherapy for the treatment of ALL for initial treatment or subsequent salvage therapy - Age ≥ 18 years - 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 - Ability to understand and willingness to sign a written informed consent - Signed and dated written informed consent is available <p><u>Exclusion criteria:</u></p> <ul style="list-style-type: none"> - Active ALL in the CNS or testes - Isolated extra-medullary disease - History of relevant CNS pathology or current relevant CNS pathology - Current autoimmune disease or history of autoimmune disease with potential CNS involvement - Known hypersensitivity to immunoglobulins or to any other component of the study drug formulation - Breast-feeding - 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	<p><u>Treatment</u> 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.</p> <p>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.</p> <p><u>Dose reduction and stopping rules:</u></p> <ul style="list-style-type: none"> - Consideration to <u>discontinue BLINCYTO temporarily</u> as appropriate should be made in the case of the following life-threatening (grade 4) toxicities: cytokine release syndrome, tumour lysis syndrome, neurological toxicity, elevated liver enzymes and any other clinically relevant toxicities - Consideration to <u>discontinue BLINCYTO temporarily</u> as appropriate should be made in the case of the following severe (grade 3) : cytokine release syndrome, tumour lysis syndrome, neurological toxicity, elevated liver enzymes and any other clinically relevant toxicities. - If the interruption of treatment after an adverse event is no longer than 7 days, continue the same cycle to a total of 28 days of infusion inclusive of days before and after the interruption in that cycle. If an interruption due to an adverse event is longer than 7 days, start a new cycle. If the toxicity takes more than 14 days to resolve, discontinue BLINCYTO permanently, except if described differently in the SmPC.

<p>Process to include a patient</p>	<p><u>Inclusion of a patient</u> The forms are available on request at EU_BE_Blinatumomab@amgen.com</p> <ol style="list-style-type: none"> 1. Completed and signed ICF 2. Written request of the treating physician 3. Send the request to EU_BE_Blinatumomab@amgen.com 4. Review by 3 BHS physicians 5. If positive advice: confirmation of enrolment by the responsible physician of the program <p>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.</p> <p><u>Product Supply:</u></p> <ul style="list-style-type: none"> - Blinatumomab will first 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.
<p>Duration of the program</p>	<p>This program started on 18th November 2015 and its execution is in line with the legal requirements.</p> <p>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.</p> <p>Or, until one of the following stopping criteria for ending the CU is met (whichever comes first):</p> <ul style="list-style-type: none"> - 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 2016. <p>The program is 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.</p>
<p>Responsible of the program</p>	<p><u>Responsible of the program:</u> Amgen N.V. / S.A. Arianelaan 5 1200 Brussels Phone: +32 2 775 27 11</p> <p><u>Responsible physician:</u> Dr. Jo Van der Veken</p> <p><u>Points of contact for this program:</u></p> <ul style="list-style-type: none"> - Florence Colliez Regional Medical Liaison +32 (0)472 90 06 51 fcolliez@amgen.com - Anke Van den broeck TA Head Oncology Haematology +32 (0) 2 775 27 81 +32 (0) 485 41 77 84 ankev@amgen.com
<p>Modalities for the disposal</p>	<p>Any unused or expired 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 medical need program can only be used for that particular patient.</p>
<p>The information for registration of suspected unexpected serious</p>	<p>Physicians are requested to report <u>all adverse events (non-serious and serious), other safety findings and product complaints</u> by <u>OR</u> faxing a completed, signed and dated Safety Report Form to the Amgen – Belgian Safety Department (Safety fax</p>

adverse reactions	<p>nr: 0800 80 877) within one working day <u>OR</u> mailing a completed, signed and dated Safety Report Form to the email svc-ags-in-be@amgen.com within one working day.</p> <p>The physician may be asked to provide follow-up information on the reported event.</p> <p>In case of an adverse event, the treating physician will decide on the further treatment with darbepoetin alfa, and on the actions needed to take.</p>
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