30 September 2015
EMA/COMP/508236/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

CD33-directed antibody-drug conjugate consisting of an antibody conjugated to a DNA cross-linking pyrrolobenzodiazepine dimer drug for the treatment of acute myeloid leukaemia

On 10 August 2015, orphan designation (EU/3/15/1545) was granted by the European Commission to Seattle Genetics UK, Limited, United Kingdom, for CD33-directed antibody-drug conjugate consisting of an antibody conjugated to a DNA cross-linking pyrrolobenzodiazepine dimer drug for the treatment of acute myeloid leukaemia.

What is acute myeloid leukaemia?

Acute myeloid leukaemia (AML) is a cancer of the white blood cells (cells that fight against infections). In patients with AML, the bone marrow (the spongy tissue inside the large bones, where blood cells are produced) produces large numbers of abnormal, immature white blood cells. These abnormal cells quickly build up in large numbers in the bone marrow and are found in the blood.

AML is a long-term debilitating and life-threatening disease because these abnormal immature cells take the place of the normal blood cells, causing bleeding episodes, blood clots and reducing the patient's ability to fight infections.

What is the estimated number of patients affected by the condition?

At the time of designation, AML affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

Treatment for AML is complex and depends on a number of factors including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. At

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

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the time of designation, the main treatments for AML were chemotherapy (medicines to treat cancer) and haematopoietic (blood) stem-cell transplantation (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with AML because early studies in experimental models show that it might reduce the growth of the cancer when used together with authorised treatments. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

This medicine is made up of a cytotoxic (cell-killing) substance that is linked to a type of protein called a monoclonal antibody. The monoclonal antibody has been designed to recognise and attach to CD33 receptors present on the surface of AML cells in about 90% of patients. When the antibody attaches to CD33, the AML cells are expected to absorb the antibody, as well as the cytotoxic substance attached to it. Once inside the cancer cell, the cytotoxic substance is released and is then expected to kill the cell, thereby slowing down the growth of the cancer.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with AML were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for AML or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 2015 recommending the granting of this designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	CD33-directed antibody-drug conjugate consisting of an antibody conjugated to a DNA cross-linking pyrrolobenzodiazepine dimer drug	Treatment of acute myeloid leukaemia
Bulgarian	Насочен към CD33 конюгат антитяло-лекарствен препарат, включващ антитяло свързано с лекарствен препарат (пиролобензодиазепин димер) реагиращ с ДНК	Лечение на остра миелоидна левкемия
Croatian	Konjugat protutijela usmjerenog protiv CD33 i lijeka sastavljen od protutijela konjugiranog na dimer pirolobenzodiazepinskog lijeka koji se križno povezuje s DNK	Liječenje akutne mijeloične leukemije
Czech	Konjugát protilátky s léčivem cílený na CD33, skládající se z protilátky konjugované k pyrrolobenzodiazepin dimeru, který zesíťuje DNA	Léčba akutní myeloidní leukémie
Danish	CD33-rettet antistoflægemiddelkonjugat bestående af antistof konjugeret til et DNA tværbindende pyrrolobenzodiazepin dimer lægemiddel	Behandling af akut myeloid leukæmi
Dutch	CD33-gericht antilichaam-geneesmiddel conjugaat bestaande uit het antilichaam geconjugeerd tot een DNA cross-linking pyrrolobenzodiazepine dimeer geneesmiddel	Behandeling van acute myeloïde leukemie
Estonian	CD33 vastane antikeha-ravimi konjugaat, mis koosneb antikehast, mis on konjugeeritud DNA ristsideme pürrolobensodiasepiini dimeerravimiga	Akuutse müeloidse leukeemia ravi
Finnish	CD33-vasta-aine lääkekonjugaatti, joka koostuu vasta-aineesta, johon on konjugoitu DNA:han yhdistetty pyrrolobentsodiatsepiini dimeerilääke	Akuutin myelooisen leukemian hoito
French	Médicament anticorps conjugué anti-CD33 composé d'un anticorps conjugué à un agent de réticulation de l'ADN de type pyrrolobenzodiazépine dimère	Traitement de la leucémie aiguë myéloïde
German	CD33-gerichtetes Antikörper-Medikament-Konjugat, bestehend aus dem Antikörper, der mit einem DNA-venetzten Pyrrolobenzodiazepin-Dimermedikament konjugiert ist	Behandlung der akuten myeloischen Leukämie
Greek	CD33-κατευθυνόμενο σύμπλεγμα αντισώματος φαρμάκου αποτελούμενο από ενα αντίσωμα συζευγμένο με ένα φάρμακο χιαστής σύνδεσης DNA διμερούς πυρρολο-βενζοδιαζεπίνης	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	CD33-vezérelt antitest-gyógyszerkonjugátum, amely egy pirrolobenzodiazepin dimer gyógyszert keresztkötő DNS-hez konjugált antitestet tartalmaz	Akut myeloid leukaemia kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	coniugato farmaco-anticorpo anti- CD33 consistente in unanticorpo coniugato ad un farmaco dimero di pirrolobenzodiazepina con legame trasversale DNA	Trattamento della leucemia mieloide acuta
Latvian	Pret CD33 vērsts antivielas-zāļu konjugāts, kas sastāv no antivielas, kas konjugēta ar pirolobenzodiazepīna dimēra zālēm, kas šķerseniski saista DNS	Akūtas mieloleikozes ārstēšana
Lithuanian	Į CD33-nukreiptas antikūno ir vaisto konjugatas, iš antikūno, konjuguoto su kryžminio sujungimo DNR pirolobenzodiazepino dimero vaistu	Ūmios mieloleukozės gydymas
Maltese	Konjugat bejn antikorp dirett kontra CD33 u mediċina li jikkonsisti f'antikorp konjugat ma' mediċina dimer bil-pyrrolobenzodiazepine b'rabta inkroċjata ma' DNA	Kura tal-lewkimja mjelojda akuta
Polish	Koniugat leku z przeciwciałem, zawierający przeciwciało skierowane przeciw CD33 skoniugowane z sieciującym DNA dimerem pirolobenzodiazepinu	Leczenie ostrej białaczki szpikowej
Portuguese	Anticorpo anti-CD33 conjugado com um medicamento consistindo num anticorpo ligado a um dímero de pirrolobenzodiazepina que se liga ao ADN	Tratamento da leucémia mielóide aguda
Romanian	Conjugat anticorpi anti-CD33-medicament alcătuit dintr-un anticorp conjugat cu ADN ce leagă încrucişat medicamentul dimer pirolobenzodiazepinic	Tratamentul leucemiei mieloide acute
Slovak	Konjugát protilátky s liečivom cielený na CD33, skladajúci sa z protilátky konjugovanej k pyrrolobenzodiazepínového diméru, ktorý zosieťuje DNA	Liečba akútnej myeloickej leukémie
Slovenian	Proti CD33 usmerjeno konjugirano zdravilo s protitelesi, ki ga sestavlja protitelo, konjugirano na prečno povezovalno zdravilo iz dimer pirolobenzodiazepinov DNK	Zdravljenje akutne mieloične levkemije
Spanish	Un conjugado de anticuerpo-fármaco dirigido al receptor CD33 consistiendo en un anticuerpo conjugado con el fármaco dímero pirrolobenzodiazepina entrecruzado con ADN	Tratamiento de la leucemia mieloide aguda
Swedish	CD33-riktat antikropp-läkemedel-konjugat bestående av en antikropp konjugerad till ett DNA-korsbindande pyrrolobensodiazepin-dimerläkemedel	Behandling av akut myeloisk leukemi
Norwegian	CD33-rettet antistofflegemiddel-konjugat bestående av antistoff konjugert til et DNAkrysbindende pyrrolobenzodiazepin dimerlegemiddel	Behandling av akutt myelogen leukemi
Icelandic	CD33-stjórnuð mótefnis-lyfja samtengingu sem samanstenur af mótefni og DNA kross-tengdu pýrrólóbenzódíazepín dímer lyfi.	Meðferð við bráðu kyrningahvítblæði