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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Trans-N1-((1R,2S)-2-phenylcyclopropyl)cyclohexane-1,4-diamine bis-hydrochloride for the treatment of acute myeloid leukaemia

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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 5 August 2013, orphan designation (EU/3/13/1174) was granted by the European Commission to Oryzon Genomics SA, Spain, for trans-N1-((1R,2S)-2-phenylcyclopropyl)cyclohexane-1,4-diamine bis-hydrochloride for the treatment of acute myeloid leukaemia.

The sponsorship was transferred to Roche Registration Limited, United Kingdom, in December 2014.

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 white blood cells, 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 2.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 138,000 people*, and is below the ceiling for orphan

*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.
At the time of designation, this represented a population of 512,200,000 (Eurostat 2013).

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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 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 this medicine might be of significant benefit for patients with AML because it works in a different way to current treatments, thereby offering an alternative for AML that has come back or does not respond to other treatments, and early studies in experimental models show that it might reduce the growth of the cancer. These assumptions 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 a small molecule that is expected to block the activity of an enzyme called lysine-specific demethylase 1 (LSD1), which is involved in turning genes 'on' and 'off' within cells. In AML, this medicine is expected to switch 'on' the genes that suppress the division and growth of the tumour cells. This is expected to lead to a reduction in the growth of the cancer.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with AML had been started.

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 11 July 2013 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	Trans-N1-((1R,2S)-2-phenylcyclopropyl)cyclohexane-1,4-diamine bis-hydrochloride	Treatment of acute myeloid leukaemia
Bulgarian	Транс N1-((1R,2S)-2-фенил циклопропил) циклохексан-1, 4-диамин бис-хидрохлорид	Лечение на остра миелоидна левкемия
Croatian	Trans-N1-((1R, 2S)-2-fenilciklopropil)cikloheksan-1,4-diamin bis-hidroklorid	Liječenje akutne mijeloične leukemije
Czech	Trans N1-((1R,2S)-2-phenylcyclopropyl) cyclohexan-1, 4-diamin bis-hydrochlorid	Léčba akutní myeloidní leukémie
Danish	Trans N1-((1R,2S)-2-phenylcyclopropyl) cyclohexan-1 ,4-diamin-bis-hydrochlorid	Behandling af akut myeloid leukæmi
Dutch	Trans N1-((1R,2S)-2-phenylcyclopropyl) cyclohexaan-1, 4- diamine bis-hydrochloride	Behandeling van acute myeloïde leukemie
Estonian	Trans N1-((1R,2S)-2-fenüültsüklopropüül) tsükloheksaan-1, 4-diamiini bis-hüdrokloriid	Akuutse müeloidse leukeemia ravi
Finnish	Trans N1-((1R,2S)-2-fenyylisyklopropyyli) sykloheksaani-1, 4-diamiini-bis-hydrokloridi	Akuutin myelooisen leukemian hoito
French	Trans N1-((1R,2S)-2-phénylcyclopropyl)-cyclohexan-1, 4-diamine bis-chlorhydrate	Traitement de la leucémie aiguë myéloïde
German	Trans N1-((1R,2S)-2-Phenylcyclopropyl)-cyclohexan-1 ,4-diamin bis-hydrochlorid	Behandlung der akuten myeloischen Leukämie
Greek	Trans N1-((1R,2S)-2-φαινυλο-κυκλοπροπυλο) κυκλοεξανο-1, 4-διαμίνη δις-υδροχλωρική	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	Trans N1-((1R,2S)-2-fenilciklopropil)-ciklohexán-1, 4-diamin bisz-hidroklorid	Akut myeloid leukaemia kezelése
Italian	Trans N1-((1R,2S)-2-fenilciclopropil) cicloesano-1, 4-diammina biscloridrato	Trattamento della leucemia mieloide acuta
Latvian	Trans N1-((1R,2S)-2-fenilciklopropil) cikloheksāna-1, 4-diamīn bis-hidrohlorīds	Akūtas mieloleikozes ārstēšana
Lithuanian	Trans N1-((1R,2S)-2-fenilciklopropil) cikloheksano-1, 4-diamino bis hidrochloridas	Ūmios mieloleukozės gydymas
Maltese	Trans N1-((1R,2S)-2-phenylcyclopropyl) cyclohexane-1, 4-diamine bis-hydrochloride	Kura tal-lewkimja mjelojda akuta

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Trans N1-((1R,2S)-2-fenylo-cyklopropylo)cykloheksano-1, 4 diaminy bis-chlorowodorek	Leczenie ostrej białaczki szpikowej
Portuguese	Trans N1-((1R,2S)-2-fenil-ciclopropil)-ciclohexano-1, 4-diamina bis-cloridrato	Tratamento da leucémia mielóide aguda
Romanian	Trans N1-((1R,2S)-2-fenilciclopropil) ciclohexan-1, 4-diamină bis-clorhidrat	Tratamentul leucemiei mieloide acute
Slovak	Trans N1-((1R,2S)-2-fenylcyklopropyl) cyklohexán-1, 4-diamín bis-hydrochlorid	Liečba akútnej myeloickej leukémie
Slovenian	Trans N1-((1R,2S)-2-fenilciklopropil) cikloheksan-1, 4-diamin bis-hidroklorid	Zdravljenje akutne mieloične levkemije
Spanish	Trans N1-((1R,2S)-2-fenilciclopropil) ciclohexano-1, 4-diamina bis-clorhidrato	Tratamiento de la leucemia mieloide aguda
Swedish	Trans N1-((1R,2S)-2-fenyl-cyklopropyl) cyklohexan-1, 4-diamin bishydroklorid	Behandling av akut myeloisk leukemi
Norwegian	Trans N1-((1R,2S)-2-fenylsyklopropyl) sykloheksan-1, 4-diamin bishydroklorid	Behandling av akutt myelogen leukemi
Icelandic	Trans-N1-((1R,2S)-2-phenýlcýklóprópýl) cýklóhexan-1,4-díamín bis-hýdróklóríð	Meðferð við bráðu kyrningahvítblæði