23 September 2014
EMA/COMP/433740/2014
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide for the treatment of acute myeloid leukaemia

On 22 August 2014, orphan designation (EU/3/14/1313) was granted by the European Commission to Clinipace GmbH, Germany, for (Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide 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 1.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 56,000 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 the time of designation, the main treatments for AML were chemotherapy (medicines to treat cancer)

*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 511,100,000 (Eurostat 2014).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
**Telephone** +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
**Send a question via our website** www.ema.europa.eu/contact

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 early studies show a positive response in patients with progressive disease who cannot be treated with existing therapies. 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 expected to work in patients with AML by blocking the action of a protein called exportin1 (XPO1). XPO1 is found at higher levels in many cancer cells, where it prevents the actions of proteins that help stop cancer growth. By blocking XPO1, the medicine is expected to enhance the action of these anti-cancer proteins and bring about the death of the cancer cells, thereby slowing the progression of the disease.

## 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. Orphan designation of the medicine had been granted in the United States for the treatment of this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 2014 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:

Clinipace GmbH
Landsbergerstrasse 408
81241 München
Germany
Tel. +1 617 6580 600
E-mail: development@karyopharm.com

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 | (Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide | Treatment of acute myeloid leukaemia |
| Bulgarian | (Z)-3-(3-(3,5-бис(трифлуорометил)фенил-1H-1,2,4-триазол-1-ил)-N'-(пиразин-2-ил)акрил хидразид | Лечение на остра миелоидна левкемия |
| Croatian | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)akrilhidrazid | Liječenje akutne mijeloične leukemije |
| Czech | (Z)-3-(3-(3,5-bis(trifluorometyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid | Léčba akutní myeloidní leukémie |
| Danish | (Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid | Behandling af akut myeloid leukæmi |
| Dutch | (Z)-3-(3-(3,5-bis(trifluormethyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylhydrazide | Behandeling van acute myeloïde leukemie |
| Estonian | (Z)-3-(3-(3,5-bis(trifluorometüül)fenüül-1H-1,2,4-triasool-1-üül)-N'-(pürasiin-2-yl)akrüül-hüdrasiin | Akuutse müeloidse leukeemia ravi |
| Finnish | (Z)-3-(3-(3,5-bis(trifluorometyyli)fenyyli-1H-1,2,4-triatsoli-1-yl)-N'-(pyratsiini-2-yl)akryylihydratsidi | Akuutin myelooisen leukemian hoito |
| French | (Z)-3-(3-(3,5-bis(trifluorométhyl)phényl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylhydrazide | Traitement de la leucémie aiguë myéloïde |
| German | (Z)-3-(3-(3,5-bis(Trifluormethyl)phenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylhydrazid | Behandlung der akuten myeloischen Leukämie |
| Greek | (Z)-3-(3-(3,5-δις(τριφθορομεθυλο)φαινυλο-1H-1,2,4-τριαζολ-1-υλο)-N'-(πυραζιν-2-υλο)ακρυλυδραζίδιο | Θεραπεία της οξείας μυελοειδούς λευχαιμίας |
| Hungarian | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-yl)-N'-(pirazin-2-yl)akrilhidrazid | Akut myeloid leukaemia kezelése |
| Italian | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-yl)-N'-(pirazina-2-yl)acrilidrazide | Trattamento della leucemia mieloide acuta |
| Latvian | (Z)-3-(3-(3,5-bis(trifluormetil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazīn-2-il)akrilhidrazīds | Akūtas mieloleikozes ārstēšana |
| Lithuanian | (Z)-3-(3-(3,5-bis(trifluorometil)fenil)-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)akrilhidrazidas | Ūmios mieloleukozės gydymas |
| Maltese | (Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide | Kura tal-lewkimja mjelojda akuta |
| Polish | (Z)-3-(3-(3,5-bis(trifluorometylo)fenylo-1H-1,2,4-triazol-1-yl)-N'-(pirazyn-2-yl)akrylohydrazyd | Leczenie ostrej białaczki szpikowej |
| Portuguese | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)acrilhidrazida | Tratamento da leucémia mielóide aguda |
| Romanian | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)acrilhidrazidă | Tratamentul leucemiei mieloide acute |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Slovak | (Z)-3-(3-(3,5-bis(trifluórometyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazín-2-yl)akrylhydrazid | Liečba akútnej myeloickej leukémie |
| Slovenian | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)akrilhidrazid | Zdravljenje akutne mieloične levkemije |
| Spanish | (Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)acrilhidrazida | Tratamiento de la leucemia mieloide aguda |
| Swedish | (Z)-3-(3-(3,5-bis(trifluorometyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid | Behandling av akut myeloisk leukemi |
| Norwegian | (Z)-3-(3-(3,5-bis(trifluormetyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid | Behandling av akutt myelogen leukemi |
| Icelandic | (Z)-3-(3-(3,5-bis(þríflúórómetýl)fenýl-1H-1,2,4-tríasól-1-ýl)-N'-(pýrasín-2-ýl)akrýlhýdrasíð | Meðferð við bráðu kyrningahvítblæði |