19 May 2015
EMA/COMP/211415/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride for the treatment of tularaemia

On 24 April 2015, orphan designation (EU/3/15/1476) was granted by the European Commission to Arno Therapeutics UK, Limited, United Kingdom, for 1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride for the treatment of tularaemia.

What is tularaemia?

Tularaemia is a bacterial infection caused by an organism called *Francisella tularensis*. These bacteria normally infect animals, but humans can be infected by handling infected animals or by being bitten by a parasite such as a mosquito or tick that has fed on an infected animal. The infection can affect various organs throughout the body and symptoms may be long-lasting and difficult to treat.

Tularaemia is a serious and long-term debilitating condition due to the development of symptoms such as skin ulcers, diarrhoea, pneumonia, and lymphadenopathy (swollen glands in the neck, armpits and groin).

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

At the time of designation, tularaemia affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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?

At the time of designation, tularaemia was mainly treated with gentamicin or streptomycin, members of a class of antibiotics known as aminoglycosides. Other types of antibiotics might also be used.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with tularaemia because it works in a different way to existing medicines and

[*]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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laboratory studies suggest that it may increase the outcome of patients when used in combination with gentamicin. 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?

The medicine is thought to work against the bacterial cells via a number of mechanisms, including increasing the ability of cells of the immune system (the body's natural defences) to destroy the bacteria, and blocking several enzymes important for the growth and survival of bacteria.

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 this medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with tularaemia had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for tularaemia 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 19 March 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	1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride	Treatment of tularaemia
Bulgarian	1-(4-(N-глициламидо)фенил)-3-трифлуорометил-5-(фенантрен-2-ил)-пиразол-хидрохлорид	Лечение на туларемия
Croatian	1-(4-(N-glicilamido)fenil)-3-trifluorometil-5-(fenantren-2-il)-pirazolklorid	Liječenje tularemije
Czech	1-(4-(N-glycylamido)fenyl)-3-trifluormethyl-5-(fenantren-2-yl)pyrazol-hydrochlorid	Léčba tularemie
Danish	1-(4-(N-glycylamido)phenyl)-3-trifluormethyl-5-(phenanthren-2-yl)pyrazol-hydrochlorid	Behandling af tularæmia
Dutch	1-(4-(N-glycylamido)fenyl)-3-trifluormethyl-5-(fenantreen-2-yl)pyrazool-hydrochloride	Behandeling van tularemie
Estonian	1-(4-(N-glütsüülamido)fenüül)-3-trifluorometüül-5-(fenantreen-2-üül)pürasool-hüdrokloriid	Ravi tularaemia
Finnish	1-(4-(N-glysyyliamido)fenyyli)-3-trifluorimetyyli-5-(fenantren-2-yyli)pyratsoli-hydrokloridi	Tularemian hoito
French	Chlorhydrate de 1-(4-(N-glycylamide)phényl)-3-trifluorométhyl-5-(phénanthrén-2-yl)pyrazole	Traitement de la tularémie
German	1-(4-(N-glycylamido)phenyl)-3-trifluormethyl-5-(phenanthren-2-yl)-pyrazol-hydrochlorid	Behandlung von Tularämie
Greek	1-(4-(N-γλυκυλάμιδο)φαινυλ)-3-τριφθορομεθυλ-5-(φαιναν θρεν-2-υλ)πυραζολο-υδροχλωρίδιο	Θεραπεία της τουλαραιμίας
Hungarian	1-(4-(N-glicil)fenil)-3-trifluoro-5-(fenantrén-2-il)-pirazol hidroklorid	Tularaemia kezelése
Italian	1-(4-(N-glycylamido)fenil)-3-trifluorometil-5-(phenanthren-2-il)-pirazolo-cloridrato	Trattamento della tularemia
Latvian	1-(4-(N-glicilamido)fenil)-3-trifluormetil-5-(fenantrēn-2-il)pirazol-hidrohlorīds	Tularēmijas ārstēšana
Lithuanian	1-(4-(N-glicilamido)fenil)-3-trifluormetil-5-(fenantren-2-il)-pirazolo-hidrochloridas	Tuliaremijos gydymas
Maltese	1-(4-(N-glycylamido)phenyl)-3-trifluoromethyl-5-(phenanthren-2-yl)-pyrazole-hydrochloride	Kura tat-tularemija
Polish	1-(4-(N-glicyloamido)fenylo)-3-trifluorometylo-5-(fenantren-2-ylo)pirazol chlorowodorek	Leczenie tularemii
Portuguese	Cloridrato de 1-(4-(N-glicilamido)fenil)-3-trifluorometil-5-(fenantren-2-il)-pirazol	Tratamento de tularémia
Romanian	Clorhidrat de 1-(4-(N-glicilamido)fenil)-3-trifluormetil-5-(fenantren-2-il)pirazol	Tratamentul tularemiei
Slovak	1-(4-(N-glycylamido)fenyl)-3-trifluórmetyl-5-(fenantrén-2-yl)pyrazol-hydrochlorid	Liečba tularémie

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	1-(4-(N-glicilamido)fenil)-3-trifluorometil-5-(fenanthren-2-il)pirazol-hidroklorid	Zdravljenje tularemije
Spanish	clorhidrato de 1-(4-(N-glycylamido)fenil)-3-trifluorometil-5-(fenantren-2-il)pirazol-	Tratamiento de la tularemia
Swedish	1-(4-(N-gycylamido)fenyl)-3-trifluormetyl-5-(fenantren-2-yl)pyrazol-hydroklorid	Behandling av tularemia
Norwegian	1-(4-(N-glysylamido)fenyl)-3-trifluormetyl-5-(fenantren-2-yl)pyrazolhydroklorid	Behandling av tularemi
Icelandic	1-(4-(N-glýkýlamídó)fenýl)-3-tríflúormetýl-5-(fenantren-2-ýl)pýrazól-hýdróklóríð	Meðferð tularemiu