



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(2R,3S)-2-(4-cyclopentylaminophenyl)-1-(2-fluoro-6-methylbenzoyl)piperidine-3-carboxylic acid(4-methyl-3-trifluoromethylphenyl)amide for the treatment of granulomatosis with polyangiitis

On 19 November 2014, orphan designation (EU/3/14/1373) was granted by the European Commission to ChemoCentryx Limited, United Kingdom, for (2R,3S)-2-(4-cyclopentylaminophenyl)-1-(2-fluoro-6-methylbenzoyl)piperidine-3-carboxylic acid(4-methyl-3-trifluoromethylphenyl)amide for the treatment of granulomatosis with polyangiitis.

What is granulomatosis with polyangiitis?

Granulomatosis with polyangiitis (previously known as Wegener's granulomatosis) is a type of inflammation of small to medium-sized arteries and veins, characterised by 'granulomas' (clumping of white blood cells into small granular lumps that result in inflammation). Often the small blood vessels (capillaries) of the nose, throat, lungs and kidneys are affected, which causes symptoms such as itchy, runny nose, breathing problems and reduced kidney function or kidney failure. Other symptoms of the disease include fever, skin rash, muscle and joint pain. Although its causes are not well understood, granulomatosis with polyangiitis is an auto-immune disease, a disease which is caused by the body's immune system attacking normal tissue and which causes inflammation.

Granulomatosis with polyangiitis is a long-term debilitating and life-threatening condition, due to the damage to the kidneys and lungs which may cause kidney and respiratory failure.

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

At the time of designation granulomatosis with polyangiitis affected approximately 1.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 82,000 people^{*}, and is

^{*}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).



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, the medicine rituximab, in combination with corticosteroids, was authorised for granulomatosis with polyangiitis in the EU. Several other medicines, including cyclophosphamide with corticosteroids, were also used. Patients with severely impaired kidney function might be given plasmapheresis (a process similar to kidney dialysis in which the liquid part of the blood, or plasma, is separated from the cells in order to remove antibodies).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with granulomatosis with polyangiitis because early studies show that it could improve kidney function in patients with the condition. 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 blocks a receptor called 'complement 5a receptor' (C5aR), which is normally activated by C5a, one of a group of proteins in the blood ('the complement system') that form part of the immune system.

When C5a attaches to C5aR it attracts and activates certain immune cells called neutrophils, which are thought to contribute to the inflammation of small blood vessels in granulomatosis with polyangiitis. By blocking C5aR, the medicine is expected to reduce inflammation of blood vessels, thus improving the symptoms 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 granulomatosis with polyangiitis were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for granulomatosis with polyangiitis. Orphan designation for this 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 9 October 2014 recommending the granting of this designation.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(2R,3S)-2-(4-cyclopentylaminophenyl)-1-(2-fluoro-6-methylbenzoyl)piperidine-3-carboxylic acid(4-methyl-3-trifluoromethylphenyl)amide	Treatment of granulomatosis with polyangiitis
Bulgarian	(2R,3S)-2-(4-Циклопентиламинофенил)-1-(2-флуоро-6-метилбензоил)пиперидин-3-карбоксилна киселина(4-метил-3-трифлуорометил-фенил)амид	Лечение на грануломатоза с полиангиит
Croatian	(4-metil-3-trifluorometilfenil)amid(2R,3S)-2-(4-ciklopentilaminofenil)-1-(2-fluoro-6-metilbenzoil)piperidin-3-karboksilatne kiseline	Liječenje granulomatoze s poliangiitismom
Czech	(4-methyl-3-trifluormethylfenyl)amid(2R,3S)-2-(4-cyklopentylaminofenyl)-1-(2-fluor-6-methylbenzoyl)piperidin-3-karboxylové kyseliny	Léčba granulomatózy s polyangiitidou
Danish	(2R,3S)-2-(4-cyclopentylaminophenyl)-1-(2-fluoro-6-methylbenzoyl)piperidin-3-carboxylsyre(4-methyl-3-trifluoromethylphenyl)amid	Behandling af granulomatose med polyangiitis
Dutch	(2R,3S)-2-(4-cyclopentylaminofenyl)-1-(2-fluoro-6-methylbenzoyl)piperidine-3-carbonzuur(4-methyl-3-trifluoromethylfenyl)amide	Behandeling van granulomatose met polyangiitis
Estonian	(2R,3S)-2-(4-tsüklopentüülaminofenüül)-1-(2-fluoro-6-metüülbensoüül)piperidiin-3-karboksüülhappe(4-metüül-3-trifluorometüülfenüül)amiid	Polüangiidiga kulgeva granulomatoosi ravi
Finnish	(2R,3S)-2-(4-syklopentyyliaminofenyylä)-1-(2-fluori-6-metyylibentsoyyli)piperidiini-3-karboksyylihappo(4-metyyli-3-trifluorimetyylifenyylä)amidi	Granulomatoottisen polyangiitin hoito
French	(4-méthyl-3-trifluorométhylphényl)amide d'acide pipéridine-3-carboxylique{(2R,3S)-2-(4-cyclopentylaminophényl)-1-(2-fluoro-6-méthylbenzoyle)}	Traitement de la granulomatose avec polyangéite
German	(2R,3S)-2-(4-cyclopentylaminophenyl)-1-(2-fluoro-6-methylbenzoyl)piperidin-3-carbonsäure(4-methyl-3-trifluoromethylphenyl)amid	Behandlung der granulomatösen Polyangiitis (M. Wegener)
Greek	(2R,3S)-2-(4-κυκλοπενταμινοφαινόληκυκλοπενταμινοφαινυλ)-1-(2-φθόριο-6-μεθυλοβενζόλιομεθυλοβενζούλ)πιπεριδίνη-3-καρβοξυλικό οξύ(4-μεθυλο-3-τριφθοριούχος τριφθορομεθυλοφαινόληυλ)αμίδιο	Θεραπεία της κοκκιωμάτωσης με πολυαγγειίτιδα

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	(2R,3S)-2-(4-ciklopentilaminofenil)-1-(2-fluoro-6-metilbenzoil)-piperidin-3-karbonsav-(4-metil-3-trifluoro-metilfenil)amid	Granulomatosis polyangiitis kezelése
Italian	(2R,3S)-2-(4-Ciclopentilaminofenil)-1-(2-fluoro-6-metilbenzil)piperidina-3-carbossilico(4-metil-3-trifluorometilfenil)ammide	Trattamento della granulomatosi con poliangite
Latvian	(2R,3S)-2-(4-ciklopentilaminofenil)-1-(2-fluoro-6-metilbenzoil)piperidīna-3-karboksilskābes(4-metil-3-trifluorometilfenil)amīds	Granulomatozes ar poliangiītu ārstēšana
Lithuanian	(2R,3S)-2-(4-ciklopentilaminofenil)-1-(2-fluoro-6-metilbenzoil)piperidin-3-karboksilo rūgštis(4-metil-3-trifluorometilfenil)amidas	Granuliomatozės su poliangitu gydymas
Maltese	(2R,3S)-2-(4-Cyclopentylaminophenyl)-1-(2-fluoro-6-methylbenzoyl)piperidine-3-carboxylic acid(4-methyl-3-trifluoromethylphenyl)amide	Kura tal-granulomatjosi bil-poliangite
Polish	(4-metylo-3-trifluorometylofenylo)amid kwasu (2R,3S)-2-(4-cyklopentyloaminofenylo)-1-(2-fluoro-6-metylobenzoilo)piperidyno-3-karboksylowego	Leczenie ziarniniakowatości z zapaleniem naczyń
Portuguese	Ácido (2R,3S)-2-(4-ciclopentil amino fenil)-1-(2-fluoro-6-metil benzoil)piperidina-3-carboxil(4-metil-3-trifluorometilfenil)amida	Tratamento da granulomatose com poliangeite
Romanian	(4-metil-3-trifluoro-metil-fenil) amida acidului piperidin 3-carboxilic{(2R,3S)-2-(4-ciclopentilaminofenil)-1-(2-fluoro-6-metil-benzoil)}	Tratamentul granulomatozei cu poliangeită
Slovak	4-metyl-3-trifluórmetylfenylamid kyseliny (2R,3S)-2-(4-cyklopentylaminofenyl)-1-(2-fluór-6-metylbenzoyl)piperidín-3-karboxylovej	Liečba granulomatózy s polyangiitídou
Slovenian	(4-metil-3-trifluorometilfenil)amid(2R,3S)-2-(4-ciklopentilaminofenil)-1-(2-fluoro-6-metilbenzoil)piperidin-3-karboksilne kisline	Zdravljenje granulomatoze s poliangiitisom
Spanish	(4-metil-3-trifluorometilfenil)amida del ácido(2R,3S)-2-(4-ciclopentilaminofenil)-1-(2-fluoro-6-metilbenzoil)piperidina-3-carboxílico	Tratamiento de granulomatosis con poliangeitis
Swedish	(2R,3S)-2-(4-cyklopentylaminofenyl)-1-(2-fluor-6-metylbensoyl)piperidin-3-karboxylsyra(4-metyl-3-trifluormetylfenyl)amid	Behandling av granulomatös polyangiit
Norwegian	(2R,3S)-2-(4-syklopentylaminofenyl)-1-(2-fluoro-6-metylbenzoyl)piperidin-3-karboksylsyre(4-metyl-3-trifluormetylfenyl)amid	Behandling av granulomatose med polyangiitt
Icelandic	(2R,3S)-2-(4-sýklópentýlaminófenýl)-1-(2-flúor-6-metylbensóyl)píperidín-3-karboxýlsýra(4-metyl-3-triflúormetylfenýl)amið	Meðferð við hnúðageri með fjölæðabólgu