



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide for the treatment of C3 glomerulopathy

On 21 March 2018, orphan designation (EU/3/18/1989) was granted by the European Commission to FGK Representative Service GmbH, Germany, for (2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide (also known as ACH-0144471) for the treatment of C3 glomerulopathy.

### What is C3 glomerulopathy?

C3 glomerulopathy is a condition in which a protein of the immune system (body's natural defences) known as C3 builds up in the kidneys, damaging them and impairing their function.

Patients with C3 glomerulopathy usually have signs of kidney problems, such as blood or protein in urine, high blood pressure, blurred vision and swelling in the hands and feet.

C3 glomerulopathy is life threatening and debilitating in the long term because it can lead to kidney failure.

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

At the time of designation, C3 glomerulopathy affected approximately 1.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 57,000 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 orphan designation, no satisfactory treatments were authorised in the EU for C3 glomerulopathy. Because the disease involves the body's immune system, immunosuppressant medicines (that reduce the activity of the immune system) were usually used. Other treatments

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\*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 517,400,000 (Eurostat 2018).



included plasmapheresis (a procedure to remove unwanted substances from plasma, the liquid part of the blood), infusion of healthy plasma, and medicines to reduce blood pressure and protein in the urine. Some patients developing end-stage kidney disease received dialysis and kidney transplantation.

### **How is this medicine expected to work?**

The damaging build-up of the C3 protein in kidneys of patients with C3 glomerulopathy mostly results from overactivity of an enzyme called C3 convertase. This medicine blocks another protein called factor D, which is involved in the production of C3 convertase. By blocking factor D and hence production of C3 convertase, the medicine is expected to reduce the build-up of the C3 protein and relieve 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 C3 glomerulopathy were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for C3 glomerulopathy 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 15 February 2018 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Treatment of C3 glomerulopathy
Bulgarian	(2S,4R)-1-(2-(3-ацетил-5-(2-метилпиримидин-5-ил)-1H-индазол-1-ил)ацетил)-N-(6-бромопиридин-2-ил)-4-флуоропирролидин-2-карбоксамид	Лечение на C3 гломерулопатия
Croatian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirolidin-2-karboksamid	Liječenje C3 glomerulopatije
Czech	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Léčba C3 glomerulopatie
Danish	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-carboxamid	Behandling af C3 glomerulopati
Dutch	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Behandeling van C3 glomerulopathie
Estonian	(2S,4R)-1-(2-(3-atsetüül-5-(2-metüülpürimidiin-5-üül)-1H-indasool-1-üül)atsetüül)-N-(6-bromopüridiin-2-üül)-4-fluoropürrolidiin-2-karboksamiid	C3 glomerulopaatia ravi
Finnish	(2S,4R)-1-(2-(3-asetyyli-5-(2-metyylipyrimidin-5-yyli)-1H-indatsol-1-yyli)asetyyli)-N-(6-bromopyrimidin-2-yyli)-4-fluoropyrrolidiini-2-karboksamidi	C3 glomerulopatian hoito
French	(2S,4R)-1-(2-(3-acetyl-5-(2-méthylpyrimidine-5-yl)-1H-indazol-1-yl)acétyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Traitement de la glomérulopathie à dépôts de C3
German	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-carboxamid	Behandlung von C3 Glomerulopathie
Greek	(2S,4R)-1-(2-(3-ακετυλ-5-(2-μεθυλπυριμιδιν-5-υλ)-1H-ινδαζολ-1-υλ)ακετυλ)-N-(6-βρωμοπυριδιν-2-υλ)-4-φθοροπυρρολιδιν-2-καρβοξαμιδιό	Θεραπεία της C3 σπειραματοπάθειας
Hungarian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirolidin-2-karboxamid	C3 glomerulopátia kezelése
Italian	(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide	Trattamento della glomerulopatia C3
Latvian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidīn-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridīn-2-il)-4-fluoropirolidīn-2-karboksamīds	C3 glomerulopātijas ārstēšana

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Lithuanian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidino-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridino-2-il)-4-fluoropirolidino-2-karboksamidas	C3 glomerulopatijos gydymas
Maltese	(2S,4R)-1-(2-(3-aċetil-5-(2-metilpirimidina-5-il)-1H-indazol-1-il)aċetil)-N-(6-bromopiridina-2-il)-4-fluworopirrolidina-2-karboksamid	Kura tal-glomerulopatija C3
Polish	(2S,4R)-1-(2-(3-acetyl-5-(2-metylpirimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopiridin-2-yl)-4-fluoropirolidin-2-karboksamid	Leczenie glomerulopatii C3
Portuguese	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirrolidina-2-carboxamida	Tratamento da glomerulopatia por C3
Romanian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidină-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridină-2-il)-4-fluoropirolidină-2-carboxamidă	Tratamentul glomerulopatiei C3
Slovak	(2S,4R)-1-(2-(3-acetyl-5-(2-metylpyrimidín-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridín-2-yl)-4-fluoropyrolidín-2-karboxamid	Liečba C3 glomerulopatie
Slovenian	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidin-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridin-2-il)-4-fluoropirolidin-2-karboksamid	Zdravljenje C3 glomerulopatije
Spanish	(2S,4R)-1-(2-(3-acetil-5-(2-metilpirimidina-5-il)-1H-indazol-1-il)acetil)-N-(6-bromopiridina-2-il)-4-fluoropirolidina-2-carboxamida	Tratamiento de la glomerulopatía C3
Swedish	(2S,4R)-1-(2-(3-acetyl-5-(2-metylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-karboxamid	Behandling av C3 glomerulopati
Norwegian	(2S,4R)-1-(2-(3-acetyl-5-(2-metylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidin-2-karboksamid	Behandling av C3-glomerulopati
Icelandic	(2S,4R)-1-(3 acetýl-5-(2-methýl pýrimidín-5-ýl)-1 H-indazól-1-ýl)-N-brómópýridín-2 ýl)-4-flúórópýrrólídín-2-carboxamíð	Meðferð við C3 glomerulopathy