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Public summary of opinion on orphan designation

2-[3-(2-chloro-4-{[5-cyclopropyl-3-(2,6-dichlorophenyl)-1,2-oxazol-4-yl]methoxy}phenyl)-3-hydroxyazetidin-1-yl]pyridine-4-carboxylic acid-2-amino-2-(hydroxymethyl)propane-1,3-diol (1/1) for the treatment of primary sclerosing cholangitis

On 1 April 2019, orphan designation (EU/3/19/2147) was granted by the European Commission to Gilead Sciences Ireland UC, Ireland, for 2-[3-(2-chloro-4-{[5-cyclopropyl-3-(2,6-dichlorophenyl)-1,2-oxazol-4-yl]methoxy}phenyl)-3-hydroxyazetidin-1-yl]pyridine-4-carboxylic acid-2-amino-2-(hydroxymethyl)propane-1,3-diol (1/1) (also known as GS-9674) for the treatment of primary sclerosing cholangitis.

What is primary sclerosing cholangitis?

Primary sclerosing cholangitis is a disease in which there is long-term damage to the small bile ducts in the liver. These ducts transport fluid called bile from the liver towards the intestines, where it is used to help digest fats. Because of the damage to the ducts, bile acids, essential components of bile, build up in the liver causing damage to liver tissue and leading to liver cirrhosis (scarring of the liver). Early symptoms of the disease include tiredness and itching. The disease is more common in middle-aged men.

Primary sclerosing cholangitis is a long-term debilitating and life-threatening disease because, when the disease progresses, it may lead to liver cirrhosis and liver failure, and may increase the risk of liver cancer.

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

At the time of designation, primary sclerosing cholangitis affected approximately 2.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 140,000 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).

*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 518,400,000 (Eurostat 2019).

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What treatments are available?

At the time of designation, ursodeoxycholic acid was authorised in a number of EU countries for the treatment of primary sclerosing cholangitis. In advanced cases, the patient may need a liver transplant.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with primary sclerosing cholangitis. Preliminary data showed that it may improve the outcome of patients intolerant to ursodeoxycholic acid. 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 by attaching to and activating receptors (targets) called 'farnesoid X receptors (FXR)', which control the production of bile acid. By activating FXRs, this medicine is expected to reduce the production of bile acid in the liver, preventing it from building up and damaging the liver tissue.

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 primary sclerosing cholangitis were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for primary sclerosing cholangitis 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 21 February 2019 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:

Contact details of the current sponsor for this orphan designation can be found on the EMA website.

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	2-[3-(2-chloro-4-{[5-cyclopropyl-3-(2,6-dichlorophenyl)-1,2-oxazol-4-yl]methoxy}phenyl)-3-hydroxyazetidin-1-yl]pyridine-4-carboxylic acid-2-amino-2-(hydroxymethyl)propane-1,3-diol (1/1)	Treatment of primary sclerosing cholangitis
Bulgarian	2-[3-(2-хлоро-4-{[5-циклопропил-3-(2,6-дихлорфенил)-1,2-оксазол-4-ил]метокси}фенил)-3-хидроксиазетидин-1-ил]пиридин-4-карбоксилна киселина—2-амино-2-(хидроксиметил)пропан-1,3-диол (1/1)	Лечение на първичен склерозиращ холангит
Croatian	2-[3-(2-kloro-4-{[5-ciklopropil-3-(2,6-diklorofenil)-1,2-oksazol-4-il]metoksi}fenil)-3-hidroksiazetidin-1-il]piridin-4-karboksilna kiselina—2-amino-2-(hidroksimetil)propan-1,3-diol (1/1)	Liječenje primarnog sklerozirajućeg kolangitisa
Czech	Kyselina 2-[3-(2-chlor-4-{[5-cyklopropyl-3-(2,6-dichlorfenyl)-1,2-oxazol-4-yl]methoxy}fenyl)-3-hydroxyazetidin-1-yl]pyridin-4-karboxylová—2-amino-2-(hydroxymethyl)propan-1,3-diol (1/1)	Léčba primární sklerotizující cholangoitidy
Danish	2-[3-(2-chloro-4-{[5-cyclopropyl-3-(2,6-dichlorophenyl)-1,2-oxazol-4-yl]methoxy}phenyl)-3-hydroxyazetidin-1-yl]pyridin-4-carboxylsyre—2-amino-2-(hydroxymethyl)propan-1,3-diol (1/1)	Behandling af primær skleroserende cholangitis
Dutch	2-[3-(2-chloor-4-{[5-cyclopropyl-3-(2,6-dichloorfenyl)-1,2-oxazol-4-yl]methoxy}fenyl)-3-hydroxyazetidine-1-yl]pyridine-4-carboxylzuur—2-amino-2-(hydroxymethyl)propaan-1,3-diol (1/1)	Behandeling van primaire scleroserende cholangitis
Estonian	2-[3-(2-kloro-4-{[5-tsüklopropüül-3-(2,6-diklorofenüül)-1,2-oksasool-4-üül]metoksü}fenüül)-3-hüdroksüasetidiin-1-üül]püridiin-4-karboksüülhape—2-amino-2-(hüdroksümetüül)propaan-1,3-diool (1/1)	Primaarse skleroseeriva kolangiidi ravi
Finnish	2-[3-(2-kloro-4-{[5-syklopropyyli-3-(2,6-diklorofenyyli)-1,2-oksatsoli-4-yyli]metoksi}fenyyli)-3-hydroksiatsetidiini-1-yyli]pyridiini-4-karboksyylihappo-2-amino-2-(hydroksimetyyli)propaani-1,3-dioli (1/1)	Primaarisen sklerosoivan kolangiitin hoito

[1] At the time of designation

Language	Active ingredient	Indication
French	Acide 2-[3-(2-chloro-4-{[5-cyclopropyl-3-(2,6-dichlorophényl)-1,2-oxazol-4-yl]méthoxy}phényl)-3-hydroxyazétidine-1-yl]pyridine-4-carboxylique—2-amino-2-(hydroxyméthyl)propane-1,3-diol (1/1)	Traitement de la cholangite sclérosante primitive
German	2-[3-(2-Chlor-4-{[5-cyclopropyl-3-(2,6-dichlorphenyl)-1,2-oxazol-4-yl]methoxy}phenyl)-3-hydroxyazetidin-1-yl]pyridin-4-carbonsäure—2-amino-2-(hydroxymethyl)propan-1,3-diol (1/1)	Behandlung der primär sklerosierenden Cholangitis
Greek	2-[3-(2-χλωρο-4-{[5-κυκλοπροπυλο-3-(2,6-διχλωροφαινυλο)-1,2-οξαζολ-4-υλο]μεθοξυ}φαινυλο)-3-υδροξυαζετιδιν-1-υλο]πυριδινο-4-καρβοξυλικό οξύ—2-αμινο-2-(υδροξυμεθυλο)προπανο-1,3-διόλη (1/1)	Θεραπεία της πρωτοπαθούς σκληρυντικής χολαγγειίτιδας
Hungarian	2-[3-(2-klór-4-{[5-ciklopropil-3-(2,6-diklórfenil)-1,2-oxazol-4-il] metoxi}fenil)-3-hidroxiazetidin-1-il]piridin-4-karboxilsav—2-amino-2-(hidroximetil)propán-1,3-diol (1/1)	Primer sclerotizáló cholangitis kezelése
Italian	2-[3-(2-cloro-4-{[5-ciclopropil-3-(2,6-diclorofenil)-1,2-ossazol-4-ile]metossi}fenil)-3-idrossiazetidin-1-ile]acido piridin-4-carbossilico—2-ammino-2-(idrossimetil)propano-1,3-diolo (1/1)	Trattamento della colangite sclerosante primitiva
Latvian	2-[3-(2-hlor-4-{[5-ciklopropil-3-(2,6-dihlorfenil)-1,2-oksazol-4-il]metoksi}fenil)-3-hidroksiazetidīn-1-il]piridīn-4-karbonskābes-2-amino-2-(hidroksimetil)propān-1,3-diols (1/1)	Primārā sklerozējošā holangīta ārstēšana
Lithuanian	2-[3-(2-chloro-4-{[5-ciklopropil-3-(2,6-dichlorofenil)-1,2-oksazol-4-il]metoksi}fenil)-3-hidroksiazetidin-1-il]piridin-4-karboksirūgšties—2-amino-2-(hidroksimetil)propano-1,3-diolis (1/1)	Pirminio sklerozuojančio cholangito gydymas
Maltese	2-[3-(2-kloro-4-{[5-ċiklopropil-3-(2,6-diklorofenil)-1,2-ossażol-4-il]metossi}fenil)-3-idrossiażetidin-1-il]piridina-4-aċidu karbossiliku—2-ammino-2-(idrossimetil)propan-1,3-diol (1/1)	Kura tal-kolanġite sklerosanti primarja
Polish	Kwas 2-[3-(2-chloro-4-{[5-cyklopropylo-3-(2,6-dichlorofenylo)-1,2-oksazolo-4-ylo]metoksy}fenylo)-3-hydroksyazetydyno-1-ylo]pirydyno-4-karboksylowy — 2-amino-2-(hydroksymetylo)propano-1,3-diol (1/1)	Leczenie pierwotnego stwardniającego zapalenia dróg żółciowych
Portuguese	Ácido 2-[3-(2-cloro-4-{[5-ciclopropil-3-(2,6-diclorofenil)-1,2-oxazol-4-il]metoxi}fenil)-3-hidroxiazetidin-1-il]piridina-4-carboxílico—2-amino-2-(hidroximetil)propano-1,3-diol (1/1)	Tratamento da colangite esclerosante primária

Language	Active ingredient	Indication
Romanian	Acid 2-[3-(2-cloro-4-{[5-ciclopropil-3-(2,6-diclorofenil)-1,2-oxazol-4-il]metoxi}fenil)-3-hidroxiazetidin-1-il]piridin-4-carboxilic—2-amino-2-(hidroximetil)propan-1,3-diol (1/1)	Tratamentul colangitei sclerozante primare
Slovak	kyselina 2-[3-(2-chlór-4-{[5-cyklopropyl-3-(2,6-dichlórfenyl)-1,2-oxazol-4-yl]metoxy}fenyl)-3-hydroxyazetidín-1-yl]pyridín-4-karboxylová—2-amino-2-(hydroxymetyl)propán-1,3-diol (1/1)	Liečba primárnej sklerotizujúcej cholangitídy
Slovenian	2-[3-(2-kloro-4-{[5-ciklopropil-3-(2,6-diklorofenil)-1,2-oksazol-4-il]metoksi}fenil)-3-hidroksiazetidin-1-il]piridin-4-karboksilna kislina—2-amino-2-(hidroksimetil)propan-1,3-diol (1/1)	Zdravljenje primarnega sklerozirajočega holangitisa
Spanish	ácido 2-[3-(2-cloro-4-{[5-ciclopropil-3-(2,6-diclorofenil)-1,2-oxazol-4-il]metoxi}fenil)-3-hidroxiazetidin-1-il]piridina-4-carboxílico — 2-amino-2-(hidroximetil)propano-1,3-diol (1/1)	Tratamiento de colangitis esclerosante primaria
Swedish	2-[3-(2-klor-4-{[5-cyklopropyl-3-(2,6-diklorfenyl)-1,2-oxazol-4-yl]metoxy}fenyl)-3-hydroxyazetidin-1-yl]pyridin-4-karboxylsyra—2-amino-2-(hydroxymetyl)propan-1,3-diol (1/1)	Behandling av primär skleroserande kolangit
Norwegian	2-[3-(2-klor-4-{[5-syklopropyl-3-(2,6-diklorfenyl)-1,2-oksazol-4-yl]metoksy}fenyl)-3-hydroksyazetidin-1-yl]pyridin-4-karboksylsyre-2-amino-2-(hydroksymetyl)propan-1,3-diol(1/1)	Behandling av primær skleroserende cholangitt
Icelandic	2-[3-(2-klór-4-{[5-cýklóprópýl-3-(2,6-díklórfenýl)-1,2-oxasól-4-ýl]metoxý}fenýl)-3-hýdroxýasetidín-1-ýl]pýridín-4-karboxýlsýru-2-amínó-2-(hýdroxýmetýl)própan-1,3-díól (1/1)	Meðferð við frumkominni herslisgallrásarbólgu