



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

(S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid for the treatment of primary sclerosing cholangitis

On 16 October 2017, orphan designation (EU/3/17/1914) was granted by the European Commission to Pharma Gateway AB, Sweden, for (S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (also known as IDN-7314) 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 1.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 83,000 people<sup>\*</sup>, 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).

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<sup>\*</sup>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 515,700,000 (Eurostat 2017).



## **What treatments are available?**

At the time of designation, ursodeoxycholic acid was authorised in the EU 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 because laboratory studies indicate that it significantly reduces death of liver cells. 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?**

It is thought that the process of normal cell death (apoptosis) can be increased in liver disease and contribute to the liver damage seen in patients with primary sclerosing cholangitis. This medicine works by blocking a group of proteins called caspases, which are involved in apoptosis and the formation of inflammatory substances. By blocking caspases, the medicine is expected to reduce death of liver cells and slow down 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, no clinical trials with the medicine in patients with primary sclerosing cholangitis had been started.

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 7 September 2017 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	(S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid	Treatment of primary sclerosing cholangitis
Bulgarian	(S)-3-((S)-2-(2-((2,6-дифлуорофенил)амино)-2-оксоацетамидо)пропанамидо)-4-оксо-5-(2,3,5,6-тетрафлуорофенокси)пентанова киселина	Лечение на първичен склерозиращ холангит
Croatian	(S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-oksoacetamido)propanamido)-4-okso-5-(2,3,5,6-tetrafluorofenoksi)pentanoična kiselina	Liječenje primarnog sklerozirajućeg kolangitisa
Czech	(S)-3-((S)-2-(2-((2,6-difluorofenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorofenoxy)-pentanová kyselina	Léčba primární sklerotizující cholangitidy
Danish	(S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentansyre	Behandling af primær skleroserende cholangitis
Dutch	(S)-3-((S)-2-(2-((2,6-difluorfenyl)amino)-2-oxoacetamide)propanamide)-4-oxo-5-(2,3,5,6-tetrafluorofenoxy)pentaanzuur	Behandeling van primaire scleroserende cholangitis
Estonian	(S)-3-((S)-2-(2-((2,6-difluorofenüül)amino)-2-oksoatsetamido)propaanamido)-4-okso-5-(2,3,5,6-tetrafluorofenoksü)pentaanhape	Primaarse skleroseeriva kolangiidi ravi
Finnish	(S)-3-((S)-2-(2-((2,6-difluorifenyyli)amino)-2-oksoasetamido)propaaniamido)-4-oksi-5-(2,3,5,6-tetrafluorifenoksi)pentaanihappo	Primaarisen sklerosoivan kolangiitin hoito
French	Acide (S)-3-((S)-2-(2-((2,6-difluorophényl)amino)-2-oxoacétamido)propanamido)-4-oxo-5-(2,3,5,6-tétrafluorophénoxy)pentanoïque	Traitement de la cholangite sclérosante primitive
German	(S)-3-((S)-2-(2-((2,6-Difluorphenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentansäure	Behandlung der primär sklerosierenden Cholangitis
Greek	(S)-3-((S)-2-(2-((2,6-διφθοροφαινυλ)αμινο)-2-οξοακεταμιδο)προπαναμιδο)-4-οξο-5-(2,3,5,6-τετραφθοροφαινοξυ)πεντανοϊκό οξύ	Θεραπεία της πρωτοπαθούς σκληρυντικής χολαγγειίτιδας
Hungarian	(S)-3-((S)-2-(2-((2,6-difluorofenil)-amino)-2-oxoacetamid)-propanamid)-4-oxo-5-(2,3,5,6-tetrafluoro-fenoxi)pentánsav	Primer sclerotizáló cholangitis kezelése
Italian	Acido (S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-ossoacetamido)propanamido)-4-osso-5-(2,3,5,6-tetrafluorofenossi)pentanoico	Trattamento della colangite sclerosante primitiva

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

Language	Active ingredient	Indication
Latvian	(S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-oksoacetamīd)propānamīd)-4-okso-5-(2,3,5,6-tetrafluorofenoksi)pentānskābe	Primārā sklerozējošā holangīta ārstēšana
Lithuanian	(S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-oksoacetamido)propanamido)-4-okso-5-(2,3,5,6-tetrafluorofenoksi)pentanoinė rūgštis	Pirminio sklerozuojančio cholangito gydymas
Maltese	(S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid	Kura tal-kolangite sklerosanti primarja
Polish	Kwas (S)-3-((S)-2-(2-((2,6-difluorofenyl)amino)-2-oksoacetamido)propanamido)-4-okso-5-(2,3,5,6-tetrafluorofenoksy)pentanowy	Leczenie pierwotnego stwardniającego zapalenia dróg żółciowych
Portuguese	Ácido (S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorofenoxi) pentanoico	Tratamento da colangite esclerosante primária
Romanian	Acid (S)-3-((S)-2-(2-((2,6-difluorfenil)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorfenoxi)pentanoic	Tratamentul colangitei sclerozante primare
Slovak	Kyselina (S)-3-((S)-2-(2-((2,6-difluórofenyl)amino)-2-oxoacetamido)propánamido)-4-oxo-5-(2,3,5,6-tetrafluórofenoxý)pentánová	Liečba primárnej sklerotizujúcej cholangitídy
Slovenian	(S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-oksoacetamido)propanamido)-4-okso-5-(2,3,5,6-tetrafluorofenoksi)pentanojska kislina	Zdravljenje primarnega sklerozirajočega holangitisa
Spanish	Ácido (S)-3-((S)-2-(2-((2,6-difluorofenil)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorofenoxi)pentanoico	Tratamiento de colangitis esclerosante primaria
Swedish	(S)-3-((S)-2-(2-((2,6-difluorofenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorofenoxy)pentansyra	Behandling av primär skleroserande kolangit
Norwegian	(S)-3-((S)-2-(2-((2,6-difluorofenyl)amino)-2-oksoacetamido)propanamido)-4-okso-5-(2,3,5,6-tetrafluorofenoksy)pentansyre	Behandling av primær skleroserende cholangitt
Icelandic	(S)-3-((S)-2-(2-((2,6-tvíflúorfenýl)amínó)-2-oxóasetamíð)própanamíð)-4-oxó-5-(2,3,5,6-tetraflúorfenoxý)valerínsýra	Meðferð við frumkominni herslisgallrásarbólgu