



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate] for the treatment of biliary tract cancer

On 16 October 2017, orphan designation (EU/3/17/1916) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for 5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate] (also known as Debio 1347) for the treatment of biliary tract cancer.

### What is biliary tract cancer?

Biliary tract cancer is cancer of the bile ducts and gallbladder. These are parts of the digestive system that transport and store bile, a fluid which is produced by the liver and released into the intestines after a meal to help digest fats. The cancer is characterised by various features such as abnormal liver function tests, pain in the belly, yellowish discoloration of the skin and weight loss.

Biliary tract cancer is a long-term debilitating and life-threatening disease due to liver failure and problems caused when the cancer blocks the bile ducts.

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

At the time of designation, biliary tract cancer affected approximately 1.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 77,000 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, no satisfactory methods were authorised in the EU for the treatment of biliary tract cancer. Some patients with early disease could undergo surgery to remove the cancer. Other treatments included chemotherapy (medicines to treat cancer).

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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 515,700,000 (Eurostat 2017).



## How is this medicine expected to work?

This medicine is a tyrosine kinase inhibitor, which blocks the activity of enzymes known as tyrosine kinases, particularly those that are part of receptors called fibroblast growth factor receptors (FGFRs). FGFRs are found on the surface of cells and are involved in the growth and spread of cancer cells. By blocking the tyrosine kinases in the FGFR receptors, this medicine is expected to prevent or slow down the growth of biliary tract cancer.

## 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 including patients with biliary tract cancer were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for biliary tract cancer 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	5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate]	Treatment of biliary tract cancer
Bulgarian	5-амино-1-(2-метил-1H-бензо[d]имидазол-5-ил)-1H-пиразол-4-ил 1H-индол-2-ил кетон моно[(S)-2-хидроксисукцинат]	Лечение на рак на жлъчните пътища
Croatian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il keton mono[(S)-2-hidroksisukcinat]	Liječenje raka bilijarnog trakta
Czech	5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate]	Léčba karcinomu žlučových cest
Danish	5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinat]	Behandling af galdegangscancer
Dutch	5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate]	Behandeling van galweg kanker
Estonian	5-amino-1-(2-metüül-1H-benzo[d]imidazool-5-üül)-1H-pürazool-4-üül 1H-indool-2-üül ketoon mono[(S)-2-hüdroksüsuksinaat]	Sapiteede kasvaja ravi
Finnish	5-amino-1-(2-metyyli-1H-bentso[d]imidatsol-5-yyli)-1H-pyratsol-4-yyli 1H-indol-2-yyli ketoni mono[(S)-2-hydroksisukkinaatti]	Sappiteiden syövän hoito
French	5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate]	Traitement du cancer des voies biliaires
German	5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinat]	Behandlung von Tumoren der Gallenwege
Greek	5-αμινο-1-(2-μεθυλ-1H βενζο[d]ιμιδαζολ-5-υλ)1H-πυραζολ-4-υλ 1H-ινδολ-2-υλ κετόνη μονο[(S)-2-υδροξυ σουκκινική]	Θεραπεία του καρκίνου της χοληφόρου οδού
Hungarian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il keton mono[(S)-2-hidroxiszukcinát]	Epeúti rák kezelése
Italian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-idroxysuccinato]	Trattamento del carcinoma delle vie biliari
Latvian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il ketona mono[(S)-2-hidroksisukcināts]	Žultsvadu sistēmas vēža ārstēšana

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

Language	Active ingredient	Indication
Lithuanian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il ketono mono[(S)-2-hidroksisukcinatas]	Tulžies latakų vėžio gydymas
Maltese	5-ammino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il keton mono[(S)-2-idrossisuccinat]	Kura tal-kanċer tal-apparat tal-bili
Polish	5-amino-1-(2-metylo-1H-benzo[d]imidazolo-5-ylo)-1H-pirazolo-4-ylo 1H-indolo-2-ylo keton mono[(S)-2-hydroksybursztynianu]	Leczenie raka dróg żółciowych
Portuguese	Mono[(S)-2-hidroxisuccinato de 5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il cetona]	Tratamento da neoplasia das vias biliares
Romanian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il cetonă mono[(S)-2-hidroxisuccinat]	Tratamentul cancerului de căi biliare
Slovak	5-amino-1-(2-metyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketón mono[(S)-2-hydroxysuccinát]	Liečba karcinómu žlčových ciest
Slovenian	5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-yl 1H-indol-2-il ketone mono[(S)-2-hidroksisuccinat]	Zdravljenje raka žolčnih vodov
Spanish	Mono[(S)-2-hidroxisuccinato de 5-amino-1-(2-metil-1H-benzo[d]imidazol-5-il)-1H-pirazol-4-il 1H-indol-2-il cetona]	Tratamiento del cáncer del árbol biliar
Swedish	5-amino-1-(2-metyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl keton mono[(S)-2-hydroxysuccinat]	Behandling av gallvägscancer
Norwegian	5-amino-1-(2-metyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl keton mono[(S)-2-hydroxysuccinat]	Behandling av gallegangskreft
Icelandic	5-amínó-1-(2-metýl-1H-benzó[d]ímidazól-5-ýl)-1H-pýrazól-4-ýl 1H-índól-2-ýl ketón mónó[(S)-2-hýdroxýsuccínat]	Meðferð við krabbameini í gallvegum