



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

1-[(3S)-3-{4-amino-3-[(3,5-dimethoxyphenyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-one for the treatment of biliary tract cancer

On 1 April 2019 orphan designation (EU/3/19/2146) was granted by the European Commission to Taiho Pharma Europe Limited, United Kingdom, for 1-[(3S)-3-{4-amino-3-[(3,5-dimethoxyphenyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-one (also known as TAS-120) for the treatment of biliary tract cancer.

What is biliary tract cancer?

Biliary tract cancer affects the bile ducts and gallbladder. These are parts of the digestive system that transport and store bile, a fluid produced by the liver and released into the intestines to help digest fats. The cancer is characterised by 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 78,000 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 (medicines to treat cancer), although these were not authorised for biliary tract cancer.

*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).



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 (targets) 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 in 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. Orphan designation of the medicine had been granted in the United States for the treatment of cholangiocarcinoma (bile duct cancer).

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	1-[(3S)-3-{4-amino-3-[(3,5-dimethoxyphenyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-one	Treatment of biliary tract cancer
Bulgarian	1-[(3S)-3-{4-амино-3-[(3,5-диметоксифенил)етинил]-1H-пиразоло[3,4-д]пиримидин-1-ил}пирролидин-1-ил]-2-пропен-1-он	Лечение на рак на жлъчните пътища
Croatian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksifenil)etnil]-1H-pirazolo[3,4-d]pirimidin-1-il}pirolidin-1-il]-2-propen-1-on	Liječenje raka bilijarnog trakta
Czech	1-[(3S)-3-{4-amino-3-[(3,5-dimethoxyfenyl)ethynyl]-1H-Pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-on	Léčba karcinomu žlučových cest
Danish	1-[(3S)-3-{4-amino-3-[(3,5-dimethoxyphenyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-one	Behandling af galdegangscancer
Dutch	1-[(3S)-3-{4-amino-3-[(3,5-dimethoxyfenyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidine-1-yl]-2-propen-1-one	Behandeling van galwegkanker
Estonian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksüfenüül)etünüül]-1H-pürasolo[3,4-d]pürimidiin-1-üül}pürrolidiin-1-üül]-2-propeen-1-oon	Sapiteedekasvaja ravi
Finnish	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksifenyyli)etynyyli]-1H-pyratsolo[3,4-d]pyrimidin-1-yyli}pyrrolidin-1-yyli]-2-propen-1-oni	Sappiteidensyövän hoito
French	1-[(3S)-3-{4-amino-3-[(3,5-diméthoxyphényl)éthynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propén-1-one	Traitement du cancer des voies biliaires
German	1-[(3S)-3-{4-Amino-3-[(3,5-dimethoxyphenyl)ethynyl]-1H-Pyrazol[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-one	Behandlung von Tumoren der Gallenwege
Greek	1-[(3S)-3-{4-αμινό-3-[(3,5-διμεθοξυφαινυλ)αιθινυλ]-1H-πυραζολο[3,4-d]πυριμιδιν-1-υλο}πυρρολιδιν-1-υλο]-2-προπεν-1-όνη	Θεραπεία του καρκίνου της χοληφόρου οδού

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoxi-fenil)-etinil]-1H-pirazolo[3,4-d]pirimidin-1-il}-pirrolidin-1-il]-2-propen-1-on	Epeútirák kezelése
Italian	1-[(3S)-3-{4-amino-3-[(3,5-dimetossifenil)etinil]-1H-pirazolo[3,4-d]pirimidin-1-il}pirrolidin-1-il]-2-propen-1-one	Trattamento del carcinoma delle vie biliari
Latvian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksifenil)etinil]-1H-pirazolo[3,4-d]pirimidīn-1-il}pirolidīn-1-il]-2-propēn-1-ons	Žultsvadu sistēmas vēža ārstēšana
Lithuanian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksifenil)etinil]-1H-pirazolo[3,4-d]pirimidin-1-il}pirolidin-1-il]-2-propen-1-onas	Tulžies latakų vėžio gydymas
Maltese	1-[(3S)-3-{4-ammino-3-[(3,5-dimetossifenil)etinil]-1H-pirazolo[3,4-d]pirimidina-1-il}pirrolidin-1-il]-2-propen-1-one	Kuratal-kancertal-apparattal-bili
Polish	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksyfenylo)etynyl]-1H-pirazolo[3,4-d]pirimidyn-1-ylo}pirolidyn-1-ylo]-2-propen-1-on	Leczenie raka dróg żółciowych
Portuguese	1-[(3S)-3-{4-amino-3-[(3,5-dimetoxifenil)etinil]-1H-pirazolo[3,4-d]pirimidin-1-il}pirrolidin-1-il]-2-propen-1-ona	Tratamento da neoplasia das vias biliares
Romanian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoxifenil)etinil]-1H-pirazol[3,4-d]pirimidin-1-il}pirolidin-1-il]-2-propen-1-onă	Tratamentul cancerului de căi biliare
Slovak	1-[(3S)-3-{4-amino-3-[(3,5-dimetoxifyfenyl)etinyl]-1H-pyrazol[3,4-d]pyrimidín-1-yl}pyrolidín-1-yl]-2-propén-1-ón	Liečba karcinómu žlčových ciest
Slovenian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksifenil)etinil]-1H-pirazolo[3,4-d]pirimidin-1-il}pirolidin-1-il]-2-propen-1-one	Zdravljenje raka žolčnih vodov
Spanish	1-[(3S)-3-{4-amino-3-[(3,5-dimetoxifenil)etinil]-1H-pirazolo[3,4-d]pirimidin-1-il}pirrolidin-1-il]-2-propen-1-ona	Tratamiento del cáncer del árbol biliar
Swedish	1-[(3S)-3-{4-amino-3-[(3,5-dimetoxifyfenyl)etynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}-pyrrolidin-1-yl]-2-propen-1-one	Behandling av gallväggscancer
Norwegian	1-[(3S)-3-{4-amino-3-[(3,5-dimetoksyfenyl)etynyl]-1H-pyrazolo[3,4-d]pyrimidin-1-yl}pyrrolidin-1-yl]-2-propen-1-on	Behandling av gallegangskreft
Icelandic	1-[(3S)-3-{4-amínó-3-[(3,5-dímetoxýfenýl)etýnýl]-1H-pýrasóló[3,4-d]pýrimídín-l-ýl}pýrrólídín-l-ýl]-2-própen-1-ón	Meðferð við krabbameini í gallvegum