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EMA/COMP/309638/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(R)-6-(2-fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amine dihydrochloride for the treatment of biliary tract cancer

On 30 May 2016, orphan designation (EU/3/16/1657) was granted by the European Commission to Coté Orphan Consulting UK Limited, United Kingdom, for (R)-6-(2-fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amine dihydrochloride 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 clinical 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 which is often diagnosed when the disease has reached a late stage, worsening the prognosis for the patient.

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, choice of treatment for biliary tract cancer depended mainly on how advanced the disease was. Some patients with early disease could undergo surgery to remove the cancer. Other treatments included chemotherapy (medicines to treat 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 513,700,000 (Eurostat 2016).

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The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with biliary tract cancer because early studies suggest that it might improve the outcome of patients whose disease returns after previous treatments. 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 a tyrosine kinase inhibitor. This means that it blocks the activity of enzymes known as tyrosine kinases, particularly tyrosine kinases that are present in 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 the growth of biliary tract cancer.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with biliary tract cancer were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for biliary tract cancer. Orphan designation of this medicine had been granted in the United States of America for cholangiocarcinoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 April 2016 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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	(R)-6-(2-fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amine dihydrochloride	Treatment of biliary tract cancer
Bulgarian	(R)-6-(2-флуорофенил)-N-(3-(2-((2-метоксиетил)амино)етил)фенил)-5,6-дихидробензо[h]квиназолин-2-амин дихидрохлорид	Лечение на рак на жлъчните пътища
Croatian	(R)-6-(2-fluorofenil)-N-(3-(2-((2-metoksietil)amino)etil)fenil)-5,6-dihidrobenzo[h]kinazolin-2-amin dihidroklorid	Liječenje raka bilijarnog trakta
Czech	(R)-6-(2-fluorfenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)fenyl)-5,6-dihydrobenzo[h]chinazolin-2-amin dihydrochlorid	Léčba karcinomu žlučových cest
Danish	(R)-6-(2-fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amin dihydrochlorid	Behandling af galdegangscancer
Dutch	(R)-6-(2-fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amine dihydrochloride	Behandeling van galweg kanker
Estonian	(R)-6-(2-fluorofenüül)-N-(3-(2-((2-metoksüetüül)amino)etüül)fenüül)-5,6-dihüdrobenso[h]kinasoliin-2-amiini dihüdrokloriid	Sapiteede kasvaja ravi
Finnish	(R)-6-(2-fluorifenyyli)-N-(3-(2-((2-metoksietyyli)amino)etyyli)fenyyli)-5,6-dihydrobentso[h]kinatsolin-2-amiinidihydrokloridi	Sappiteiden syövän hoito
French	Dichlorhydrate (R)-6-(2-fluorophényle)-N-(3-(2-((2-méthoxyéthyle)amino)éthyl)phényle)-5,6-dihydrobenzo[h]quinazoline-2-amine	Traitement du cancer des voies biliaires
German	(R)-6-(2-Fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amindihydrochlorid	Behandlung von Tumoren der Gallenwege
Greek	Διυδροχλωρική (R)-6-(2-φθοριοφαινυλ)-N-(3-(2-((2-μεθοξυαιθυλ)αμινο)αιθυλ)φαινυλ)-5,6-διυδροβενζο[h]κιναζολιν-2-αμίνη	Θεραπεία του καρκίνου της χοληφόρου οδού
Hungarian	(R)-6-(2-fluorofenil)-N-(3-(2-((2-metoxietil)amino)etil)fenil)-5,6-dihidrobenzo[h]quinazolin-2-amin dihidroklorid	Epeúti rák kezelése
Italian	(R)-6-(2-fluorofenil)-N-(3-(2-((2-metossietil)amino)etil)fenil)-5,6-diidrobenzo[h]quinazolina-2-amina dicloridrato	Trattamento del carcinoma delle viebiliari

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	(R)-6-(2-fluorfenil)-N-(3-(2-((2-metoksietil)amino)etil)fenil)-5,6-dihidrobenzo[h]hinazolīn-2-amīna dihidrohlorīds	Žultsvadu sistēmas vēža ārstēšana
Lithuanian	(R)-6-(2-fluorfenil)-N-(3-(2-((2-metoksietil)amin)etil)fenil)-5,6-dihidrobenzo[h]kvinazolin-2-amino dihidrochloridas	Tulžies latakų vėžio gydymas
Maltese	(R)-6-(2-fluorophenyl)-N-(3-(2-((2-methoxyethyl)amino)ethyl)phenyl)-5,6-dihydrobenzo[h]quinazolin-2-amine dihydrochloride	Kura tal-kanċer tal-apparat tal-bili
Polish	(R)-6-(2-fluorofenyl)-N-(3-(2-((2-metoksyetyl)amino)etyl)fenyl)-5,6-dihydrobenzo[h]chinazolina-2-amino dihydrochlorek	Leczenie raka dróg żółciowych
Portuguese	Dicloridrato de (R)-6-(2-fluorofenil)-N-(3-(2-((2-metoxietil)amino)etil)fenil)-5,6-di-hidrobenzo[h]quinazolina-2-amina	Tratamento da neoplasia das vias biliares
Romanian	Diclorhidrat de (R)-6-(2-fluorofenil)-N-(3-(2-((2-metoxietil)amino)etil)fenil)-5,6-dihidrobenzo[h]chinazolin-2-amină	Tratamentul cancerului de căi biliare
Slovak	(R)-6-(2-fluorofenyl)-N-(3-(2-((2-metoxyetyl)amino)etyl)fenyl)-5,6-dihydrobenzo[h]chinazolin-2-amín dihydrochlorid	Liečba karcinómu žlčových ciest
Slovenian	(R)-6-(2-fluorofenil)-N-(3-(2-((2-metoksietil)amino)etil)fenil)-5,6-dihidrobenzo[h]kinazolin-2-amindihidroklorid	Zdravljenje raka žolčnih vodov
Spanish	(R)-6-(2-fluorofenil)-N-(3-(2-((2-metoxietil)amino)etil)fenil)-5,6-dihidrobenzo[h]quinazolina-2-amina diclorhidrato	Tratamiento del cáncer del árbol biliar
Swedish	(R)-6-(2-fluorfenyl)-N-(3-(2-((2-metoxietyl)amino)etyl)fenyl)-5,6-dihydrobenzo[h]kinazolin-2-amin-dihydroklorid	Behandling av gallvägscancer
Norwegian	(R)-6-(2-fluorofenyl)-N-(3-(2-((2-metoksyetyl)amino)etyl)fenyl)-5,6-dihydrobenzo[h]kinazolin-2-amin-dihydroklorid	Behandling av gallegangskreft
Icelandic	(R)-6-(2-flúorfenýl)-N-(3-(2-((2-metoxýethýl)amínó)etýl)fenýl)-5,6-díhýdróbensó[h]kínasólín-2-amíndíhýdróklóríð	Meðferð við krabbameini í gallvegum