



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-β-D-glucopyranosyl]-oxy]-5-(4-
({(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy}carbonyl}oxy)-3,5-
dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-
6(5aH)-one for the treatment of biliary tract cancer

On 4 June 2014, orphan designation (EU/3/14/1270) was granted by the European Commission to CellAct Pharma GmbH, Germany, for (5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-β-D-glucopyranosyl]-oxy]-5-(4-((2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one 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 1.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 87,000 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 511,100,000 (Eurostat 2014).



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).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with biliary tract cancer because early studies suggest that it might improve the outcome of patients who did not respond to standard 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 'prodrug' of a substance called etoposide, which has been authorised in the EU for many years to treat cancer. It consists of etoposide linked to another substance called an ester group. The medicine is broken down in the body by enzymes called carboxylesterases, releasing the active etoposide. Because these enzymes are present in high levels in the digestive system, including the biliary tract, high levels of etoposide are expected to be produced within the cancerous tissue, where they damage the DNA of cancer cells, killing them and reducing the growth of the 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 the 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 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 9 April 2014 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:

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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	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-β-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy))-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one	Treatment of biliary tract cancer
Bulgarian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Етилиден]-β-D-глюкопиранозил]-окси]-5-(4-({[(2,2-диметил-1,3-диоксолан-4-ил)метокси]карбонил}окси))-3,5-диметоксифенил)-5,8,8a,9-тетрахидроизобензофуоро[5,6-φ][1,3]бензодиоксол-6(5aH)-едно	Лечение на рак на жлъчните пътища
Croatian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etiliden]-β-D-glukopiranozil]-oksi]-5-(4-({[(2,2-dimetil-1,3-dioksolan-4-il)metoksi]karbonil}oksi))-3,5-dimetoksifenil)-5,8,8a,9-tetrahidroizobenzofuro[5,6-f][1,3]benzodioksol-6(5aH)-on	Liječenje raka bilijarnog trakta
Czech	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-ethyliden]-beta-D-glukopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)metoxy]karbonyl}oxy))-3,5-dimethoxyfenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-on	Léčba karcinomu žlučových cest
Danish	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-ethyliden]-beta-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy))-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-on	Behandling af galdegangscancer
Dutch	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylideen]-beta-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolaan-4-yl)methoxy]carbonyl}oxy))-3,5-dimethoxyfenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one	Behandeling van galweg kanker
Estonian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etüülideen]-beeta-D-glükopüranosüül]-oksü]-5-(4-({[(2,2-dimetüül-1,3-dioksolaan-4-üül)metoksü]karbonüül}oksü))-3,5-dimetoksüfenüül)-5,8,8a,9-tetrahüdroisobensofuro[5,6-f][1,3]bensodioksool-6(5aH)-üks	Sapiteede kasvaja ravi

¹ At the time of designation

Language	Active ingredient	Indication
Finnish	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etyyliideeni]-beeta-D-glukopyranosyyli]-oksi]-5-(4-({[(2,2-dimetyyli-1,3-dioksolaani-4-yyli)metoksi]karbonyyli}oksi)-3,5-dimetoksifenyli)-5,8,8a,9-tetrahydroisobentsofuro[5,6-f][1,3]bentsodioksoli-6(5aH)-oni	Sappiteiden syövän hoito
French	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Éthylidène]-bêta-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-diméthyl-1,3-dioxolan-4-yl)méthoxy]carbonyl}oxy)-3,5-diméthoxyphényl)-5,8,8a,9-tétrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one	Traitement du cancer des voies biliaires
German	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-beta-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one	Behandlung von Tumoren der Gallenwege
Greek	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-αιθυλιδενο]-β-D-γλυκοπυρανοσυλ]-οξυ]-5-(4-({[(2,2-διμεθυλο-1,3-διοξολαν-4-υλ)μεθοξυ]καρβονυλ}οξυ)-3,5-διμεθοξυφαινυλο)-5,8,8a,9-τετραϋδροϊσοβενζοφουρο[5,6-f][1,3]βενζοδιοξολ-6(5aH)-όνη	Θεραπεία του καρκίνου της χοληφόρου οδού
Hungarian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etilidén]-béta-D-glukopiranozil]-oxi]-5-(4-({[(2,2-dimetil-1,3-dioxolán-4-il)metoxi]karbonil}oxi)-3,5-dimetoxifenil)-5,8,8a,9-tetrahidroizobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-on	Epeüti rák kezelése
Italian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-beta-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one	Trattamento del carcinoma delle vie biliari
Latvian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etilidēn]-beta-D-glikopiranozil]-oksi]-5-(4-({[(2,2-dimetil-1,3-dioksolan-4-il)metoksi]karbonil}oksi)-3,5-dimetoksifenil)-5,8,8a,9-tetrahidroizobenzofuro[5,6-f][1,3]benzodioksol-6(5aH)-ons	Žultsvadu sistēmas vēža ārstēšana
Lithuanian	(5R, 5aR, 8aR, 9S)-9-[[4,6-O-[(R)-etilideno]-β-D-glukopiranozil]-oksi]-5-(4-({[(2,2-dimetil-1,3-dioksolan-4-il)metoksi]karbonil}oksi)-3,5-dimetoksifenil)-5,8,8a,9- tetrahidroizobenzofuro [5,6-f][1,3]benzodioksol-6(5aH)-onas	Tulžies latakų vėžio gydymas

Language	Active ingredient	Indication
Maltese	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-beta-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy))-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one	Kura tal-kanċer tal-apparat tal-bili
Polish	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etylideno]-beta-D-glukopiranozylo]-oksy]-5-(4-({[(2,2-dimetylo-1,3-dioksolano-4-ilo)metoksy]carbonylo}oksy))-3,5-dimetoksyfenylo)-5,8,8a,9-tetrahydroizobenzofuro[5,6-f][1,3]benzodioksol-6(5aH)-on	Leczenie raka dróg żółciowych
Portuguese	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etilideno]-beta-D-glucopiranosil]-oxi]-5-(4-({[(2,2-dimetil-1,3-dioxolan-4-il)metoxi]carbonil}oxi))-3,5-dimetoxifenil)-5,8,8a,9-tetrahidroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-ona	Tratamento da neoplasia das vias biliares
Romanian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etiliden]-beta-D-glucopiranozil]-oxi]-5-(4-({[(2,2-dimetil-1,3-dioxolan-4-il)metoxi]carbonil}oxi))-3,5-dimetoxifenil)-5,8,8a,9-tetrahidroizobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-onă	Tratamentul cancerului de căi biliare
Slovak	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etylidén]-beta-D-glukopyranozyl]-oxy]-5-(4-({[(2,2-dimetyl-1,3-dioxolan-4-yl)metoxy]carbonyl}oxy))-3,5-dimetoxyfenyl)-5,8,8a,9-tetrahydroizobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-ón	Liečba karcinómu žľčových ciest
Slovenian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etiliden]-beta-D-glukopiranozil]-oksi]-5-(4-({[(2,2-dimetil-1,3-dioksolan-4-il)metoksi]karbonil}oksi))-3,5-dimetoksifenil)-5,8,8a,9-tetrahidroizobenzofuro[5,6-f][1,3]benzodioksol-6(5aH)-on	Zdravljenje raka žolčnih vodov
Spanish	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-etilideno]-beta-D-glucopiranosil]-oxi]-5-(4-({[(2,2-dimetil-1,3-dioxolan-4-il)metoxi]carbonil}oxi))-3,5-dimetoxifenil)-5,8,8a,9-tetrahidroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-on	Tratamiento del cáncer del árbol biliar
Swedish	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Etyliden]-beta-D-glukopyranosyl]-oxi]-5-(4-({[(2,2-dimetyl-1,3-dioxolan-4-yl)metoxi]karbonyl}oxi))-3,5-dimetoxifenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-on	Behandling av gallvägscancer

Language	Active ingredient	Indication
Norwegian	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Etyliden]-beta-D-glukopyranosyl]-oksy]-5-(4-({[(2,2-dimetyl-1,3-dioksolan-4-yl)metoksy]karbonyl}oksy)-3,5-dimetoksyfenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioksol-6(5aH)-on	Behandling av gallegangskreft
Icelandic	(5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Etylíden]-beta-D-glúkópýranósýl]-oxý]-5-(4-({[(2,2-dímetyl-1,3-díoxólan-4-ýl)metoxý]karbónýl}oxý)-3,5-dímetoxýfenýl)-5,8,8a,9-tetrahýdrísóbensófúró[5,6-f][1,3]bensódíoxól-6(5aH)-ón	Meðferð við krabbameini í gallvegum