



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 February 2019
EMA/830039/2018

Public summary of opinion on orphan designation

(2S)-2-{{(2R)-2-[[{3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid for the treatment of biliary atresia

On 14 December 2018, orphan designation (EU/3/18/2103) was granted by the European Commission to Albireo AB, Sweden, for (2S)-2-{{(2R)-2-[[{3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid (also known as A4250) for the treatment of biliary atresia.

What is biliary atresia?

Biliary atresia is a condition in which the bile ducts that transport bile from the liver towards the intestines are blocked or absent. As a result, the bile – which is used to digest fats – stays in the liver where it accumulates and causes damage. Symptoms of the disease appear a few weeks after birth.

Biliary atresia is a long-term debilitating and life-threatening disease because of the long term damage to the liver, including loss of liver tissue and function, and cirrhosis (scarring of the liver).

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

At the time of designation, biliary atresia affected approximately 0.15 in 10,000 people in the European Union (EU). This was equivalent to a total of around 8,000 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 application for orphan designation, there was no medicine authorised for biliary atresia. Patients had surgery to restore flow of the bile, and liver transplantation. They also received antibiotics, medicines to encourage bile flow, vitamin supplements and nutritional support.

^{*}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 517,400,000 (Eurostat 2018).



How is this medicine expected to work?

The medicine blocks certain channels called IBATs through which the bile acids (a major component of bile) leave the intestines to reach the blood vessels that carry them back to the liver. By blocking these channels, the medicine is expected to reduce the amount of bile acids in the liver, thereby reducing the liver damage.

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 biliary atresia had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for biliary atresia 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 8 November 2018 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	(2S)-2-{{(2R)-2-[[[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl}amino} butanoic acid	Treatment of biliary atresia
Bulgarian	(2S)-2-{{(2R)-2-[[[3,3-дибутил-7-(метилтио)-1,1-диоксидо-5-фенил-2,3,4,5-тетраhydro-1,2,5-бензотиадиазепин-8-ил]окси}ацетил)амино]-2-(4-хидроксифенил)ацетил}амино} бутаноева киселина	Лечение на атрезия на жлъчните пътища
Croatian	(2S)-2-{{(2R)-2-[[[3,3-dibutil-7-(metiltio) -1,1-dioksido-5-fenil-2,3,4,5-tetrahydro-1,2,5-benzotiadiazepin-8-il] oksi} acetil) amino]-2-(4-hidroksifenil) acetil} amino} maslačna kiselina	Liječenje bilijarne atrezije
Czech	(2S)-2-{{(2R)-2-[[[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl}amino} butanová kyselina	Léčba atrezie žlučových cest
Danish	(2S)-2-{{(2R)-2-[[[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl}amino} butansyre	Behandling af biljær atresi
Dutch	(2S)-2-{{(2R)-2-[[[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl}amino} butanoïczuur	Behandeling van biliaire atresie
Estonian	(2S)-2-{{(2R)-2-[[[3,3-dibutüül-7-(metüültio)-1,1-dioksido-5-fenüül-2,3,4,5-tetrahydro-1,2,5-bensotiadiasepiin-8-üül]oksü}atsetüül)amino]-2-(4-hüdroksüfenüül)atsetüül}amino} butaanhape	Sapiteede atreesia ravi
Finnish	(2S)-2-{{(2R)-2-[[[3,3-dibuutyl-7-(metyylitio)-1,1-dioksidi-5-fenyyl-2,3,4,5-tetrahydro-1,2,5-bentsotiadiatsepiini-8-yl]oksi}asetyyli)amino]-2-(4-hydroksyfenyyl)asetyyil}amino} voihippo	Biliaarisen atresian hoito
French	Acide (2S)-2-{{(2R)-2-[[[3,3-dibutyl-7-(méthylthio)-1,1-dioxido-5-phényl-2,3,4,5-tétrahydro-1,2,5-benzothiadiazépine-8-yl]oxy}acétyl)amino]-2-(4-hydroxyphényl)acétyl}amino} butanoïque	Traitement de l'atrésie biliaire

¹ At the time of designation

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German	(2S)-2-{{(2R)-2-[[{3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy} acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino} buttersäure	Behandlung von Gallengangsatresie
Greek	(2S)-2-{{(2R)-2-[[{3,3-διβούτυλο-7-(μεθυλθειο)-1,1-διοξειδο-5-φαινυλο-2,3,4,5-τετραϋδρο-1,2,5-βενζοθειαδιαζεπιν-8-υλ]οξυ}ακετυλ)αμινο]-2-(4-υδροξυφαινυλ)ακετυλ]αμινο}βουτανοϊκό οξύ	Θεραπεία της ατρησίας των χοληφόρων
Hungarian	(2S)-2-{{(2R)-2-[[{3,3-dibutil-7-(metiltio)-1,1-dioxido-5-fenil-2,3,4,5-tetrahidro-1,2,5-benzothiadiazepin-8-il]oxi} acetil]amino]-2-(4-hidroxifenil) acetil]amino}butánsav	Epeút-elzáródás kezelése
Italian	(2S)-2-{{(2R)-2-[[{3,3-dibutil-7-(metiltio)-1,1-diossido-5-fenil-2,3,4,5-tetraidro-1,2,5-benzotiodiazepin-8-yl]oxy} acetil]amino]-2-(4-idrossifenil)acetil]amino}acido butanoico	Trattamento dell'atresia delle vie biliari
Latvian	(2S)-2-{{(2R)-2-[[{3,3-dibutil-7-(metiltio)-1,1-dioksido-5-fenil-2,3,4,5-tetrahidro-1,2,5-benzotiadiazepīn-8-il]oksi} acetil]amino]-2-(4-hidroksifenil)acetil]amino}sviestskābe	Biliārās atrēzijas ārstēšana
Lithuanian	(2S)-2-{{(2R)-2-[[{3,3-dibutil-7-(metiltio)-1,1-dioksido-5-fenil-2,3,4,5-tetrahidro-1,2,5-benzotiadiazepin-8-il]oksi} acetil]amino]-2-(4-hidroksifenil)acetil]amino}sviesto rūgštis	Tulžies latakų atrezijos gydymas
Maltese	(2S)-2-{{(2R)-2-[[{3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy} acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino} butanoic acid	It-trattament tal-atresja biljari
Polish	Kwas (2S)-2-{{(2R)-2-[[{3,3-dibutyl-7-(metylotio)-1,1-dioksydo-5-fenyl-2,3,4,5-tetrahydro-1,2,5-benzotiadiazepin-8-yl]oksy} acetyl)amino]-2-(4-hydroksyfenyl)acetyl]amino}butanowy	Leczenie atrezji układu żółciowego
Portuguese	Ácido (2S)-2-{{(2R)-2-[[{3,3-dibutil-7-(metiltio)-1,1-dióxido-5-fenil-2,3,4,5-tetrahidro-1,2,5-benzotiadiazepin-8-il]oxi} acetil]amino]-2-(4-hidroxifenil)acetil]amino}butanóico	Tratamento da atresia das vias biliares
Romanian	Acid (2S)-2-{{(2R)-2-[[{3,3-dibutil-7-(metiltio)-1,1-dioxido-5-fenil-2,3,4,5-tetrahidro-1,2,5-benzotiadiazepin-8-il]oxi} acetil]amino]-2-(4-hidroxifenil)acetil]amino}butanoic	Tratamentul atreziei biliare
Slovak	(2S)-2-{{(2R)-2-[[{3,3-dibutyl-7-(metylthio)-1,1-dioxido-5-fenyl-2,3,4,5-tetrahydro-1,2,5-benzotiadiazepin-8-yl]oxy} acetyl)amino]-2-(4-hydroxypfenyl)acetyl]amino}butánová kyselina	Liečba biliárnej atrezie

Language	Active ingredient	Indication
Slovenian	(2S)-2-{{(2R)-2-[[3,3-dibutil-7-(metiltio)-1,1-dioksido-5-fenil-2,3,4,5-tetrahydro-1,2,5-benzotiadiazepin-8-il]oksi} acetil)amino]-2-(4-hidroksifenil)acetil}amino} butanojska kislina	Zdravljenje atrezije žolčevodov
Spanish	Ácido (2S)-2-{{(2R)-2-[[3,3-dibutil-7-(metiltio)-1,1-dioxido-5-fenil-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-il]oxi} acetil)amino]-2-(4-hidroxifenil)acetil}amino} butanoico	Tratamiento de la atresia biliar
Swedish	(2S)-2-{{(2R)-2-[[3,3-dibutyl-7-(metylthio)-1,1-dioxido-5-fenyl-2,3,4,5-tetrahydro-1,2,5-benzotiadiazepin-8-yl]oxy} acetyl)amino]-2-(4-hydroxyfenyl)acetyl}amino} butansyra	Behandling av biliär atresi
Norwegian	(2S)-2-{{(2R)-2-[[3,3-dibutyl-7-(metylthio)-1,1-dioksido-5-fenyl-2,3,4,5-tetrahydro-1,2,5-benzotiadiazepin-8-yl]oksy} acetyl)amino]-2-(4-hydroksyfenyl)acetyl}amino} butansyre	Behandling av biliær atresi
Icelandic	(2S)-2-{{(2R)-2-[[3,3-dibútýl-7-(methýlthíó)-1,1-díoxídó-5-phenýl-2,3,4,5-tetrahydró-1,2,5-benzóthíadíazepín-8-ýl]oxý} acetýl)amínó]-2-(4-hýdroxyphenýl)acetýl}amínó} bútanóik sýra	Meðferð við gallgangalokun