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Public summary of opinion on orphan designation

1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one for the treatment of Stargardt's disease

On 25 May 2018, orphan designation (EU/3/18/2014) was granted by the European Commission to IQVIA RDS Ireland Limited, Ireland, for 1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one (also known as LBS-008) for the treatment of Stargardt's disease.

What is Stargardt's disease?

Stargardt's disease is a hereditary disorder of the eye that leads to progressive loss of sight. Stargardt's disease is caused by abnormalities in a gene called *ABCA4*. The *ABCA4* gene is responsible for the production of a protein called ABCR that regulates the transport of substances in and out of some cells in the retina (the light-sensitive surface at the back of the eye). In patients with Stargardt's disease, ABCR does not work properly. This causes deposits known as lipofuscins made of fats and proteins to build up inside the retina cells, which become damaged and eventually die.

Stargardt's disease is a long-term debilitating disease because the patient's sight becomes progressively worse and eventually leads to blindness.

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

At the time of designation, Stargardt's disease affected approximately 1.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 67,000 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 Stargardt's disease.

*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 lipofuscin deposits in the retina of patients with Stargardt's disease are made up of substances called bisretinoids. The process that forms bisretinoids in the eye involves attachment of vitamin A (retinol) to a substance called retinol-binding protein 4 (RBP4).

This medicine is expected to work by blocking RBP4. This is expected to reduce the formation of bisretinoids in the eye and so decrease damage caused by lipofuscin deposits.

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 Stargardt's disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Stargardt's disease. Orphan designation of the medicine had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 April 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 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one	Treatment of Stargardt's disease
Bulgarian	1-(3-{4-[3,4-дифлуоро-2-(трифлуорометил)фенил]пиперидин-1-карбонил}-1H,4H,5H,6H,7H-пиразоло[3,4-с]пиридин-6-ил)етан-1-он	Лечение на болест на Stargardt
Croatian	1-(3-{4-[3,4-difluor-2-(trifluorometil)fenil]piperidin-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-on	Liječenje Stargardtove bolesti
Czech	1-(3-{4-[3,4-difluoro-2-(trifluorometil)fenil]piperidin-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-on	Léčba Stargardtovy choroby
Danish	1-(3-{4-[3,4-difluor-2-(trifluormethyl)phenyl]piperidin-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-on	Behandling af Stargardt sygdom
Dutch	1-(3-{4-[3,4-difluor-2-(trifluormethyl)fenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-on	Behandeling van de ziekte van Stargardt
Estonian	1-(3-{4-[3,4-difluoro-2-(trifluorometüül)fenüül]piperidiin-1-karbonüül}-1H,4H,5H,6H,7H-pürasolo[3,4-c]püridiin-6-üül)etaan-1-oon	Stargardt'tõve ravi
Finnish	1-(3-{4-[3,4-difluori-2-trifluorimetyyli]fenyyli]piperidiini-1-karbonyyli}-1H,4H,5H,6H,7H-pyratsolo[3,4-c]pyridin-6-yyli)etan-1-oni	Stargardtin taudin hoito
French	1-(3-{4-[3,4-difluoro-2-(trifluorométhyl)phényl]pipéridine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridine-6-yl)ethan-1-one	Traitement de la maladie de Stargardt
German	1-(3-{4-[3,4-Difluor-2-(trifluormethyl)phenyl]piperidin-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)Ethan-1-on	Behandlung der Stargardt-Krankheit
Greek	1-(3-{4-[3,4-διφθορο-2-(τριφθορομεθυλο)φαινυλο]πιπεριδινο-1-καρβονυλο}-1H,4H,5H,6H,7H-πυραζολο[3,4-с]πυριδιν-6-υλ)αιθαν-1-όνη	Θεραπεία της νόσου Stargardt

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	1-(3-{4-[3,4-difluor-2-(trifluorometil)-fenil]-piperidin-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)-etán-1-on	Stargardt-kór kezelése
Italian	1-(3-{4-[3,4-difluoro-2-(trifluorometil)fenil]piperidina-1-carbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-one	Trattamento della malattia di Stargardt
Latvian	1-(3-{4-[3,4-difluor-2-(trifluorometil)fenil]piperidīn-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridīn-6-il)etān-1-ons	Stargardta slimības ārstēšana
Lithuanian	1-(3-{4-[3,4-difluor-2-(trifluorometil)fenil]piperidino-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-onas	Stargardt ligos gydymas
Maltese	1-(3-{4-[3,4-difluoro-2-(trifluorometil)fenil]piperidina-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridina-6-il)etan-1-wieħed	Kura tal-marda ta' Stargardt
Polish	1-(3-{4-[3,4-difluoro-2-(trifluorometylo)fenylo]piperydino-1-karbonylo}-1H,4H,5H,6H,7H-pirazolo[3,4-c]pirydino-6-yl)etan-1-on	Leczenie choroby Stargardta
Portuguese	1-(3-{4-[3,4-difluoro-2-(trifluorometil)fenil]piperidina-1-carbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-ona	Tratamento da doença de Stargardt
Romanian	1-(3-{4-[3,4-difluor-2-(trifluorometil)fenil]piperidin-1-carbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-onă	Tratamentul bolii Stargardt
Slovak	1-(3-{4-[3,4-difluor-2-(trifluórmetyl)fenyl]piperidín-1-karbonyl}-1H,4H,5H,6H,7H-pyrazol[3,4-c]pyridín-6-yl)etán-1-on	Liečba Stargardtovej choroby
Slovenian	1-(3-{4-[3,4-difluoro-2-(trifluorometil)fenil]piperidin-1-karbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-il)etan-1-on	Zdravljenje Stargardtjeve bolezni
Spanish	1-(3-{4-[3,4-difluoro-2-(trifluorometil)fenil]piperidina-1-carbonil}-1H,4H,5H,6H,7H-pirazolo[3,4-c]piridin-6-yl)ethan-1-one	Tratamiento de la enfermedad de Stargardt
Swedish	1-(3-{4-[3,4-difluor-2-(trifluorometyl)fenyl]piperidin-1-karbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)etan-1-on	Behandling av Stargadts sjukdom
Norwegian	1-(3-{4-[3,4-difluor-2-(trifluormetyl)fenyl]piperidin-1-karbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)etan-1-on	Behandling av Stargadts sykdom
Icelandic	1-(3-{4-[3,4-díflúoró-2-(tríflúormetýl)fenýl]píperidín-1-karbónýl}-1H,4H,5H,6H,7H-pýrasóló[3,4-c]pýridín-6-ýl)etan-1-ón	Meðferð við Stargadts sjúkdómi