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EMA/COMP/348492/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Antisense oligonucleotide directed against TGF- β 2 mRNA for the prevention of scarring post glaucoma filtration surgery

On 19 June 2015, orphan designation (EU/3/15/1506) was granted by the European Commission to Isarna Therapeutics GmbH, Germany, for antisense oligonucleotide directed against TGF- β 2 mRNA for the prevention of scarring post glaucoma filtration surgery.

What is scarring post glaucoma filtration surgery?

Glaucoma is a disease in which the pressure in the eye rises because the fluid inside the eye cannot drain away properly. The pressure affects the optic nerve (the nerve that sends signals from the eye to the brain) and can cause loss of vision. Glaucoma can be treated using 'filtration surgery', whereby the surgeon makes a small hole in the sclera (the white of the eye), to create a drainage channel, so that the fluid that has built up in the eye can drain away. After surgery, as part of the body's normal healing process, specialised cells called fibroblasts build up scar tissue which helps to repair the wound. However, scarring can sometimes be excessive and seal the channel up, causing the pressure inside the eye to build up again.

Scarring post glaucoma filtration surgery is a long-term debilitating condition because it may lead to loss of vision.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of scarring post glaucoma filtration surgery was estimated to be approximately 1.9 people in 10,000 in the European Union (EU). This was equivalent to a total of around 97,000 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 at risk of developing 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 512,900,000 (Eurostat 2015).

What methods of prevention are available?

At the time of designation, no satisfactory methods were authorised in the EU for the prevention of scarring post glaucoma filtration surgery. Medicines that block and kill fibroblasts, such as mitomycin C or 5-fluorouracil (which are also used to treat cancer), were applied to the eye during surgery to slow down the formation of scar tissue and prevent the channel from sealing up.

How is this medicine expected to work?

This medicine is an 'anti-sense oligonucleotide', a very short piece of synthetic genetic material. This anti-sense oligonucleotide specifically attaches to a type of genetic material (called the 'sense RNA') responsible for producing the TGF- β 2 protein. This protein is found in high levels in the eye of glaucoma patients and it is thought to promote scarring. When given by injection into the eye, the medicine is expected to block the production of excess TGF- β 2 protein, thus preventing scarring after glaucoma filtration surgery and so stopping the pressure in the eye from building up again.

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 scarring post glaucoma filtration surgery had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for scarring post glaucoma filtration surgery 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 13 May 2015 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	Antisense oligonucleotide directed against TGF- β 2 mRNA	Prevention of scarring post glaucoma filtration surgery
Bulgarian	Антисенс олигонуклеотид, насочен срещу тРНК на TGF- β 2	Превенция на белези след филтрираща операция при глаукома
Croatian	Protusmisleni oligonukleotid usmjeren protiv mRNK za TGF- β 2	Prevenција ožiljkavanja nakon filtracijske operacije glaukoma
Czech	Protisměrný oligonukleotid proti TGF- β 2 mRNA	Prevence jizvení po glaukomatozní filtrační operace
Danish	Antisense oligonukleotid rettet mod TGF- β 2 mRNA	Forebyggelse af ardannelse efter glaukom filterings-operation
Dutch	Antisense oligonucleotide gericht tegen TGF- β 2 mRNA	Preventie van littekenvorming na glaucoomfiltratiechirurgie
Estonian	TGF- β 2 mRNA vastu suunatud antisense-oligonukleotiid	Glaukoomi filtratsioonkirurgia järgsete armide ennetamine
Finnish	Antisense-oligonukleotidi, joka on suunnattu TGF- β 2-mRNA:ta vastaan	Arpikudoksen kasvun esto glaukooman kirurgisen hoidon jälkeen
French	Oligonucléotide antisens dirigé contre TGF- β 2 mRNA	Prévention des cicatrices après chirurgie filtrante du glaucome
German	Antisense-Oligonukleotid, das gegen TGF- β 2 mRNA gerichtet ist	Prävention von Narbenbildung nach Glaukom-Filtrations-Operation
Greek	Αντιπληροφοριακό ολιγονουκλεοτιδίο που κατευθύνεται έναντι του TGF- β 2 mRNA	Πρόληψη ουλών μετά από εγχείριση διήθησης γλαυκώματος
Hungarian	TGF-beta2 mRNS elleni antisense oligonukleotid	Glaucoma filtrációs műtétet követő hegesedés kialakulásának megelőzése
Italian	Oligonucleotide antisenso diretto contro il TGF- β 2 mRNA	Prevenzione delle cicatrici post intervento chirurgico filtrante per glaucoma
Latvian	Antisenses oligonukleotīds, kas vērsts pret TGF- β 2 mRNS	Rētaudu veidošanās profilakse pēc glaukomas filtrēšanas operācijas
Lithuanian	Priešprasminis oligonukleotidas, nukreiptas prieš TGF- β 2 mRNR	Randų po glaukomos filtracijos operacijos prevencija
Maltese	Oligonucleotide antisens dirett kontra mRNA TGF- β 2	Prevenzjoni ta' ċikatriċi wara kirurġija ta' filtrazzjoni għal glawkoma
Polish	Oligonukleotyd antysensowny skierowany przeciwko mRNA TGF- β 2	Zapobieganie bliznom po operacji udrożnienia kąta przesączania w jaskrze
Portuguese	Oligonucleótido anti-senso dirigido contra o ARNm do TGF- β 2	Prevenção de cicatrizes no pós-operatório de filtração do glaucoma
Romanian	Oligonucleotid antisens îndreptat împotriva ARNm TGF- β 2	Prevenirea cicatrizării după intervenția chirurgicală de filtrare în glaucom
Slovak	Protismerný oligonukleotid namierený proti TGF- β 2 mRNA	Prevenca jazvenia po filtračnej operácii glaukómu

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	Protismerni oligonukleotid, usmerjen proti TGF- β 2 mRNA	Preprečevanje brazgotin po filtracijski operaciji glavkoma
Spanish	Oligonucleótido antisentido dirigido contra el ARNm del TGF- β 2	Prevención de la cicatrización posterior a la cirugía de filtración del glaucoma
Swedish	Antisense-oligonukleotid riktad mot TGF- β 2-mRNA	Förebyggande av ärrbildning efter fistulerande ingrepp för behandling av glaukom
Norwegian	Antisense-oligonukleotid rettet mot TGF- β 2 mRNA	Forebygging av arrdannelse etter filtrasjonskirurgi for glaukom
Icelandic	Andþáttar-óligónúkleótíð beint gegn TGF- β 2 mRNA	Til að koma í veg fyrir örmyndun eftir síunaraðgerð vegna gláku