



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

17-(dimethylaminoethylamino)-17-demethoxygeldanamycin (after administration of adeno-associated viral vector encoding an inducible short hairpin RNA targeting claudin-5) for the treatment of retinitis pigmentosa

On 28 November 2012, orphan designation (EU/3/12/1007) was granted by the European Commission to Avena Therapeutics Ltd, Ireland, for 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin (after administration of adeno-associated viral vector encoding an inducible short hairpin RNA targeting claudin-5) for the treatment of retinitis pigmentosa.

### What is retinitis pigmentosa?

Retinitis pigmentosa is a group of hereditary diseases of the eye that lead to progressive loss of sight. In patients with retinitis pigmentosa, cells in the retina (the light-sensitive surface at the back of the eye) become damaged and eventually die.

Retinitis pigmentosa is a long-term debilitating disease because it can cause night blindness and tunnel vision, which can progress to total blindness.

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

At the time of designation, retinitis pigmentosa affected less than 3.7 in 10,000 people in the European Union (EU)\*. This is equivalent to a total of fewer than 187,000 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 submission of the application for orphan designation, no satisfactory methods were authorised in the EU for treating retinitis pigmentosa. Patients with the condition were given sunglasses to slow down the damage to the retina, genetic counselling (discussion of the risks of passing the condition on to children) and general 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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).



## How is this medicine expected to work?

The medicine contains the active substance '17-(dimethylaminoethylamino)-17-demethoxygeldanamycin' (17-DMAG), which is expected to attach to a protein called heat shock protein (Hsp90), triggering a reaction that is expected to protect cells in the retina against further damage.

Before it can have its effect, however, 17-DMAG needs to cross the barrier separating the circulating blood from the retinal tissue. For that to happen, a virus containing genetic material will first be injected into the eye followed by a substance called doxycycline. Doxycycline is expected to activate the virus, which will cause the barrier to become temporarily permeable to 17-DMAG.

The type of virus used in this medicine ('adeno-associated virus') does not cause disease in humans.

## What is the stage of development of this medicine?

The effects of the medicinal product have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicinal product in patients with retinitis pigmentosa had been started.

At the time of submission, the medicinal product was not authorised anywhere in the EU for retinitis pigmentosa 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 11 May 2012 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:

Avena Therapeutics Ltd  
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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 languages<sup>1</sup>, Norwegian and Icelandic

| Language  | Active ingredient                                                                                                                                                                                      | Indication                                           |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| English   | 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin (after administration of adeno-associated viral vector encoding an inducible short hairpin RNA targeting claudin-5)                              | Treatment of retinitis pigmentosa                    |
| Bulgarian | 17-(диметиламиноетиламино)-17-деметоксигелданамицин (след приложение на адено-асоцииран вирусен вектор, кодиращ индуцируема къса hairpin РНК насочена срещу клаудин 5)                                 | Лечение на пигментен ретинит                         |
| Czech     | 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin (po podání adeno-asociovaného virového vektoru kódující indukovatelnou krátkou vlásenku RNA cílenou na claudine-5)                               | Léčba pigmentosní retinitidy                         |
| Danish    | 17-(Dimetylaminøetylaminø)-17-demetoxygeldanamycin (efter administration af adenoassocieret viral vektor kodende for en inducerbar kort RNA hårnål rettet mod claudin-5)                               | Behandling af retinitis pigmentosa                   |
| Dutch     | 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin (na toediening van adeno-geassocieerde virale vector welke codeert voor een induceerbaar kort haarpin RNA doelend op claudine-5)                 | Behandeling van retinitis pigmentosa                 |
| Estonian  | 17-Dimetüülaminoetüülamino-17-demetoksügeldanamütsiin (peale adenoviirusega seotud viirusvektori sisestamist, mis kodeerib inducible short hairpin RNA targeting claudin-5)                            | Pigmentoosse võrkkestapõletiku ravi                  |
| Finnish   | 17-(dimetyyliaminoetyyliamino)-17-demetoksigidanamysiini, jota ennenannetaan adenovirusvektori, joka koodaa indusoitavaa, klaudiini-5:een kohdennettua "short hairpin" RNA:ta                          | Verkkokalvorappeuman hoito                           |
| French    | 17-(Diméthylaminoéthylamino)-17-déméthoxygeldanamycine (après administration de vecteur viral adéno-associé codant pour un court ARN inductible en épingle à cheveu dirigé contre la claudine 5)       | Traitement de la rétinite pigmentaire                |
| German    | 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin (nach Verabreichung eines adeno-assoziierten viralen Vektors, der für eine gegen claudin-5 gerichtete, induzierbare "short hairpin RNA" kodiert) | Behandlung der Retinopathia Pigmentosa               |
| Greek     | 17-(Διμεθυλαμινοεθυλαμινο)- 17 δεμεθοξυγελδαναμικίνη (μετά από χορήγηση αδενο-σχετιζόμενου ιικού φορέα που κωδικοποιεί για μια βραχεία φουρκέτα RNA (shRNA) που στοχεύει την κλωνίνη-5)                | Αγωγή κατά της μελαγχρωστικής αμφιβληστροειδοπάθειας |
| Hungarian | 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin (claudin-5-öt célzó indukálható rövid hajtű-RNS-t kódoló adeno-asszociált vírus vektor adagolása után)                                           | Retinitis pigmentosa kezelése                        |
| Italian   | 17-( Diméthylaminoéthylamino)-17-demetossigeldanamicina (dopo somministrazione del vettore virale adeno-associato                                                                                      | Trattamento della retinite pigmentosa                |

<sup>1</sup> At the time of designation

| Language   | Active ingredient                                                                                                                                                                       | Indication                           |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
|            | codificante un hairpin RNA corto inducibile diretto alla claudina-5                                                                                                                     |                                      |
| Latvian    | 17-(dimetilaminoetilamino)-17-demetoksigeldanamicīns (pēc adenovīrusa asociētā vektora, kas iekodēts inducētā īsā harpina RNS arm mērķi – kladīns 5, ievadišanas)                       | Retinitis pigmentosa ārstēšana       |
| Lithuanian | 17-(dimetilaminoetilamino)-17-demetoksigeldanamicinas (po adeno asocijuoto viruso vektoriaus, koduojančio inicijuojamą smeigtuko tipo RNR nukreiptą prieš kladiną-5, paskyrimo)         | Pigmentinio retinito gydymas         |
| Maltese    | 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin (wara l-amministrazzjoni ta' vettur imnissel mill-adenovirus li jikkodifika hairpin RNA qasir inducibbli immirat għall-claudin-5) | Kura tar-retinite pigmentuża         |
| Polish     | 17-(dimetyloaminoetyloamino)-17-demetoksygeldanamycyna (po podaniu wektora adenowirusowego kodującego induktywny shRNA przeciw kładynie-5)                                              | Leczenie retinopatii barwnikowej     |
| Portuguese | 17 - (Dimetilaminoetilamino)-17-desmetoxigeldanamicina (após a administração de um vetor adenoviral codificando um curto grampo de ARN indutível, dirigido à claudina-5)                | Tratamento da retinite pigmentosa    |
| Romanian   | 17-(dimetilaminoetilamino)-17-demetoxigeldanamicină (post administrarea unui vector viral adeno-asociat ce codifică hairpină ARN scurtă inductibilă direcționată împotriva claudinei 5) | Tratamentul retinitei pigmentare     |
| Slovak     | 17-(dimetylaminoetylamino)-17-demetoxygeldanamycín (po podaní adeno-asociovaného vírusového vektora kódujúceho indukovateľnú krátku hairpin RNA cielenú na kladín-5)                    | Liečba retinitis pigmentosa          |
| Slovenian  | 17-(dimetilaminoetilamino)-17-demetoksigeldanamicin (vnešen po vnosu adenoasociacijskega virusnega vektorja, kodiranega z shRNA, usmerjeno proti kladinu-5)                             | Zdravljenje pigmentozne retinopatije |
| Spanish    | 17-(Dimetilaminoetilamino)-17-demetoxigeldanamicina (administrado tras el vector adeno-asociado que codifica para ARN corto en horquilla inducible dirigido contra claudina-5)          | Tratamiento de retinosis pigmentaria |
| Swedish    | 17-(Dimetylaminoetylamino)-17-demetoxygeldanamycin (efter administrering av adeno-associerad viral vektor som kodar en inducerbar kort RNA hårpinne riktad mot claudin-5)               | Behandling av retinitis pigmentosa   |
| Norwegian  | 17-(Dimetylaminoetylamino)-17-demetoksygeldanamycin (etter administrering av adenoassosiert virus vektor som koder for et induserbart kort hårnåls RNA rettet mot claudin-5)            | Behandling av retinitis pigmentosa   |
| Icelandic  | 17-(Dimetýletýlámínó)-17-demetoxýgeldanamýcín (eftir gjöf adenó tengdri veirufurju sem kóðar fyrir hvetjandi stutt hárnálar RNA sem beinist gegn claudín-5)                             | Meðferð á retinitis pigmentosa       |