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Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Synthetic double-stranded siRNA oligonucleotide directed against the keratin 6a N171K mutation for the treatment of pachyonychia congenita

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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 19 June 2013, orphan designation (EU/3/13/1141) was granted by the European Commission to Alan Irvine, Ireland, for synthetic double-stranded siRNA oligonucleotide directed against the keratin 6a N171K mutation for the treatment of pachyonychia congenita.

### What is pachyonychia congenita?

Pachyonychia congenita is an inherited skin condition in which the patient has symptoms such as painful blisters and callouses on the palms and soles of the feet, thickened finger and toe nails, and lesions on the inside of the mouth.

Pachyonychia congenita is caused by mutations (defects) in the genes for keratin, the tough fibrous protein found in the skin and nails. A patient normally has a 50% chance of passing it on to their offspring as one defective gene from one parent is usually enough for a person to have the condition.

Pachyonychia congenita is a chronically debilitating disease because the painful blisters and callouses make walking difficult or impossible.

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

At the time of designation, pachyonychia congenita affected less than 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 1,000 people*, and is below the

*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 509,000,000 (Eurostat 2013).

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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 the application for orphan designation, no satisfactory methods were authorised in the EU for treating pachyonychia congenita. Treatment focused on the relief of symptoms, personal hygiene to help blisters heal, to avoid infections and to protect the skin from damage and the treatment of any infections that may occur in the affected skin.

## How is this medicine expected to work?

The medicine is made of a small strand of synthetic genetic material, called 'small interfering RNA' (siRNA) that interferes with the function of certain genes. It has been designed to target a defective gene called KRT6a causing pachyonychia congenita in some people, where it is expected to block the production of the abnormal keratin and reverse the disease by restoring the ability of the cells in the skin to produce normal keratin.

## 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 pachyonychia congenita had been started.

At the time of submission, the medicinal product was not authorised anywhere in the EU for pachyonychia congenita 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 15 May 2013 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

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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[1], Norwegian and Icelandic

| Language | Active ingredient | Indication |
|---|---|---|
| English | Synthetic double-stranded siRNA oligonucleotide directed against the keratin 6a N171K mutation | Treatment of pachyonychia congenita |
| Bulgarian | Синтетичен двойно-верижна siRNA олигонуклеотид насочен срещу кератин 6a мутация N171K | Лечение на вродена пахионхия |
| Czech | Syntetický dvouvláknový oligonukleotid siRNA namířené proti keratin 6a mutaci N171K | Léčba pachyonychia congenita |
| Danish | Syntetisk dobbeltstrenget siRNA oligonukleotid rettet mod keratin 6a N171K mutation | Behandling af pachyonychia congenita |
| Dutch | Synthetische dubbelstrengig siRNA oligonucleotide gericht tegen de keratine 6a N171K mutatie | Behandeling van pachyonychia congenitaal |
| Estonian | Sünteetiline kaheahelaline siRNA oligonukleotiidide suunatud keratiini 6a N171K mutatsioon | Kaasasündinud i pachyonychia ravi |
| Finnish | Synteettinen kaksijuosteinen siRNA oligonukleotidi, joka on kohdistettu keratiini 6a N171K mutaatioon | Synnynnäisen pakyonykian hoito |
| French | Oligonucléotide siRNA double brin synthétique dirigé contre la mutation de la kératine 6a N171K | Traitement des pachyonychie congénitale |
| German | Synthetisches doppelsträngiges siRNA Oligonucleotid, das gegen die Keratin 6a N171K Mutation gerichtet ist | Behandlung von Pachyonychia congenita |
| Greek | Συνθετικό δίκλωνο ολιγονουκλεοτίδιο siRNA που κατευθύνεται έναντι της μετάλλαξης N171K της κερατίνης 6α | Η θεραπεία του συγγενούς pachyonychia |
| Hungarian | Keratin 6a N171K mutáció-elleni szintetikus kétszálú siRNS oligonukleotid | Veleszületett pachyonychia kezelése |
| Italian | Oligonucleotide sintetico a doppio filamento siRNA diretto contro la cheratina 6A mutazione N171K | Trattamento della Pachionichia congenita |
| Latvian | Sintētiskās dubultvijuma siRNS oligonukleotīds, kas vērsts pret keratīna 6a N171K mutāciju | Iedzimtas pahionīcijas ārstēšana |
| Lithuanian | Sintetinis dvigrandės siRNR oligonukleotidas, nukreiptas prieš keratino 6a N171K mutaciją | Įgimtos pachionichijos gydymas |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Maltese | Oligonukleotide sintetiku tas-siRNA b'katina doppja dirett kontra l-mutazzjoni tal-keratina 6a N171K | Kura tal-pakionikja konġenitali |
| Polish | Syntetyczny dwuniciowy oligonukleotyd siRNA skierowany przeciwko mutacji N171K keratyny 6a | Leczenie wrodzonego zgrubienia paznokci |
| Portuguese | Oligonucleotídeo sintético siRNA de cadeia dupla dirigido contra a mutação N171K da queratina 6a | Tratamento de paquioníquia congénita |
| Romanian | Oligonucleotidă de sinteză si ARN dublucatenar îndreptată împotriva mutaţiei 6a N171K a keratinei | Tratamentul pachyonychia congenitala |
| Slovak | Syntetický dvojvláknový oligonukleotid siRNA namierený proti rohovej mutácii keratínu 6a N171K | Liečba pachyonychia congenita |
| Slovenian | Sintetični dvojno vijačni siRNK oligonukleotid usmerjen proti mutaciji keratina 6a N171K | Zdravljenje pachyonychia congenita |
| Spanish | Oligonucleótido sintético de doble cadena de siRNA dirigido contra la mutación 6a N171K de la queratina | Tratamiento de la paquioniquia congénita |
| Swedish | Syntetisk dubbelsträngad siRNA-oligonukleotid riktad mot keratin 6a N171K mutationen | Behandling av pachyonychia congenita |
| Norwegian | Syntetisk dobbelt-trådet siRNA oligonukleotid rettet mot keratin 6a N171K mutasjonen | Behandling av pachyonychia congenita |
| Icelandic | Tilbúinn tvístrengja siRNA ólígónúkleótíð beint gegn keratín 6a N171K stökkbreytingu | Meðferð pachyonychia congenita |