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EMA/COMP/116731/2015  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### 6-ethoxy-7-methoxy-2-(2-methylsulfanyphenyl)-3,1-benzoxazin-4-one for the treatment of Netherton syndrome

On 19 March 2015, orphan designation (EU/3/15/1454) was granted by the European Commission to Sixera Pharma AB, Sweden, for 6-ethoxy-7-methoxy-2-(2-methylsulfanyphenyl)-3,1-benzoxazin-4-one for the treatment of Netherton syndrome.

#### What is Netherton syndrome?

Netherton syndrome is an inherited skin condition in which the patient, usually a new born baby, has red, scaly skin, which cannot properly protect against infection or retain heat, water and proteins. Many babies also have a 'bamboo-type' hair structure, with strands of varying diameter. Babies born with the syndrome may fail to thrive in their first years of life.

Netherton syndrome is caused by a mutation (change) in the gene responsible for producing a protein called LEKT1, which regulates the action of enzymes called kallikreins. Kallikreins are involved in the shedding of the skin. As a result of the mutation in the *LEKT1* gene, kallikreins become overactive, causing excessive shedding and damage to the skin.

Netherton syndrome is a long-term debilitating and life-threatening condition because of the skin damage and associated infections, and failure to thrive.

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

At the time of designation, Netherton syndrome affected approximately 0.05 in 10,000 people in the European Union (EU). This was equivalent to a total of around 2,600 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).

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\*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 512,900,000 (Eurostat 2015).

## **What treatments are available?**

At the time of submission for orphan designation, no satisfactory methods were authorised in the EU for the treatment of Netherton syndrome. To reduce the inflammation of the skin in patients with Netherton syndrome, creams containing medicines such as steroids and calcineurin inhibitors were used in addition to general moisturisers and emollients (substances that soften or smooth the skin).

## **How is this medicine expected to work?**

The medicine is a molecule that blocks the effect of kallikreins. It is expected that when applied to the skin in patients with Netherton syndrome it will block the excess kallikrein activity and so allow the skin to function more normally, relieving the symptoms of the condition.

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

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with this medicine in patients with Netherton syndrome had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Netherton syndrome 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 12 February 2015 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:

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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	6-ethoxy-7-methoxy-2-(2-methylsulfanylphenyl)-3,1-benzoxazin-4-one	Treatment of Netherton syndrome
Bulgarian	6-етокси-7-метокси-2-(2-метилсулфанилфенил)-3,1-бензоксазин-4-он	Лечение на синдрома на Netherton
Croatian	6-etoksi-7-metoksi-2-(2-metilsulfanilfenil)-3,1-benzoksazin-4-on	Liječenje Nethertonovog sindroma
Czech	6-ethoxy-7-methoxy-2-(2-methylsulfanylfenyl)-3,1-benzoxazin-4-on	Léčba Nethertonova syndromu
Danish	6-ethoxy-7-methoxy-2-(2-methylsulfanylphenyl)-3,1-benzoxazin-4-on	Behandling af Nethertons syndrom
Dutch	6-ethoxy-7-methoxy-2-(2-methylsulfanylfenyl)-3,1-benzoxazin-4-one	Behandeling van het syndroom van Netherton
Estonian	6-etoksü-7-metoksü-2-(2-metüülsulfanüülfenüül)-3,1-bensoaksiin-4-oon	Nehertoni sündroomi ravi
Finnish	6-etoksi-7-metoksi-2-(2-metyylisulfanyylifenyyli)-3,1-bentsoksatsin-4-oni	Nethertonin oireyhtymän hoito
French	6-éthoxy-7-méthoxy-2-(2-méthylsulfanylphényl)-3,1-benzoxazin-4-one	Traitement du syndrome de Netherton
German	6-Ethoxy-7-methoxy-2-(2-methylsulfanylphenyl)-3,1-benzoxazin-4-on	Behandlung des Netherton Syndroms
Greek	6-αιθοξυ-7-μεθοξυ-2-(2-μεθυλοσουλφανυλοφαινυλο)-3,1-βενζοξαζιν-4-όνη	Θεραπεία του συνδρόμου Netherton
Hungarian	6-etoxi-7-metoxi-2-(2-metil-szulfanil-fenil)-3,1-benzoxazin-4-on	Netherton szindróma kezelése
Italian	6-etossi-7-metossi-2-(2-metilsulfanilfenil)-3,1-benzossazina-4-one	Trattamento della sindrome di Netherton
Latvian	6-etoksi-7-metoksi-2-(2-metilsulfanilfenil)-3,1-benzoksazīn-4-ons	Netertona sindroma ārstēšana
Lithuanian	6-etoksi-7-metoksi-2-(2-metilsulfanilfenil)-3,1-benzoksazin-4-onas	Nethertono sindromo gydymas
Maltese	6-ethoxy-7-methoxy-2-(2-methylsulfanylphenyl)-3,1-benzoxazin-4-one	Kura tas-sindrome ta' Netherton

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

Language	Active ingredient	Indication
Polish	6-etoksy-7-metoksy-2-(2-metylo)sulfanylo)fenylo)-3,1-benzoksazyn-4-on	Leczenie zespołu Nethertona
Portuguese	6-etoxi-7-metoxi-2-(2-metilsulfanilfenil)-3,1-benzoxazin-4-ona	Tratamento da síndrome de Netherton
Romanian	6-etoxi-7-metoxi-2-(2-metilsulfanilfenil)-3,1-benzoxazin-4-onă	Tratamentul sindromului Netherton
Slovak	6-etoxy-7-metoxy-2-(2-metylsulfanylfenyl)-3,1-benzoxazín-4-ón	Liečba Nethertonovho syndrómu
Slovenian	6-etoksi-7-metoksi-2-(2-metilsulfanilfenil)-3,1-benzoksazin-4-on	Zdravljenje Nethertonovega sindroma
Spanish	6-etoxi-7-metoxi-2-(2-metilsulfanilfenil)-3,1-benzoxazina-4-ona	Tratamiento del síndrome de Netherton
Swedish	6-etoxi-7-metoxi-2-(2-metylsulfanylfenyl)-3,1-bensoxazin-4-one	Behandling av Nethertons syndrom
Norwegian	6-etoksy-7-metoksy-2 (2-metylsulfanylfenyl)-3,1-benzoksazin-4-on	Behandling av Nethertons syndrom
Icelandic	6-etoxý-7-metoxý-2-(2-metýlsúlfanýlfenýl)-3,1-benzoxazín-4-ón	Meðhöndlun á Netherton heilkenni