

29 October 2013
EMA/COMP/554682/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Zoledronic acid for the treatment of complex regional pain syndrome

On 7 October 2013, orphan designation (EU/3/13/1192) was granted by the European Commission to Axsome Therapeutics Limited, United Kingdom, for zoledronic acid for the treatment of complex regional pain syndrome.

What is complex regional pain syndrome?

Complex regional pain syndrome is a condition characterised by persistent disabling pain, often starting in a limb. Although the condition usually develops after an injury, the pain experienced is greater than what would normally be expected from the injury. The skin of the affected area can become very sensitive and even a simple touch can cause pain. As the disease progresses, it often spreads beyond the affected limb.

Complex regional pain syndrome is a long-term debilitating condition because of the persistent pain which may impair the ability to move and perform daily activities.

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

At the time of designation, complex regional pain syndrome affected less than 3 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 154,000 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 time of designation, no satisfactory methods were authorised in the EU for the treatment of complex regional pain syndrome. Patients were mainly treated with medicines to reduce the pain and physiotherapy.

*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 512,200,000 (Eurostat 2013).

How is this medicine expected to work?

Zoledronic acid belongs to a group of medicines called 'bisphosphonates'. It stops the action of the osteoclasts, the cells in the body that are involved in breaking down the bone tissue. Zoledronic acid has been authorised in the EU for several years to treat diseases affecting the bones such as osteoporosis.

The way zoledronic acid works in complex regional pain syndrome is not fully elucidated, but laboratory studies showed that it has a favourable effect on pain mainly by reducing the activity of the osteoclasts and suppressing the release of substances involved in inflammation.

What is the stage of development of this medicine?

The effects of zoledronic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with zoledronic acid in patients with complex regional pain syndrome had been started.

At the time of submission, zoledronic acid was not authorised anywhere in the EU for complex regional pain syndrome. Orphan designation of zoledronic acid had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 September 2013 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	Zoledronic acid	Treatment of complex regional pain syndrome
Bulgarian	Золедронова киселина	Лечение на комплексен регионален болков синдром
Czech	Kyselina zolendrová	Léčba komplexního regionálního bolestivého syndromu
Croatian	Zoledronatna kiselina	Liječenje kompleksnog regionalnog bolnog sindroma
Danish	Zoledronsyre	Behandling af komplekst regionalt smerte syndrom
Dutch	Zoledroninezuur	Behandeling van complex regionaal pijnsyndroom
Estonian	Zoledroonhape	Komplekse piirkondliku valu sündroomi ravi
Finnish	Tsoledronihappo	Monimutkaisen alueellisen kipuoireyhtymän hoito
French	Acide zoledronique	Traitement du syndrome douloureux régional complexe
German	Zoledronsäure	Behandlung des komplexen regionalen Schmerzsyndroms
Greek	Ζολεδρονικό οξύ	Θεραπεία του συνδρόμου σύμπλοκου περιοχικού πόνου
Hungarian	Zoledronsav	Komplex regionális fájdalom szindróma kezelése
Italian	Acido zoledronico	Trattamento della sindrome dolorosa regionale complessa
Latvian	Zoledronskābe	Kompleksa reģionālās sāpju sindroma
Lithuanian	Zoledrono rūgštis	Komplikuoto regioninio skausmo sindromo gydymas
Maltese	Zoledronic acid	Kura tas-sindrome ta' uġiġħ reġjonali kumpless
Polish	Kwas zoledronowy	Leczenie kompleksowego zespołu bólu regionalnego
Portuguese	Ácido zoledrónico	Tratamento da síndrome de dor regional complexa
Romanian	Acid zoledronic	Tratamentul Sindromului dureros regional complex
Slovak	Kyselina zoledrónová	Liečba syndrómu komplexnej regionálnej bolesti
Slovenian	Zoledronska kislina	Zdravljenje kompleksnega regionalnega bolečinskega sindroma
Spanish	Ácido zoledrónico	Tratamiento del síndrome de dolor regional complejo
Swedish	Zoledronsyra	Behandling av komplexa regionala smärtsyndrom
Norwegian	Zoledronsyre	Behandling av komplekst regionalt smertesyndrom
Icelandic	Zóledrónic sýra	Meðferð flókinna svæðistengdra sársauka heilkennis

¹ At the time of designation