27 May 2016
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(1E,6E)-1,7-bis(3,4-dimethoxyphenyl)-4-cyclobutylmethyl-1,6-heptadiene-3,5-dione for the treatment of X-linked spinal and bulbar muscular atrophy (Kennedy's disease)

On 28 April 2016, orphan designation (EU/3/16/1639) was granted by the European Commission to Coté Orphan Consulting UK Limited, United Kingdom, for (1E,6E)-1,7-bis(3,4-dimethoxyphenyl)-4-cyclobutylmethyl-1,6-heptadiene-3,5-dione for the treatment of X-linked spinal and bulbar muscular atrophy (Kennedy's disease).

What is X-linked spinal and bulbar muscular atrophy?

X-linked spinal and bulbar muscular atrophy (also known as Kennedy's disease) is a genetic disease that affects the motor neurons (nerves from the brain and spinal cord that control muscle movements), causing muscle weakness and wasting, and difficulty in speech articulation and swallowing.

The condition is caused by mutations (changes) in a gene on the X chromosome and usually occurs in adulthood. Because men have only one X chromosome, the condition occurs almost exclusively in men (in women a second, undamaged copy can compensate for the mutated gene). Affected men may also have other symptoms such as breast enlargement, impotence and reduced fertility.

X-linked spinal and bulbar muscular atrophy is debilitating in the long-term because of the progressive muscle weakness. It can be life-threatening when it affects muscles involved in breathing and swallowing.

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

At the time of designation, X-linked spinal and bulbar muscular atrophy affected approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 21,000 people[*], and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the

[1] Correction of EU Registration number, 29 November 2016.
[*]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 513,700,000 (Eurostat 2016).

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information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of X-linked spinal and bulbar muscular atrophy.

How is this medicine expected to work?

Patients with X-linked spinal and bulbar muscular atrophy have mutations in the gene for a protein called 'androgen receptor'. This medicine works by stimulating the proteasome, which is a system within cells that breaks down proteins when they are no longer needed. By stimulating the proteasome, the abnormal androgen receptors produced by the mutated gene are expected to be broken down and cleared away faster. This is expected to help alleviate muscle weakness and other symptoms of the disease.

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 X-linked spinal and bulbar muscular atrophy had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for X-linked spinal and bulbar muscular atrophy 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 23 March 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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[2], Norwegian and Icelandic

Language	Active ingredient	Indication
English	(1E,6E)-1,7-bis(3,4-dimethoxyphenyl)-4-cyclobutylmethyl-1,6-heptadiene-3,5-dione	Treatment of X-linked spinal and bulbar muscular atrophy (Kennedy's disease)
Bulgarian	(1E,6E)-1,7-бис(3,4-диметоксифенил)-4-циклобутил метил-1,6-хепта-3,5-дион	Лечение на Х-свързана спинална и булбарна мускулна атрофия (болест на Кенеди)
Croatian	(1E,6E)-1,7-bis(3,4-dimetoksifenil)-4-ciklobutil-metil-1,6-heptadien 3,5-dion	Liječenje X-vezane bulbospinalne mišićne atrofije (Kennedyjeve bolesti)
Czech	(1E,6E)-1,7-bis(3,4-dimethoxyfenyl)-4-methyl-cyklobutyl 1,6-heptadien-3,5-dion	Léčba X-vázané spinální a bulbární muskulární atrofie (Kennedyho choroby)
Danish	(1E,6E)-1,7-bis(3,4-dimethoxyphenyl)-4-cyclobutyl methyl-1,6-heptadien-3,5-dion	Behandling af X-bundet spinal og bulbær muskulær atrofi (Kennedys sygdom)
Dutch	(1E,6E)-1,7-bis(3,4-dimethoxyfenyl)-4-cyclobutyl methyl-1,6-heptadieen-3,5-dion	Behandeling van x-linked spinobulbaire musculaire atrofie (ziekte van Kennedy)
Estonian	(1E,6E)-1,7-bis(3,4-dimetoksüfenüül)-4-tsüklobutüül metüül-1,6-heptadiene-3,5-dioon	X-liitelise spinobulbaarse lihasatroofia (Kennedy haiguse) ravi
Finnish	(1E,6E)-1,7-bis(3,4-dimetoksifenyyli)-4-syklobutyyli metyyli-1,6-heptadieeni-3,5-dioni	X-kromosomaalisen, spinaalisen ja bulbaarisen lihasatrofian (Kennedyn tauti) hoito
French	(1E,6E)-1,7-bis(3,4-diméthoxyphényl)-4-méthyl cyclobutyle -1,6 -heptadiène-3,5-dione	Traitement de l'atrophie musculaire spinale et bulbaire liée à l'X (maladie de Kennedy)
German	(1E,6E)-1,7-Bis(3,4-dimethoxyphenyl)-4-cyclobutyl Methyl-1,6-heptadien-3,5-dion	Behandlung der x-chromosomalen spinobulbären Muskelatrophie Typ Kennedy (Kennedy-Krankheit)
Greek	(1E,6E)-1,7-δις(3,4-διμεθοξυφαινυλο)-4-κυκλοβουτυλ μεθυλ-1,6-επταδιένιο-3,5-διόνη	Θεραπεία της φυλοσύνδετης νωτιαίας και βολβικής μυϊκής ατροφίας (νόσος Kennedy)
Hungarian	(1E,6E)-1,7-bisz(3,4-dimetoxi-fenil)-4-ciklobutil-metil-1,6-heptadién-3,5-dion	X-hez kötött gerinci és nyúltagyi izomatrófia (Kennedy-betegség) kezelésére
Italian	(1E,6E)-1,7-bis(3,4-dimetossifenil)-4-metil-ciclobutile 1,6-eptadiene-3,5-dione	Trattamento dell'atrofia muscolare spinale bulbare X-linked (malattia di Kennedy)
Latvian	(1E,6E)-1,7-bis(3,4-dimetoksifenil)-4-ciklobutilmetil-1,6-heptadiēna-3,5-dions	Ar X hromosomu saistītās spinālās un bulbārās muskuļu atrofijas (Kenedija slimības) ārstēšana
Lithuanian	(1E,6E)-1,7-bis(3,4-dimetoksifenil)-4-ciklobutilmetil 1,6-heptadieno-3,5-dionas	Su X chromosoma susijusios spinalinės ir bulbarinės raumenų atrofijos (*Kennedy* liga) gydymas

[2] At the time of designation

Language	Active ingredient	Indication
Maltese	(1E,6E)-1,7-bis(3,4-dimethoxyphenyl)-4-cyclobutylmethyl-1,6-heptadiene-3,5-dione	Kura tal-atrofija muskulari spinali u bulbari marbuta mal-kromosoma X (marda ta' Kennedy)
Polish	(1E,6E)-1,7-bis(3,4-dimetoksyfenylo) -4-cyklobutylo-metylo-1,6-heptadien-3,5-dion	Leczenie sprzężonego z chromosomem X rdzeniowo-opuszkowego zaniku mięśni (choroby Kennedy'ego)
Portuguese	(1E,6E)-1,7-bis(3,4-dimetoxifenil)-4-metil-ciclobutilo 1,6-heptadieno-3,5-diona	Tratamento da atrofia muscular espinhal e bulbar ligada ao cromossoma X (doença de Kennedy)
Romanian	(1E,6E)-1,7-bis(3,4-dimetoxifenil)-4-ciclobutil metil-1,6-heptadiena-3,5-diona	Tratarea atrofiei musculare spinale și bulbare X-linkate (bolii Kennedy)
Slovak	(1E,6E)-1,7-bis(3,4-dimetoxyfenyl)-4-metyl-cyklobutyl 1,6-heptadién-3,5-dión	Liečba X-chromozómovej spinálnej a bulbárnej svalovej atrofie (Kennedyho ochorenia)
Slovenian	(1E,6E)-1,7-bis(3,4-dimetoksifenil)-4-ciklobutil metil-1,6-heptadien-3,5-dion	Zdravljenje bulbospinalne mišične atrofije vezane na kromosom X (Kennedyjeve bolezni)
Spanish	(1E,6E)-1,7-bis(3,4-dimetoxifenil)-4-ciclobutil metil-1,6-heptadieno-3,5-diona	Tratamiento de la atrofia muscular espinobulbar ligada al cromosoma X (enfermedad de Kennedy)
Swedish	(1E,6E)-1,7-bis(3,4-dimetoxifenyl)-4-cyklobutyl metyl-1,6-heptadien-3,5-dion	Behandling av X-kromosombunden spinobulbär muskelatrofi (Kennedys sjukdom)
Norwegian	(1E,6E)-1,7-bis(3,4-dimetoksyfenyl)-4-cyklobutyl metyl-1,6-heptadien-3,5-dion	Behandling av x-bundet spinal og bulbær muskelatrofi (Kennedys sykdom)
Icelandic	(1E,6E)-1,7-bis(3,4-dímetoxýfenýl)-4-sýklóbútýl metýl-1,6-heptadíen-3,5-díón	Meðferð við X-tengdri vöðvarýrnun í mænu og mænukylfu (Kennedy-sjúkdómi)