



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27 May 2016
EMA/COMP/242793/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Combination of 4-hydroxyandrostenedione, *Serenoa serrulata* fruit extract and alpha lipoic acid for the treatment of multiple symmetric lipomatosis

On 28 April 2016, orphan designation (EU/3/16/1646) was granted by the European Commission to Dr. Regenold GmbH Development·Regulatory·Market Access, Germany, for a combination of 4-hydroxyandrostenedione (also called formestane), *Serenoa serrulata* fruit extract and alpha lipoic acid (also called thioctic acid) for the treatment of multiple symmetric lipomatosis.

What is multiple symmetric lipomatosis?

Multiple symmetric lipomatosis is a disorder of the way in which parts of the body produce and store fat. As a result, large symmetrical masses of fat build up under the skin of the neck, shoulders and upper arms. These can result in disfigurement and symptoms such as nerve damage and pain, muscle cramps, increased heart rate, excessive sweating, impotence, reduced blood flow to the hands, deep ulcers and deformity of the fingers. The disease affects mostly men and is thought to be associated with alcohol abuse.

Multiple symmetric lipomatosis is long-term debilitating and life threatening, with a reduction in life-expectancy and an increased risk of sudden death.

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

At the time of designation, multiple symmetric lipomatosis affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 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 designation, no satisfactory methods were authorised in the EU for the treatment of multiple symmetric lipomatosis. Patients were encouraged to abstain from alcohol. Surgery or

*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).



liposuction were sometimes used to reduce the fat masses and provide temporary relief of symptoms caused by the fat pressing on other tissues. Some patients with early-stage disease were also given the medicine salbutamol.

How is this medicine expected to work?

The medicine is being developed as a cream that contains 3 active substances. The substance 4-hydroxyandrostenedione and the extract of *Serenoa serrulata* (saw palmetto) fruit work in different ways to alter the balance of sex hormones in fat cells beneath the skin and reduce the build-up of fat. The antioxidant alpha lipoic acid helps to control substances called free radicals that can damage cells and may be involved in the disease process. By applying the cream to the affected areas, it is expected that the absorbed active substances will reduce the build-up of fat in multiple symmetric lipomatosis.

What is the stage of development of this medicine?

The effects of each component in this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with multiple symmetric lipomatosis were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for multiple symmetric lipomatosis or designated as an orphan medicinal product elsewhere for this condition. The individual active substances have been approved separately in some EU member states for other uses.

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.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Combination of 4-hydroxyandrostenedione, <i>Serenoa serrulata</i> fruit extract and alpha lipoic acid	Treatment of multiple symmetric lipomatosis
Bulgarian	Комбинация от 4-хидрокси-андростендион, екстракт от плодовете на <i>Serenoa serrulata</i> и тиоктова киселина	Лечение на множествена симетрична липоматоза
Croatian	Kombinacija 4-hidroksi-androstenediona, ekstrakta ploda <i>Serenoa serrulata</i> i alfa lipoične kiseline	Liječenje multiple simetrične lipomatoze
Czech	Kombinace 4-hydroxy-androstenedion, extrakt z plodů rostliny <i>Serenoa serrulata</i> a kyselina alfa lipoová	Léčba mnohočetné symetrické lipomatózy
Danish	Kombination af 4-hydroxy-androstendion, <i>Serenoa serrulata</i> frugt ekstrakt og alfa-liponsyre	Behandling af multiple symmetrisk lipomatose
Dutch	Combinatie van 4-hydroxy-androsteendion, <i>Serenoa serrulata</i> vrucht extract en alfa liponzuur	Behandeling van multipele symmetrische lipomatose
Estonian	Kombinatsioon 4-hüdroksüandrosteendioonist, <i>Serenoa serrulata</i> viljade ekstraktist ja ja alfalipoehapest	Multiibelse sümmeetrilise lipomatoosi ravi
Finnish	4-hydroksi-androstenedionin, sahapalmun hedelmäuutteen ja alfalipoiinihapon yhdistelmä	Multippelin symmetrisen lipomatoosin hoito
French	Association de 4-hydroxy-androstènedione, extrait de fruits de <i>Serenoa serrulata</i> et acide alpha-lipoïque	Traitement de la lipomatose multiple symétrique
German	Kombination von 4-Hydroxy-Androstendion, <i>Serenoa serrulata</i> Fruchtextrakt und Alpha-Liponsäure	Behandlung von multipler symmetrischer Lipomatose
Greek	Συνδυασμός 4-υδροξυ- ανδροστενεδιόνης, εκχυλίσματος φρούτου <i>Serenoa serrulata</i> και άλφα λιποϊκού οξέος	Θεραπεία πολλαπλής συμμετρικής λιπωμάτωσης
Hungarian	4-hidroxi-androszténdion, szabalpálma termés kivonat és alfa-liponsav kombinációja	Szimmetrikus multiplex lipomatosis kezelése
Italian	Combinazione di 4-idrossi-androstenedione, estratto di frutto di <i>Serenoa serrulata</i> e acido alfa lipoico	Trattamento della lipomatosi multipla simmetrica
Latvian	4-hidroksi androstendiona, <i>Serenoa serrulata</i> augļu ekstrakta un alfalipoiskābes kombinācija	Multiplās simetriskās lipomatozes ārstēšana
Lithuanian	4-hidroksiandrostenediono, <i>Serenoa serrulata</i> vaisių ekstraktas ir alfa lipo rūgšties darinys	Dauginės simetrinės lipomatozės gydymas
Maltese	4-hydroxy-androstenedione, <i>Serenoa serrulata</i> fruit extract u alpha lipoic acid magħqudin ma' xulxin	Kura tal-lipomatosi multipla simmetrika
Polish	Połączenie 4-hydroksy-androstenedionu, ekstraktu owoców palmy sabal i kwasu liponowego	Rozsiana, symetryczna tłuszczakowatość
Portuguese	Associação de 4-hidroxiandrostenediona, <i>Serenoa repens</i> e ácido lipóico	Tratamento da lipomatose simétrica múltipla

¹ At the time of designation

Language	Active ingredient	Indication
Romanian	Combinajie de 4-hidroxi-androstendionă, extract de fructe de <i>Serrenoa serulata</i> și acid alfa lipoic	Tratamentul lipomatozei simetrice multiple
Slovak	Kombinácia 4-hydroxy-androstenedion, extrakt z plodov serenoy a kyselina lipoová	Liečba mnohopočetnej symetrickej lipomatózy
Slovenian	Kombinacija 4-hidroksi-androstendiona, ekstrakta sadeža žagastolistne palme in alfa lipoične kisline	Zdravljenje multiple simetrične lipomatoze
Spanish	Combinación de 4-hidroxi-androstenediona, extracto del fruto de <i>Serenoa serrulata</i> y ácido alfa lipóico	Tratamiento de la lipomatosis simétrica múltiple
Swedish	Kombination av 4-hydroxi-androstendion, <i>Serenoa serrulata</i> fruktextrakt och alfa.liponsyra	Behandling av multipel symmetrisk lipomatos
Norwegian	Kombinasjon av 4-hydroksy-androstenedion, ekstrakt av <i>Serenoa serrulata</i> frukt og alfa-liponsyre	Behandling av multippel symmetrisk lipomatose
Icelandic	Blanda af 4-hýdroxý-andróstendíon, þykkni úr ávexti Freyspálma og alfa-lípóínsýra	Til meðferðar við samhverfu fituhnútageri