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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Clonidine hydrochloride for the prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy

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Rev.1: sponsor's name change	4 March 2015
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 27 October 2011, orphan designation (EU/3/11/919) was granted by the European Commission to Bioalliance Pharma SA, France, for clonidine hydrochloride for the prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy.

In October 2014, BioAlliance Pharma changed name to Onxeo.

What is oral mucositis?

Oral mucositis is inflammation of the lining of the mouth which results in symptoms such as ulcers, severe pain, bleeding and inflammation. Patients with head and neck cancer are prone to developing oral mucositis because of the radiation therapy they receive. Radiation therapy employs high-dose X-rays or other high-energy rays to kill the cancer cells in the head and neck. Unfortunately the radiation therapy is also likely to cause inflammation in the surrounding cells and tissues.

Oral mucositis in head and neck cancer patients undergoing radiation therapy is a long-term debilitating and life threatening disease because it can lead to pain, poor nutrition, infections and make the patient less likely to comply with their radiotherapy treatment.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of oral mucositis was estimated to be approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

102,000 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 methods of prevention are available?

At the time of designation, mouth rinses containing calcium phosphate and povidone iodine were authorised in some EU countries for preventing oral mucositis in head and neck cancer patients undergoing radiation therapy.

The sponsor has provided sufficient information to show that clonidine hydrochloride might be of significant benefit for mucositis in head and neck cancer patients undergoing radiotherapy because it works in a different way to existing treatments and early studies show that it might offer benefits to patients with this condition, possibly in combination with existing methods. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Clonidine hydrochloride has been used for the treatment of high blood pressure since the 1970s. It is known to act on certain receptors in the body called ɑlpha-2 adrenergic receptors. Among other functions, these receptors are involved in the production of messenger molecules (cytokines) that are involved in inflammation. This includes cytokines that promote inflammation (pro-inflammatory) and others that reduce inflammation (anti-inflammatory). By attaching to these receptors, clonidine hydrochloride is expected to reduce the production of pro-inflammatory cytokines and increase the production of anti-inflammatory cytokines. This is expected to reduce inflammation which could help in preventing oral mucositis.

Clonidine hydrochloride is expected to be available as a tablet designed to adhere to the upper gum for several hours to allow the clonidine to dissolve slowly in the mouth.

What is the stage of development of this medicine?

The effects of clonidine hydrochloride have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with clonidine hydrochloride in patients with oral mucositis were ongoing.

At the time of submission, clonidine hydrochloride was not authorised anywhere in the EU for the prevention of oral mucositis 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 30 September 2011 recommending the granting of this designation.

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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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

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:

Onxeo
49, Bd Gal Martial Valin
F-75015 Paris
France
Tel. +33 1 45 58 76 00
Fax +33 1 45 58 08 81
E-mail: contact@onxeo.com

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	Clonidine hydrochloride	Prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy
Bulgarian	Клонидин хидрохлорид	Профилактика на орален мукозит при пациенти с карцином в областта на главата и шията, подложени на радиационна терапия
Czech	Klonidin hydrochlorid	Prevence orální mukositidy u pacientů s nádorovým onemocněním v oblasti hlavy a krku podstupujících radioterapii
Danish	Clonidin hydrochlorid	Forebyggelse af oral mucositis i patienter med kræft i hoved - og halsregionen som får strålebehandling
Dutch	Clonidinehydrochloride	Preventie van orale mucositis in hoofd- en nekkankerpatienten die stralingstherapie ondergaan
Estonian	Klonidiin hüdrokloriid	Suuõõne mukosiidi profülaktika patsientidel, kes saavad kiiritusravi pea- ja kaelapiirkonna vähi vastu
Finnish	Klonidiini hydrokloridi	Oraalisen mucositis:in ennaltaehkäisy pään- ja kaulan alueen syöpää sairastavilla potilailla, jotka saavat sädehoitoa
French	Chlorhydrate de clonidine	Prévention de la mucite bucco-pharyngée chez les patients atteints de cancer de la tête et du cou subissant une radiothérapie
German	Clonidinhydrochlorid	Prävention einer oralen Mucositis (Schleimhautentzündung im Mund) bei Patienten mit Plattenepithelkarzinomen des Kopf- und Halsbereichs im Rahmen einer Bestrahlungstherapie
Greek	Κλονιδίνη υδροχλωρική	Πρόληψη της στοματίτιδας σε ασθενείς με καρκίνο της κεφαλής και του λαιμού που υποβάλλονται σε ακτινοθεραπεία
Hungarian	Klonidin hidroklorid	Fej - és nyakrák sugárkezelését követő orális mucositis megelőzése
Italian	Clonidina cloridrato	Prevenzione delle mucositi orali in pazienti con cancro nella regione della testa e del collo sottoposti a radioterapia
Latvian	Klonidīna hidrohlorīds	Mutes gļotādas iekaisuma novēršana galvas un kakla vēža pacientiem, kas saņem staru terapiju
Lithuanian	Klonidino hidrochloridas	Burnos gleivinės uždegimo (mukozito) prevencija pacientams, kuriems taikomas radioterapinis gydymas dėl galvos ir kaklo srities vėžio
Maltese	Clonidine hydrochloride	Prevenzjoni tal-mukożite orali f'pazjenti li għandhom kanċer fir-ras u fl-għonq li qed jirċievu radjoterapija
Polish	Chlorowodorek klonidyny	Zapobieganie zapaleniu śluzówki jamy ustnej u pacjentów poddawanych radioterapii w przebiegu raka głowy i szyi

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	Cloridrato de clonidina	Prevenção da mucosite oral induzida pela radioterapia em doentes com neoplasia de cabeça e pescoço
Romanian	Clorhidrat de clonidină	Prevenirea mucozitei orale la pacienţii cu neoplasm de cap şi gât cărora li se administrează radioterapie
Slovak	Klonidín hydrochloride	Prevencia orálnej mukozitídy u pacientov podstupujúcich rádioterapiu pri liečbe rakoviny hlavy a krku
Slovenian	Klonidin hidroklorid	Preprečevanje oralnega mukozitisa pri pacientih, ki so izpostavljeni radioterapiji v območju glave in vratu
Spanish	Clorhidrato de clonidina	Prevención de la mucositis oral en pacientes tratados con radioterapia por cánceres de la región de la cabeza y el cuello
Swedish	Klonidinhydroklorid	Profylax av oral mucositis hos huvud-hals cancer patienter som får strålbehandling
Norwegian	Klonidinhydroklorid	Forebygging av oral mucositis hos pasienter med kreft i hode- og halsregionen som får strålebehandling
Icelandic	Klónidín klóríð	Vörn gegn slímubólgu í munni hjá sjúklingum í geislamedferð vegna krabbameins á höfuð-og hálssvæði