



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Genetically modified *Lactococcus lactis* bacteria containing the *human trefoil factor 1* gene for the prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy

On 27 September 2011, orphan designation (EU/3/11/903) was granted by the European Commission to ActoGeniX N.V., Belgium, for genetically modified *Lactococcus lactis* bacteria containing the *human trefoil factor 1* gene for the prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy.

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 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 disease because it can lead to pain, poor nutrition, infections and it makes 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 in the European Union (EU) with head and neck cancer at risk of oral mucositis following radiation therapy was estimated to be less than 4 in 10,000 people *. This is equivalent to a total of fewer than 203,000 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).

*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. This represents a population of 506,300,000 (Eurostat 2011).



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 genetically modified *Lactococcus lactis* bacteria containing the *human trefoil factor 1* gene might be of significant benefit for mucositis in head and neck cancer patients undergoing radiotherapy because it works in a different way to existing methods 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?

The medicine is a 'gene therapy product' that works by delivering specific genes into the body with the purpose of providing a specific protein. The medicine contains bacteria called *Lactococcus lactis* that have been genetically modified so that they produce a protein called human trefoil factor 1. This is a natural human protein found in the lining of the mouth and the gut where it is involved in protecting and repairing the cells of this lining. The medicine is expected to be available as a mouth rinse. When patients use the mouth rinse, the bacteria are expected to enter the patient's mouth and produce the human trefoil factor 1, thus helping to protect and repair the cells of the mouth lining and to prevent oral mucositis.

What is the stage of development of this medicine?

The effects of genetically modified *Lactococcus lactis* bacteria containing the *human trefoil factor 1* gene have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicinal product in head and neck cancer patients undergoing radiation therapy were ongoing.

At the time of submission, the medicinal product was not authorised anywhere in the EU for the prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy 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 8 July 2011 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	Genetically modified <i>Lactococcus lactis</i> bacteria containing the <i>human trefoil factor 1</i> gene	Prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy
Bulgarian	Генетично модифицирани <i>Lactococcus lactis</i> бактерии, съдържащи ген за човешки <i>трефоил фактор 1</i>	Профилактика на орален мукозит при пациенти с карцином в областта на главата и шията, подложени на радиационна терапия
Czech	Geneticky modifikovaná bakterie <i>Lactococcus lactis</i> obsahující lidský gen <i>trefoil factor 1</i>	Prevence orální mukositivity u pacientů s nádorovým onemocněním v oblasti hlavy a krku podstupujících radioterapii
Danish	Genetisk modificerede <i>Lactococcus lactis</i> bakterier indeholdende det humane <i>trefoil factor 1</i> gen	Forebyggelse af oral mucositis i patienter med kræft i hoved - og halsregionen som får strålebehandling
Dutch	Genetisch gemodificeerd <i>Lactococcus lactis</i> bacterie dewelke <i>humane trefoil factor 1</i> gen bevat	Preventie van orale mucositis in hoofd- en nekkankerpatienten die stralingstherapie ondergaan
Estonian	Geneetiliselt modifitseeritud <i>Lactococcus lactis</i> bakterid, mis sisaldavad inimese <i>trefoil factor 1</i> geeni	Suuõõne mukosiidi profülaktika patsientidel, kes saavad kiiritusravi pea- ja kaelapiirkonna vähi vastu
Finnish	Geneettisesti muunneltu <i>Lactococcus lactis</i> bakteeri, joka sisältää ihmisen <i>trefoil factor 1</i> geenin	Oraalisen mucositis:in ennaltaehkäisy pään- ja kaulan alueen syöpää sairastavilla potilailla, jotka saavat sädehoitoa
French	Bacille de <i>Lactococcus lactis</i> modifié génétiquement contenant le gène <i>humain trefoil facteur 1</i>	Prévention de la mucite bucco-pharyngée chez les patients atteints de cancer de la tête et du cou subissant une radiothérapie
German	Gentechnisch veränderte <i>Lactococcus lactis</i> Bakterien, die das <i>humane trefoil factor 1</i> Gen enthalten	Prävention einer oralen Mucositis (Schleimhautentzündung im Mund) bei Patienten mit Plattenepithelkarzinomen des Kopf- und Halsbereichs im Rahmen einer Bestrahlungstherapie
Greek	Γενετικά ανασυνδιασμένα βακτήρια <i>λακτόκκοκου lactis</i> που περιέχουν το ανθρώπινο γονίδιο <i>trefoil παράγοντα 1</i>	Πρόληψη της στοματίτιδας σε ασθενείς με καρκίνο της κεφαλής και του λαιμού που υποβάλλονται σε ακτινοθεραπεία
Hungarian	<i>Humán trefoil faktor 1</i> gént tartalmazó genetikailag módosított <i>Lactococcus lactis</i> baktériumok	Fej - és nyakrák sugárkezelését követő orális mucositis megelőzése
Italian	Bacillo di <i>lactococcus lactis</i> geneticamente modificato contenente il gene <i>umano trefoil factor 1</i>	Prevenzione delle mucositi orali in pazienti con cancro nella regione della testa e del collo sottoposti a radioterapia
Latvian	<i>Cilvēka trefoil faktora 1</i> gēnu saturoša <i>Lactococcus lactis</i> ģenētiski modificēta baktērija	Mutes gļotādas iekaisuma novēršana galvas un kakla vēža pacientiem, kas saņem staru terapiju

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	Genetiškai modifikuota bakterija <i>Lactococcus lactis</i> , pernešanti žmogaus <i>trefoil 1 faktoriaus</i> geną	Burnos gleivinės uždegimo (mukozito) prevencija pacientams, kuriems taikomas radioterapinis gydymas dėl galvos ir kaklo srities vėžio
Maltese	Batterji <i>Lactococcus lactis</i> modifikati ġenetikament li fihom il-ġene <i>trefoil fattur 1 uman</i>	Prevenzjoni tal-mukožite orali f'pazjenti li għandhom kanċer fir-ras u fl-għonq li qed jirċievu radjoterapija
Polish	Genetycznie zmodyfikowane bakterie <i>Lactococcus lactis</i> zawierające ludzki gen kodujący czynnik <i>TFF1</i>	Zapobieganie zapaleniu śluzówki jamy ustnej u pacjentów poddawanych radioterapii w przebiegu raka głowy i szyi
Portuguese	Bactérias <i>Lactococcus lactis</i> geneticamente modificadas contendo o gene do <i>factor trefoil 1 humano</i>	Prevenção da mucosite oral induzida pela radioterapia em doentes com neoplasia de cabeça e pescoço
Romanian	Bacterii <i>Lactococcus lactis</i> genetic modificate, ce conțin gena <i>umană trefoil factor 1</i>	Prevenirea mucozitei orale la pacienții cu neoplasm de cap și gât căroră li se administrează radioterapie
Slovak	Geneticky modifikované baktérie <i>Lactococcus lactis</i> obsahujúce ľudský gén pre <i>trefoil factor 1</i>	Prevencia orálnej mukozitídy u pacientov podstupujúcich rádioterapiu pri liečbe rakoviny hlavy a krku
Slovenian	Gensko spremenjena bakterija <i>Lactococcus lactis</i> z genom za <i>humani triperesni faktor 1</i>	Preprečevanje oralnega mukozitisa pri pacientih, ki so izpostavljeni radioterapiji v območju glave in vratu
Spanish	<i>Lactococcus lactis</i> genéticamente modificado que contiene el gen del <i>factor trébol humano 1</i>	Prevención de la mucositis oral en pacientes tratados con radioterapia por cánceres de la región de la cabeza y el cuello
Swedish	Genmodifierad <i>Lactococcus lactis</i> bakterie innehållande den <i>mänskliga trefoil factor 1</i> genen	Profylax av oral mucositis hos huvud-hals cancer patienter som får strålbehandling
Norwegian	Genmodifisert <i>Lactococcus lactis</i> bakterie inneholdende <i>human trefoil faktor 1</i> gen	Forebygging av oral mucositis hos pasienter med kreft i hode- og halsregionen som får strålebehandling
Icelandic	Erfðabreytt <i>Lactococcus lactis</i> baktería sem inniheldur <i>manna trefoil factor 1</i> gen	Vörn gegn slímubólgu í munni hjá sjúklingum í geislamedferð vegna krabbameins á höfuð-og hálssvæði