European Medicines Agency
*Pre-authorisation Evaluation of Medicines for Human Use*

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## Committee for Orphan Medicinal Products

# Public summary of positive opinion for orphan designation of type I native bovine skin collagen for treatment of systemic sclerosis

On 9 February 2009, orphan designation (EU/3/08/607) was granted by the European Commission to arGentis Autoimmune Europe Limited, United Kingdom, for type I native bovine skin collagen for the treatment of systemic sclerosis.

**What is systemic sclerosis?**
Systemic sclerosis is a complex disease in which the immune system (the body's natural defences) is overactivated, causing inflammation and overproduction of various proteins, particularly collagen. The reason why the immune system is activated is not known. Collagen is an important component of connective tissue (the tissue that supports the skin and internal organs).
The overproduction of collagen leads to abnormal growth of connective tissue, causing the skin to become thick and hard. It also damages the tissues around the blood vessels of the internal organs, such as the heart, lungs and kidneys. This makes it more difficult for the blood to move through the vessels, causing tissue damage, circulation problems and high blood pressure. The high collagen levels can also stimulate the body's immune system to attack the collagen, increasing the inflammation in the body.
Systemic sclerosis is a debilitating disease that is long lasting and may be life threatening because of its effects on the heart, lungs and kidneys.

**What treatments are available?**
At the time of designation, there were no treatments for systemic sclerosis that could stop the build-up of collagen. Treatments authorised in the EU were aimed at relieving the symptoms of the disease and limiting the damage it causes. Several medicines were used to reduce inflammation.
The sponsor has provided sufficient information to show that type I native bovine skin collagen might be of potential significant benefit for the treatment of systemic sclerosis because it might work in a different way to existing medicines and cause fewer side effects. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

**What is the estimated number of patients affected by the condition?**
At the time of designation, systemic sclerosis affected not more than 3.5 in 10,000 people in the European Union (EU)[*]. This is below the threshold for orphan designation, which is 5 in 10,000, and is equivalent to a total of not more than 176,000 people. 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 502,282,000 (Eurostat 2008).

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.europa.eu http://www.emea.europa.eu

**How is this medicine expected to work?**
Type I native bovine skin collagen is thought to work by stimulating 'oral tolerance'. Oral tolerance is a way to 'teach' the immune system not to react against an antigen (a specific structure that the body recognises as 'foreign'). It involves giving the patient a particular antigen by mouth.
Type I native bovine skin collagen is a type of collagen that is extracted from cow skin. In patients with systemic sclerosis, ingestion of this protein by mouth is expected to teach the immune system not to react to the collagen that is produced in the body. This is expected to reduce the inflammation caused by the patient's own collagen production, reducing the symptoms of the disease.

**What is the stage of development of this medicine?**
The effects of type I native bovine skin collagen have been evaluated in experimental models.
At the time of submission of the application for orphan designation, clinical trials in patients with systemic sclerosis had been completed and additional trials had been planned.
Type I native bovine skin collagen was not authorised anywhere in the world for the treatment of systemic sclerosis at the time of submission. Orphan designation of type I native skin collagen had been granted in the United States of America for the treatment of diffuse systemic sclerosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted a positive opinion on 10 December 2008 recommending the granting of this designation.

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Opinions on orphan medicinal products designations are based on the following criteria:
- the seriousness of the condition;
- the existence or not of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (considered to affect not more than 5 in 10,000 in the Community) or insufficient returns on investment.

Designated orphan medicinal are products that are still under investigation and are considered for 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 marketing authorisation.

**For more information:**
Sponsor's contact details:
arGentis Autoimmune Europe Limited
179 Portland Street
London W1W5LS
United Kingdom
Telephone: +44 20 7344 56 41
Telefax: +44 20 7344 7689
E-mail: tom@argentisrx.com

Patients' associations contact points:

**Scleroderma Liga e.V.**
Kelterstraße 23
76227 Karlsruhe
Germany
Telephone: +49 721 40 48 44
Telefax: +49 721 94 15 515
E-mail: scl@scleroliga.de

**Association des Sclérodermiques de France**
41 Rue du Pont de Fer
28260 Sorel-Moussel
France
Telephone: +33 0820 620 615
E-mail: association.asf@club-internet.fr

**Raynaud's & Scleroderma Association (RSA)**
112 Crewe Road
Alsager
Cheshire
ST7 2JA
United Kingdom
Telephone: +44 1270 87 27 76
Freephone: 0800 91 72 494 (for UK enquiries only)
Fax: +44 1270 88 35 56
Email: info@raynauds.org.uk

**Translations of the active ingredient and indication in all EU languages, Norwegian and Icelandic**

| Language | Active ingredient | Indication |
|---|---|---|
| English | Type I native bovine skin collagen | Treatment of systemic sclerosis |
| Bulgarian | Тип I нативен волски кожен колаген | Лечение на системна склероза |
| Czech | Přírodní telecí kožní kolagen typu I | Léčba systémové sklerodermie |
| Danish | Nativt type I-kollagen fra bovin hud | Behandling af systemisk sklerose |
| Dutch | Type I natief runderhuidcollageen | Behandeling van Systeem Sclerose |
| Estonian | I tüüpi töötlemata veisenaha kollageen | Süsteemse sklerodermia ravi |
| Finnish | Tyypin I natiivi naudan ihon kollageeni | Systeemisen skleroosin hoito |
| French | Collagène cutané bovin natif de type I | Traitement de la sclérose systémique |
| German | Natives bovines Hautkollagen Typ I | Behandlung der systemischen Sklerose |
| Greek | Εγγενές Βόειο Δερματικό Κολλαγόνο Τύπου I | Θεραπεία της συστηματικής σκλήρυνσης |
| Hungarian | I. típusú természetes marhabőr kollagén | Szisztémás scleroderma kezelése |
| Italian | Collagene nativo di Tipo I da cute bovina | Trattamento della sclerosi sistemica |
| Latvian | I tipa dabīgas liellopu ādas kolagēns | Sistēmiskas sklerozes ārstēšana |
| Lithuanian | Natyvus jaučio odos I tipo kolagenas | Sisteminės odos sklerozės gydymas |
| Maltese | Kollaġni tal-ġilda tal-baqar indiġenu tat-Tip I | Kura tas-sklerosi sistemika |
| Polish | Kolagen typu I otrzymywany z komórek skóry bydlęcej | Leczenie twardziny narządowej |
| Portuguese | Colagénio natural, derivado de pele de bovino (tipo I) | Tratamento da esclerose sistémica |
| Romanian | Colagen cutanat nativ bovin, de tip I | Tratamentul sclerozei sistemice |
| Slovak | Prírodný hovädzí kožný kolagén typu I | Liečba systémovej sklerózy |
| Slovenian | Nativni kožni bovini kolagen vrste I | Zdravljenje sistemske skleroze |
| Spanish | Colágeno cutáneo bovino natural de tipo I | Tratamiento de la esclerosis sistémica |
| Swedish | Nativt kollagen typ I från bovin hud | Behandling av systemisk skleros |
| Norwegian | Type I nativt bovint hudkollagen | Behandling av systemisk sklerose |
| Icelandic | Gerð I af náttúrulegu kollageni nautgripahúðar | Meðferð við dreifðum herslismeinum |