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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

A non-covalent trimer of tumour necrosis factor fused to an antibody specific to the extra-domain B of fibronectin in single-chain variable fragment format for the treatment of soft tissue sarcoma

On 14 October 2016, orphan designation (EU/3/16/1739) was granted by the European Commission to Philogen S.p.A., Italy, for a non-covalent trimer of tumour necrosis factor fused to an antibody specific to the extra-domain B of fibronectin in single-chain variable fragment format (also known as L19TNF) for treatment of soft tissue sarcoma.

What is soft tissue sarcoma?

Soft tissue sarcoma is a cancer that affects the soft tissues of the body. It can occur in muscles, blood vessels, fat tissue or in other tissues that support, surround and protect organs. Patients with soft tissue sarcoma do not usually have symptoms in the early stages of the disease. First symptoms appear when the tumour grows large enough to cause swelling and pain.

Soft tissue sarcoma is a long-term debilitating and life-threatening disease, particularly when the cancer has spread to other parts of the body.

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

At the time of designation, soft tissue sarcoma affected approximately 2.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 144,000 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, the main treatment for early-stage soft tissue sarcoma was surgery. For large sarcomas, surgery was usually followed by radiotherapy (treatment with radiation) and

*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).

chemotherapy (medicines to treat cancer) to kill any cancer cells that were left behind. Several medicines were authorised in the EU for the treatment of soft tissue sarcoma including doxorubicin.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with soft tissue sarcoma, with early data showing improved progression-free survival (how long patients lived without their disease getting worse) in patients who had received previous treatment. 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 made of two joined proteins, an antibody and tumour necrosis factor (TNF). The antibody is a protein designed to attach to blood vessels that supply the tumours, while TNF is a natural protein known to attack and kill cells. By having the antibody and TNF joined together, the medicine is expected to target and kill soft tissue sarcoma cells, helping to slow down progression of the cancer.

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, clinical trials with the medicine including patients with soft tissue sarcoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for soft tissue sarcoma 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 September 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	A non-covalent trimer of tumour necrosis factor fused to an antibody specific to the extra-domain B of fibronectin in single-chain variable fragment format	Treatment of soft tissue sarcoma
Bulgarian	Нековалентен тример на тумор некрозис фактор, свързан с антитяло специфично за допълнителния домейн B на фибронектин под формата на еднoверижeн променлив фрагмент	Лечение на сарком на меките тъкани
Croatian	Ne-kovalentni trimer faktora nekroze tumora sjedinjen s antitijelima specifičnim za ekstra-domene B fibronektina u obliku jednolančanog varijabilnog fragmenta	Liječenje sarkoma mekih tkiva
Czech	Nekovalentní trimer faktoru nekrózy nádorů fúzován s protilátku specifickou pro extra doménu B fibronektinu ve formátu jednořetězcového variabilního fragmentu	Léčba sarkomu měkkých tkání
Danish	En ikke-kovalent trimer af tumornekrosefaktor fusioneret til et antistof et specifikt for den ekstracellulære domæne B af fibronectin i single-chain variable fragment format	Behandling af bløddelssarkom
Dutch	Een niet-covalente trimeer tumornecrosefactor gefuseerd met het een antilichaam specifiek voor het extra-domein B van fibronectine in single-chain variable fragment vorm	Behandeling weke delen sarcoom
Estonian	Tuumorinekroosifaktori mittekovalentne trimeer, mis on liidetud fibronektiini ekstra-domeeni B spetsiifilise antikehaga ühekordse ahela varieeruva fragmendina	Pehmete kudede sarkoomi ravi
Finnish	Tuumorinekroositekijän ei-kovalenttinen trimeeri, fuusioituna vasta-aineeseen, joka on spesifinen fibronektiinin extra-domeeni B:lle, yksiketjuisessa vaihtelevan fragmentin muodossa	Pehmytkudossarkooman hoito
French	Un trimère non covalent du facteur de nécrose tumorale fusionné à un anticorps spécifique de l'extra domaine B de la fibronectine en format de fragment variable à chaîne unique	Traitement des sarcomes des tissus mous
German	Ein nicht-kovalente Trimer bestehend aus Tumornekrosefaktor und einem Antikörpers spezifisch für die Extra Domäne B von Fibronektin in single-chain variable fragment Format	Behandlung des Weichteilsarkoms

¹ At the time of designation

Language	Active ingredient	Indication
Greek	Ένα μη-ομοιοπολικό τριμερές του παράγοντα νέκρωσης των όγκων προσδεμένο σε ένα αντίσωμα ειδικό προς την πρόσθετη-B περιοχή της φимπρονεκτίνης σε μορφή μεταβλητής περιοχής μονής αλυσίδας	Θεραπεία του σαρκώματος των μαλακών ιστών
Hungarian	Egyláncú variábilis fragmentumú fibronectin B extra-doménjére specifikus antitesttel fuzionált tumor nekrosis faktor non-kovalens trimerje	Lágy szöveti sarcoma kezelése
Italian	Trimer non covalente del fattore di necrosi tumorale fuso con l'anticorpo specifico per l'extra-dominio B della fibronectina in formato frammento variabile a catena singola	Trattamento dei sarcomi dei tessuti molli
Latvian	Audzēja nekrozes faktora, kas sapludināts ar pret fibronektīna ekstra-domēnu B specifisku vienkāršas ķēdes variablā fragmenta formāta antivielu, , ne-kovalents trimērs	Mīksto audu sarkomas ārstēšana
Lithuanian	Nekovalentinis naviko nekrozės faktoriaus trimeras, sulietas su antikūnu, specifiniu papildomo domeno B fibronektinui, kintamo viengubos grandinės fragmento formatu	Minkštųjų audinių sarkomos gydymas
Maltese	Trimer mhux kovalenti tal-fattur tan-nekrosi tat-tumur magħqud ma’ antikorp speċifiku għall-extra-dominju B ta’ fibronectin f’għamla ta’ framment varjabbli b’katina waħda	Kura tas-sarkoma tat-tessuti rotob
Polish	Niekowalencyjny trimer czynnika martwicy nowotworu przyłączony do przeciwciała specyficznego dla dodatkowej domeny B fibronektyny w postaci jednołańcuchowego zmiennego fragmentu	Leczenie mięsaków tkanek miękkich
Portuguese	Um trímero não-covalente composto pelo fator de necrose tumoral fundido com o anticorpo específico para o domínio extra-B de fibronectina de cadeia única em formato de fragmento variável	Tratamento do sarcoma dos tecidos moles
Romanian	Un trimer non-covalent al factorului de necroză tumorală fuzionat cu un anticorp specific pentru domeniul extra-B al fibronectinei în format de fragment variabil monocatenar	Tratamentul sarcomului țesuturilor moi
Slovak	Nekovalentný trimér faktora nekrózy nádorov fúzaný s protilátkou špecifickou pre extra doménu B fibronektínu vo formáte jednoreťazcového variabilného fragmentu	Liečba sarkómu mäkkých tkanív
Slovenian	Ne-kovalentni trimer tumorje nekrotizirajočega faktorja, vezan na specifična protitelesa za ekstra domeno B fibronektina v enojni verižni obliki spremenljivega fragmenta	Zdravljenje sarkoma mehkih tkiv

Language	Active ingredient	Indication
Spanish	Un trímero no covalente de factor de necrosis tumoral fusionado a un anticuerpo de cadena única de un fragmento variable específico para el dominio adicional B de la fibronectina en formato	Tratamiento del sarcoma de tejidos blandos
Swedish	En icke-kovalent trimer av tumörnekrosfaktor fuserad till en antikroppen som är specifik för extradomän B av fibronektin i enkelkedjat variabelt fragment format	Behandling av mjukdelssarkom
Norwegian	En ikke-kovalent trimer av tumornekrosefaktor koblet til et antistoff spesifikt for ekstradomene B av fibronektin i enkeltkjede variabelt fragmentformat	Behandling av bløtvevssarkom
Icelandic	Ekki-samgilda trímer af tumour necrosis faktor áfast við sértækt mótefni í auka-ríki B af fíbrónektíni í einkeðju breytileg brotins sniðs	Meðferð við mjúkvefjasarkmeini