12 March 2013
EMA/COMP/170167/2010 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Synthetic double-stranded siRNA oligonucleotide directed against p53 mRNA for the prevention of delayed graft function after renal transplantation

On 6 June 2010, orphan designation (EU/3/10/751) was granted by the European Commission to Verius Limited, United Kingdom, for synthetic double-stranded siRNA oligonucleotide directed against p53 mRNA for the prevention of delayed graft function after renal transplantation.

In February 2013, Verius Limited changed name to ProductLife Limited.

What is delayed graft function after renal transplantation?

Delayed graft function is the failure of a transplanted organ to start working properly in the first few days after the transplant. Delayed graft function can occur following kidney transplants as a result of damage to the organ caused by the interruption and restoration of blood flow. This is called 'ischaemia/reperfusion injury' and is associated with an inflammatory reaction, caused in part by the invasion of neutrophils (a type of white blood cell) into the transplanted organ.

Delayed graft function after renal transplantation is a debilitating and life-threatening condition because of the risk of losing the transplanted kidney.

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 delayed graft function after renal transplantation was estimated to be approximately 0.4 people in 10,000 in the European Union (EU). This was equivalent to a total of around 20,000 people*, and is below the threshold 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 Lichtenstein.
At the time of designation, this represented a population of 506,300,000 (Eurostat 2010).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What methods of prevention are available?

At the time of submission of the application for orphan drug designation, no satisfactory methods were authorised in the EU for the prevention of delayed graft function after renal transplantation. Several preventative measures were commonly used to reduce the risk of delayed graft function, including careful selection of the kidney donor and preservation of the kidney during transport.

How is this medicine expected to work?

This medicine is expected to be injected into patients while they are undergoing a kidney transplant. It will then accumulate in the kidney, where it is expected to work by temporarily blocking the activity of a protein called p53. During ischaemia/reperfusion injury, this protein is overactivated and causes cell death. By temporarily inactivating p53, the medicine is expected to prevent delayed graft function by delaying the induction of cell death at the time of injury, thereby allowing natural repair mechanisms to restore the normal function of the transplanted kidney.

What is the stage of development of this medicine?

The effects of synthetic double-stranded siRNA oligonucleotide directed against p53 mRNA have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients undergoing renal transplantation were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the prevention of delayed graft function after renal transplantation. Orphan designation of this medicine had been granted in the United States of America for delayed graft function after kidney transplantation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 3 March 2010 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:

ProductLife Limited
The Jeffrey's Building
St. John's Innovation Park
Cowley Road
Cambridge CB4 0DS
United Kingdom
Telephone: +44 1223 402 660
Telefax: +44 1223 413 689
E-mail: mjohnston@quarkpharma.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	Synthetic double-stranded siRNA oligonucleotide directed against p53 mRNA	Prevention of delayed graft function after renal transplantation
Bulgarian	Синтетичен двойноспирален олигонуклеотид siRNA, действащ срещу p53 mRNA	Превенция на забавена функция на присадката след бъбречна трансплантация
Czech	Syntetický dvouvláknový oligonukleotid (siRNA) zacílený proti mRNA kódující protein p53	Prevence opožděné funkce štěpu po transplantaci ledvin
Danish	Syntetisk dobbeltstrenget siRNA oligonukleotid rettet mod p53 mRNA	Forebyggelse af forsinket graftfunktion efter nyretransplantation
Dutch	Synthetisch dubbelstreng siRNA-oligonucleotide gericht tegen p53 mRNA	Profylaxe van vertraagde transplantaatfunctie na niertransplantatie
Estonian	Sünteetiline kahe ahelaga siRNA oligonukleotiid, mis on suunatud p53 mRNA poole	Siiriku hilisfunktsiooni (delayed graft function, DGF) ennetamine peale neeru transplantatsiooni
Finnish	Synteettinen, p53 mRNA:ta vastaan suunnattu kaksoisjuosteinen siRNA-oligonukleotidi	Munuaissiirrännäisen toimintaviiveen ehkäisy
French	Oligonucléotide ARNsi bicaténaire synthétique dirigé contre l'ARNm p53	Prévention des retards fonctionnels du greffon après transplantation rénale
German	Gegen p53-mRNA gerichtetes, synthetisches doppelsträngiges siRNA-Oligonukleotid	Vorbeugung einer verzögerten Transplantatfunktion bei Nierentransplantationspatienten
Greek	Συνθετικό ολιγονουκλεοτίδιο δίκλωνου siRNA κατευθυνόμενο κατά του p53 mRNA	Πρόληψη της αργοπορημένης λειτουργίας του μοσχεύματος (DGF) μετά από μεταμόσχευση νεφρού
Hungarian	A p53 mRNS-sel szemben irányított szintetikus dupla spirális siRNS oligonukleotid	Késve induló graftműködés megelőzése vesetranszplantált betegek esetén
Italian	Oligonucleotide siRNA sintetico a doppia elica anti-p53 mRNA	Prevenzione della ritardata ripresa funzionale dopo trapianto renale
Latvian	Sintētisks divspirāļu interferences RNS oligonukleotīds, kas virzīts pret gēna p53 informācijas RNS	Aizkavētas transplantāta funkcijas profilakse pacientiem pēc nieru transplantācijas
Lithuanian	Dvigrandis sintetinis oligonunukleotidas siRNR, nukreiptas prieš p53 mRNR	Vėlyvos transplantato funkcijos profilaktika po inkstų transplantacijos
Maltese	Oligonukleotide sintetiku tas-siRNA b'katina doppja dirett kontra mRNA p53	Prevenzjoni ta' ttardjar fil-funzjonalità ta' trapjant wara trapjant tal-kliewi
Polish	Syntetyczny oligonukleotyd o podwójnym łańcuchu siRNA skierowany przeciwko p53 mRNA	Zapobieganie opóźnieniu w funkcjonowaniu przeszczepu u pacjentów po przeszczepie nerki

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	Oligonucleotídeo ARNsi de cadeia dupla sintético anti ARNm p53	Profilaxia do atraso funcional do órgão transplantado (DGF) em doentes de transplante renal
Romanian	Oligonucleotid ARNsi dublu catenar de sinteză anti-p53 ARNm	Profilaxia funcţionării întârziate a grefei la pacienţii posttransplant renal
Slovak	Syntetický dvojvláknový oligonukleotid (siRNA) zacielený proti p53 mRNA	Prevencia oneskorenia funkcie štepu po transplantácii obličky
Slovenian	sintetični oligonukleotid siRNA z dvojno vijačnico proti p53 mRNA	Preprečevanje zakasnjenega delovanja ledvičnega presadka
Spanish	Oligonucleótido sintético de ARN pequenio de interferencia de doble cadena contra el ARNm de p53	Prevención del retardo funcional del órgano trasplantado tras el trasplante renal
Swedish	Syntetisk dubbelsträngad siRNA-oligonukleotid riktad mot p53 mRNA	Profylax mot försenad transplantatfunktion (DGF) efter njurtransplantation
Norwegian	Syntetisk dobbelttrådet siRNA-oligonukleotid rettet mot p53 mRNA	Forebygging av forsinket transplantatfunksjon etter nyretransplantasjon
Icelandic	Samtengt tvíþátta siRNA fákirni beint gegn p53 mRNA	Forvörn gegn seinkun græðlingsstarfsemi eftir nýrnaígræðslu