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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

A lentiviral vector pseudotyped by the Indiana serotype of the vesicular stomatitis virus G protein encoding an antigen derived from the Tax, HBZ, p12I and p30II HTLV-1 proteins for the treatment of adult T-cell leukaemia/lymphoma

On 15 January 2015, orphan designation (EU/3/14/1417) was granted by the European Commission to Theravectis, France, for a lentiviral vector pseudotyped by the Indiana serotype of the vesicular stomatitis virus G protein encoding an antigen derived from the Tax, HBZ, p12I and p30II HTLV-1 proteins for the treatment of adult T-cell leukaemia/lymphoma.

What is adult T-cell leukaemia/lymphoma?

Adult T-cell leukaemia/lymphoma (ATL) is a cancer of a type of white blood cells, called T cells, which play an important role in the immune system (the body's natural defences). It is associated with infection by a virus known as human T-cell leukaemia virus (HTLV-1) though most people infected do not develop the condition.

In patients with ATL there is uncontrolled growth of abnormal, infected T cells in the blood, bone marrow (the tissue inside the large bones in which blood cells are formed) and lymphatic system (the network of vessels that transport fluid from tissues through the lymph nodes and into the bloodstream). Over a period of time, the abnormal cells can replace the normal blood and immune cells. Abnormal T cells may also invade other tissues such as the skin. In some patients the disease may develop slowly, whereas in others it takes a more aggressive, rapidly developing form.

In patients with symptomatic disease the condition may be associated with low numbers of normal blood cells, breakdown of bone with resultant high levels of calcium in the blood, and skin lesions (rashes or lumps). The condition is long-term debilitating and potentially life-threatening because the loss of normal immune cells in the blood leaves the patient vulnerable to severe and unusual infections.

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

At the time of designation, ATL affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 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?

Treatment of ATL depends on the stage and speed of progression. In addition to measures to relieve symptoms, at the time of designation various cancer medicines were authorised in the EU for the treatment of T-cell cancers. Patients whose disease was not progressing rapidly, and who had few or no symptoms, might be monitored until treatment became necessary.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ATL because initial results from experimental studies suggest that it can trigger the body's own natural defences to attack the abnormal T cells and shrink the cancer. 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 contains a version of HIV, the human immunodeficiency virus, which has been modified in various ways so that it can enter cells but cannot reproduce and cannot cause disease. In addition, genes have been inserted into the virus that enable it to produce a protein made up of parts of 4 different proteins produced by HTLV-1, the virus associated with ATL.

When the medicine is given, it causes the cells it enters to produce this protein, which stimulates the immune system to recognise it, and the HTLV-1 proteins that make it up, as 'foreign'. This encourages the immune system to attack and kill cells that are infected with HTLV-1, thus destroying the abnormal T cells and shrinking the cancer. Patients treated with this medicine are then given a similar medicine, containing a slightly different modified virus, in order to increase the stimulation of the immune system and strengthen its effect.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with this medicine in patients with ATL had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for ATL 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 11 December 2014 recommending the granting of this designation.

*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 511,100,000 (Eurostat 2014).

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	A lentiviral vector pseudotyped by the Indiana serotype of the vesicular stomatitis virus G protein encoding an antigen derived from the Tax, HBZ, p12I and p30II HTLV-1 proteins	Treatment of adult T-cell leukaemia/lymphoma
Bulgarian	Лентивирален вектор, получен от G протеина на серотип Indiana на вируса на везикуларния стоматит кодиращ антиген, получен от протеините Tax, HBZ, p12I и p30II HTLV-1	Лечение на Т-клетъчна левкемия/лимфома у възрастни
Croatian	Lentivirusni vektor pseudotipiziran proteinom G virusa vezikularnog stomatitisa (serotip Indiana) koji kodira za antigen dobiven iz proteina Tax, HBZ, p12I i p30II HTLV-1	Liječenje leukemije/limfoma zrelih T-stanica
Czech	Lentivirový vektor pseudotypovaný pomocí G proteinu viru vezikulární stomatitidy sérotypu Indiana, který kóduje antigen získaný z proteinů Tax, HBZ, p12I a p30II HTLV-1	Léčba leukémie/lymfomu z T-lymfocytů u dospělých pacientů
Danish	En lentiviral vektor med pseudotype efter vesikulær stomatitis virus G protein Indiana serotypen som koder for et antigen afledt af Tax, HBZ, p12I og p30II HTLV-1 proteinerne	Behandling af T-celle leukæmi/lymfom hos voksne
Dutch	Een lentivirale vector pseudogetypeerd door het Indiana serotype van het vesiculaire-stomatitisvirus G proteïne die een antigeen codeert dat afkomstig is van de Tax, HBZ, p12I en p30II HTLV-1 proteïnen	Behandeling van T-cel leukemia/lymphoma bij volwassenen
Estonian	Lentiviirus-vektor, mis on pseudotüpeeritud vesikulaase stomatiidi Indiana serotüübi viiruse G valguga kodeeritud antigeeniga, mis omakorda on saadud valkudest Tax, HBZ, p12I ja p30II HTLV-1,	Täiskasvanute T-rakulise leukeemia/lümfoomi ravi
Finnish	Lentivirusvektori, joka on pseudotyypitetty VS-viruksen G-proteiinin Indiana-serotyypin mukaisesti ja joka koodittaa antigeenia, joka on peräisin Tax-, HBZ-, p12I- ja p30II HTLV-1 -proteiinista	Aikuisen T-solu leukemian/lymfooman hoito
French	Un vecteur lentiviral pseudotypé par le sérotype Indiana de la protéine G du virus de la stomatite vésiculaire codant pour un antigène dérivé des protéines Tax, HBZ, p12I et p30II du virus HTLV-1	Traitement du lymphome/a leucémie à cellules T de l'adulte
German	Ein lentiviraler Vektor pseudotypisiert durch den Indiana-Serotyp des vesikulären Stomatitis-Virus-G-Proteins, der ein von den Tax-, HBZ-, p12I- und p30II-HTLV-1-Proteinen abgeleitetes Antigen kodiert	Behandlung der adulten T-Zell-Leukämie/Lymphome

¹ At the time of designation

Language	Active ingredient	Indication
Greek	Λεντιικός φορέας ψευδοτυπωμένος με την πρωτεΐνη G του ιού της φυσαλιδώδους στοματίτιδας του οροτύπου της Ιντιάνα που κωδικοποιεί αντιγόνο προερχόμενο από τις πρωτεΐνες Tax, HBZ, p12I και p30II του HTLV-1	Θεραπεία της T-λευχαιμίας/λεμφώματος των ενηλίκων
Hungarian	A Tax, HBZ, p12I és p30II HTLV-1 fehérjékből származó antigént kódoló vesicularis stomatitis vírus G fehérje Indiana szerotípusa által pszeidotipizált lentivirális vektor	Felnőtt T-sejtleukémia/limfómakezelése
Italian	Un vettore lentivirale pseudotipizzato con il sierotipo Indiana della proteina G del virus della stomatite vescicolare, che codifica per un antigene derivato dalle proteine Tax, HBZ, p12I e p30II di HTLV-1	Trattamento della leucemia/linfoma a cellule T dell'adulto.
Latvian	Lentivīrusa vektors, kas pseidotipēts ar vezikulārā stomatīta vīrusa <i>Indiana</i> serotipa proteīnu G, kas kodē no Tax, HBZ, p12I un p30II HTLV-1 proteīniem atvasinātu antigēnu	Pieaugušo T šūnu leikēmijas/limfomas ārstēšana
Lithuanian	Lentivirusinis vektorius, sukurtas naudojant vezikulinio stomatito Indiana serotipo viruso baltymą G ir koduojantis antigeną, išskirtą iš Tax, HBZ, p12I ir p30II HTLV-1 baltymų	Suaugusiųjų T-ląstelių leukemijos / limfomos gydymas
Maltese	Vekter lentivirali psewdotipat bis-serotip Indiana tal-proteina G tal-virus tal-istomatite vesikulari li tikkodifika antigen imnissel mill-proteini Tax, HBZ, p12I u p30II ta' HTLV-1	Kura ta' lewkimja/limfoma tač-ċelloli T tal-adult
Polish	Wektor lentiwirusowy pseudotypowany serotypem Indiana białka G wirusa pęcherzykowego zapalenia jamy ustnej, kodujący antygen uzyskany z białek Tax, HBZ, p12I i p30II HTLV-1	Leczenie chłoniaka/białaczki T-komórkowej dorosłych (ATLL)
Portuguese	Vetor lentiviral pseudotipificado pelo serotipo Indiana da proteína G do vírus da estomatite vesicular codificando um antígeno derivado das proteínas Tax, HBZ, p12I e p30II HTLV-1	Tratamento de leucémia/linfoma de células T do adulto
Romanian	Un vector lentiviral pseudotipat de serotipul Indiana al proteinei G a virusului stomatitei veziculare care codifică un antigen derivat din proteinele Tax, HBZ, p12I și p30II HTLV-1	Tratamentul leucemiei/limfomului cu celule T adulte
Slovak	Lentivírusový vektor pseudotypizovaný bielkovinou G vírusu vezikulárnej stomatitídy sérotypu Indiana kódujúci antigén odvodený od proteínov tax, HBZ, p12I a p30II vírusu HTLV-1	Liečba T-bunkovej leukémie dospelého veku/T-bunkového lymfómu dospelého veku.
Slovenian	Lentivirusni vektor, psevdotipiziran s proteinom G virusa vezikularnega stomatitisa (serotip Indiana), ki kodira antigen, pridobljen iz proteinov Tax, HBZ, p12I in p30II HTLV-1	Zdravljenje T-celične levkemije/limfoma pri odraslih

Language	Active ingredient	Indication
Spanish	Un vector lentiviral pseudotipado por el serotipo Indiana de la proteína G del virus de la estomatitis vesicular que codifica un antígeno derivado de las proteínas HTLV-1 Tax, HBZ, p12I y p30II.	Tratamiento de la leucemia-linfoma de células T en adultos
Swedish	En lentivirusvektor pseudotypade av Indiana serotypen av vesikulär stomatit virus G-proteinet som kodar för ett antigen från Tax, HBZ, p12I och p30II HTLV-1-proteiner	Behandling av vuxna T-cellsleukemi/lymfom
Norwegian	En lentiviral vektor pseudotypet av Indianaserotypen av vesikulært stomatittvirus G-protein og som koder for et antigen derivert fra Tax, p12I og p30II HTLV-1-proteiner	Behandling av adult T-celleleukemi/lymfom
Icelandic	Hæggeng veirugenaferja byggð á G-próteinum Indiana sermigerðar munnblöðrubólguveiru splæst saman við ónæmisvaka úr próteinum í Tax, HBZ, p12I og p30II HTLV-1	Meðferð á fullþroska T-frumu hvítblæði/eitlakraðbameini