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 human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) for the treatment of renal cell carcinoma

On 27 October 2006, orphan designation (EU/3/06/417) was granted by the European Commission to Immunservice GmbH, Germany, for human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) for the treatment of renal cell carcinoma.

What is renal cell carcinoma?

Renal cell carcinoma (also called cancer of the kidney or renal adenocarcinoma) is a disease in which cancer (malignant) cells are found in certain tissues of the kidney. Inside each kidney, there are tiny tubules that filter and clean the blood, taking out waste products, and making urine. Renal cell carcinoma is a cancer of the lining of the tubules in the kidney. Renal cell carcinoma accounts for approximately 85% of all kidney cancers. Signs of cancer are difficult to detect in early stages of the disease, and about half of the patients are diagnosed when the disease has spread around the kidney or to distant parts of the body. Renal cell carcinoma is life-threatening.

What are the methods of treatment available?

There are treatments for most patients with renal cell cancer. These may include surgery (taking out the cancer in an operation), chemotherapy (using drugs to kill cancer cells), radiation therapy (using high-dose x-rays or other high-energy rays to kill cancer cells), hormone therapy (using hormones to stop cancer cells from growing), and biological therapy (using the body's immune system to fight cancer). The primary therapies for advanced cancer are biologic agents, such as interleukin-2 and interferon-α. Other anticancer agents were also authorised in the Community for treatment of renal cell carcinoma at the time of submission of the application for orphan designation.
Satisfactory argumentation has been submitted by the sponsor to justify the assumption that human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) might be of potential significant benefit for the treatment of renal cell carcinoma. This could represent an additional treatment option for patients with renal cell carcinoma, when cancer cells have spread to the lungs. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, renal cell carcinoma was considered to affect approximately 3.5 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 161,000 persons.

How is this medicinal product expected to act?

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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Human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) belongs to a group of small proteins, the so-called cytokines. It is released by particular cells and has specific effects on cell-cell interaction. It also influences the behaviour of cells by binding to a specific receptor (proteins found on the surface of the cell, on which only a specific protein can bind in order to activate certain biologic reactions of that cell). Certain types of white blood cells, such as lymphocytes, carry this specific interleukin 2 receptor on their surface. These types of white blood cells seem to play a role in the control and destruction of cancer cells as part of the body's defence mechanism (immune system). By binding to these cells, it is thought that interleukin-2 may help the body's immune system to kill the cancer cells. Thus, human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) given by inhalation may be able to activate the patient's immune system against renal cell carcinoma cells that have spread to the lung.

What is the stage of development of this medicinal product?
The effects of human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with renal cell carcinoma were completed.

Human interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use) was not authorised anywhere worldwide for renal cell carcinoma or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 4 October 2006 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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

Language	Active Ingredient	Indication
English	Human Interleukin-2 (glycosylated tetrasaccharide, glycosylated trisaccharide and non-glycosylated) (inhalation use)	Treatment of renal cell carcinoma
Czech	Humánní interleukin-2 (glykosylovaný tetrasacharidem, glykosylovaný trisacharidem a neglykosylovaný) (inhalační podání)	Léčba karcinomu ledvin
Danish	Human interleukin-2 (glykosyleret tetrasaccharid, glykosyleret trisaccharid og ikke-glykosyleret) (til inhalation)	Behandling af renalcellekarcinom
Dutch	Humaan interleukine-2 (geglycosyleerd tetrasaccharide, geglycosyleerd trisaccharide en niet-geglycosyleerd) (inhalatie gebruik)	Behandeling van niercelcarcinoom
Estonian	Humaaninterleukiin-2 (glükosüülitud tetrasahhariid, glükosüülitud tetrasahhariid, glükosüülimata) (inhalatsioon)	Neeru vähi-ravi
Finnish	Ihmisinterleukiini-2 (glykosyloitunut tetrasakkaridi, glykosyloitunut trisakkaridi ja glykosyloitumaton) (inhalaatioon)	Munuaiskarsinooman hoito
French	Interleukine 2 humaine (tétrasaccharide glycosylé, trisaccharide glycosylé et non glycosylé) (voie inhalée)	Traitement du carcinome rénal
German	Humanes Interleukin-2 (glykosyliertes Tetrasaccharid, glykosyliertes Trisaccharid und nicht-glykosyliert) (zur Inhalation)	Behandlung des Nierenzellkarzinoms
Greek	ανθρώπινη ιντερλευκίνη-2 (γλυκοσυλιωμένος τετρασακχαρίτης, γλυκοσυλιωμένος τρισακχαρίτης και μη γλυκοσυλιωμένος) (Χρήση δια εισπνοής)	Θεραπεία του νεφροκυτταρικού καρκινώματος
Hungarian	Humán interleukin-2 (glikozilált tetraszacharid, glikozilált triszacharid és nem-glikozilált) (inhalációra)	Vesekarcinoma kezelése
Italian	Interleuchina-2 umana (tetrasaccaride glicosilato trisaccaride glicosilato, e non glicosilata) (per uso inalatorio)	Trattamento del carcinoma renale
Latvian	Cilvēka interleikīns-2 (glikozilēts tetrasaharīds, glikozilēts trisaharīds un neglikozilēts) (inhalācijām)	Nieru karcinomas ārstēšana
Lithuanian	Žmogaus interleukinas-2 (glikozilintas tetrasacharidas, glikozilintas trisacharidas ir neglikozilintas) (inhaliuoti)	Inkstų adenokarcinomos gydymas

Polish	Ludzka, Interleukina-2 Ludzka interleukina-2 (glikozylowany tetrasacharyd, glikozylowany trisacharyd oraz nieglikozylowana) (podanie wziewne)	Leczenie raka nerki
Portuguese	Interleucina-2 humana (tetrassacarídeos glicosilados, trissacarídeos glicosilados e não glicosilados) (via inalatoria)	Tratamento do carcinoma das células renais
Slovak	Ľudský interleukín-2 (glykozylovaný tetrasacharid, glykozylovaný trisacharid a neglykozylovaný) (inhalačné použitie)	Liečba karcinómu obličky
Slovenian	Humani interlevkin-2 (glikoziliran tetrasaharid, glikoziliran trisaharid in neglikoziliran) (za inhaliranje)	zdravljenje raka ledvičnih celic
Spanish	Interleucina-2 humana (tetrasacárido glucosilado, trisacárido glucosilado y no glucosilado) (vía inhalatoria)	Tratamiento del carcinoma de células renales
Swedish	Humant interleukin-2 (glykosylerad tetrasackarid, glykosylerad trisackarid och icke-glykosylerad) (användning för inhalation)	Behandling av njurcellscancer
Norwegian	Humant interleukin-2 (glykosylert tetrasakkarid, glykosylert trisakkararid og ikke-glykosylert) (bruk til inhalasjon)	Behandling av nyrecellekarsinom
Icelandic	Interleukin-2 manna (glýkósílerað tetrasakkaríð, glýkósílerað þrísakkaríð og óglýkósílerað) (til innöndunar)	Meðferð á nýrnafrumukrabbameini