



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

Document Date: London, 4 January 2006
Doc.Ref.: EMEA/COMP/216828/2005

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF autologous tumor-derived gp96 heat shock protein-peptide complex for the treatment of renal cell carcinoma

On 11 April 2005, orphan designation (EU/3/05/270) was granted by the European Commission to Antigenics Therapeutics Limited, Ireland, for autologous tumor-derived gp96 heat shock protein-peptide complex 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 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-alpha. Other anticancer agents had also been 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 autologous tumor-derived gp96 heat shock protein-peptide complex might be of potential significant benefit for the treatment of renal cell carcinoma because it might act in a different way than other available medicines, and thereby it might improve the long-term outcome of the patients. 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*?

According to the information provided by the sponsor, renal cell carcinoma was considered to affect about 156,000 in the European Union.

How is this medicinal product expected to act?

Autologous tumor-derived gp96 heat shock protein-peptide complex is a type of vaccine made from the so-called gp96 heat shock protein, of the tumour cells from the patient him/herself (autologous). Heat shock proteins are molecules that are triggered by various factors such as stress and cancer genes. Once extracted from the patient it is given back to the patient, whose body's defense system (immune system) will now recognize this protein as a foreign body. Since part of this vaccine is similar to parts

of the protein on the cancer cells, it is expected that the immune system will not only recognize the vaccine as foreign but also the cancer cells. Cells of the immune system could then kill the cancer cells.

What is the stage of development of this medicinal product?

The effects of autologous tumor-derived gp96 heat shock protein-peptide complex 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 ongoing.

Autologous tumor-derived gp96 heat shock protein-peptide complex was not authorised anywhere worldwide for renal cell carcinoma, at the time of submission. Orphan designation of autologous tumor-derived gp96 heat shock protein-peptide complex was granted in the United States for treatment of renal cell carcinoma.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 3 March 2005 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.

For more information:

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

Language	Active Ingredient	Indication
English	Autologous Tumor-Derived gp96 Heat Shock Protein-Peptide Complex	Treatment of renal cell carcinoma
Czech	Autologní, z tumoru derivovaný gp96 komplex peptidů a proteinů teplotního šoku	Léčba karcinomu ledvinných buněk
Danish	Autogent tumoraflødt gp96 varmekok-protein-peptidkomplex	Behandling af renalcellekarcinom
Dutch	Autoloog tumoreus afgeleid gp96 hittestok-proteïne – peptidecomplex	Behandeling van niercelcarcinoom
Estonian	Autoloogiline kasvaja tuletatud gp96 kuumashoki valgu-peptiidi kompleks	Neeru vähi ravi
Finnish	Autologinen, kasvainperäinen, gp96- lämpöshokkiproteiini-peptidi-kompleksi	Munuaiskarsinooman hoito
French	Complexe de protéine-peptide de choc thermique gp96, dérivé de cellules tumorales autologues	Traitement du carcinome rénal
German	Autologer, aus Tumorzellen gewonnener gp96 Hitzeschock-Protein-Peptidkomplex	Behandlung des Nierenzellkarzinoms
Greek	Αυτόλογο πρωτεϊνικό-πεπτιδικό σύμπλεγμα θερμικού πλήγματος gp96, προερχόμενο από νεόπλασμα	Θεραπεία του καρκινώματος νεφρών
Hungarian	Autológ tumor-eredetű gp96 hőshock fehérje-peptid komplex	Vese carcinoma kezelése
Italian	Complesso proteina gp96-peptide da shock termico derivato da tumore autologo	Trattamento del carcinoma renale
Latvian	Autologs, no audzēja atvasināts gp96 karstumšoka olbaltumvielu-peptīdu komplekss	Nieru karcinomas ārstēšana
Lithuanian	Autologinis navikinės kilmės gp96 šiluminio streso baltymų ir peptidų kompleksas	Inkstų adenokarcinomos gydymas
Polish	Otrzymywany z tkanki nowotworowej autologiczny kompleks polipeptydów gp96 białek szoku cieplnego	Leczenie raka nerki

Portuguese	Complexo de proteínas/péptidos gp96 obtido por choque térmico, derivado de tumor autólogo	Tratamento do carcinoma das células renais
Slovak	Autologový, z tumoru získaný gp96 komplex peptidov a proteínov teplotného šoku	Liečba karcinómu obličky
Slovenian	Avtologni, iz tumorskih celic s toplotnim šokom pridobljen gp96 proteinsko-peptidni kompleks	zdravljenje raka ledvičnih celic
Spanish	Complejo péptido- proteína gp96 del shock térmico derivado de tumor autólogo	Tratamiento de carcinoma de células renales
Swedish	Autologt tumörderiverat gp96 värmechock protein-peptidkomplex	Behandling av njurcellscancer
Norwegian	Autologt tumor-derivert gp96-varmesjokkprotein-peptidkompleks	Behandling av nyrecellekarsinom
Icelandic	Samkynja gp96 hitalostmyndað prótínpeptíð samband úr æxli	Meðferð á nýrnafrumukrabbameini