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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 adenoviral vector containing human p53 gene for the treatment of Li-Fraumeni syndrome

On 23 October 2006, orphan designation (EU/3/06/404) was granted by the European Commission to Gendux AB, Sweden, for adenoviral vector containing human p53 gene for the treatment of Li-Fraumeni syndrome.
The sponsorship was transferred to Gendux Molecular Limited, Ireland, in December 2007.

What is Li-Fraumeni syndrome?
Patients affected by Li-Fraumeni syndrome have a hereditary disorder that increases their risk for several cancer types with early life onset. Cancer types that are common in patients with Li-Fraumeni syndrome include osteosarcoma (cancers of the skeleton and bones), breast cancer, brain cancer, adrenocortical cancer (cancer of the adrenal glands) and leukaemia (cancer of the white blood cells). The syndrome is caused by a defect in a gene that regulates the protein p53. This protein is very important for cells' natural ability to recognise when they have been damaged. When cells lack this ability or this ability is decreased, the risk of cells starting to divide and grow uncontrollably and develop tumours increases by many folds. Li-Fraumeni syndrome is chronically debilitating and life-threatening because of the high risk for affected patients to develop several cancer tumours at an early age.

What is the estimated number of patients affected by the condition?
At the time of designation Li-Fraumeni syndrome affected less than 0.05 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of less than 2,300 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 knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?
Cancer tumours in Li-Fraumeni syndrome patients are treated in the same way as cancer tumours in other patients. Treatment depends on many factors including the type of cancer, age, sex and how advanced the tumour is at diagnosis. Most treatments for the type of cancers occurring in Li-Fraumeni patients are chemotherapy (using drugs to kill cancer cells).
Satisfactory argumentation has been submitted by the sponsor to justify the assumption that adenoviral vector containing human p53 gene might be of potential significant benefit for the treatment of Li-Fraumeni syndrome, mainly because it has a new mechanism of action and may be used in combination with other treatments. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

[*]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 Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

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How is this medicine expected to work?
Adenoviral vector containing human p53 gene is a virus-like particle that is designed to deliver healthy copies of the defective p53 gene to the cancer cells. According to the sponsor, adenoviral vector containing human p53 gene will, by providing the tumour cells with p53, make them more susceptible to be destroyed by the damage that chemotherapy drugs cause.

What is the stage of development of this medicinal product?
The effects of adenoviral vector containing human p53 gene were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with Li-Fraumeni syndrome were ongoing.

Adenoviral vector containing human p53 gene was not authorised anywhere worldwide for the treatment of Li-Fraumeni syndrome, at the time of submission of the application for orphan drug designation. Orphan designation of adenoviral vector containing human p53 gene was granted in the United States for the treatment of head and neck cancer.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 6 September 2006 a positive opinion recommending the grant of the above-mentioned 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 Community) 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.

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

Language	Active Ingredient	Indication
English	Adenoviral vector containing human p53 gene	Treatment of Li Fraumeni Syndrome
Czech	Adenovirový vektor obsahující humánní gen p53	Léčba syndromu Li Fraumeni
Danish	Adenoviral vektor med humant p53-gen	Behandling af Li Fraumenis syndrom
Dutch	Adenovirale vector bevattend het humaan p53 gen	Behandeling van Li Fraumeni syndroom
Estonian	Inimese p53 geeni sisaldav adenoviiruse vektor	Li Fraumeni sündroomi ravi
Finnish	Adenovirusvektori, joka sisältää ihmisen p53-geenin	Li Fraumeni -oireyhtymän hoito
French	Vecteur adénoviral porteur du gène humain p53	Traitement du syndrome de Li Fraumeni
German	Adenoviraler Vektor, der das humane p53-Gen trägt	Behandlung des Li Fraumeni-Syndroms
Greek	Αδενοϊικός φορέας που περιέχει το ανθρώπινο γονίδιο p53	Θεραπεία του συνδρόμου Li Fraumeni
Hungarian	Humán p53 gént tartalmazó adenovírus vektor	Li Fraumeni szindróma kezelése
Italian	Vettore adenovirale contenente il gene p53 umano	Trattamento della sindrome di Li Fraumeni
Latvian	Adenovīrusa vektors, kas satur cilvēka p53 gēnu	Li Fraumeni sindroma ārstēšana
Lithuanian	Adenovirusinis vektorius, pernešantis žmogaus p53 geną	Li Fraumeni sindromo gydymas
Polish	Wektor adenowirusowy zawierający ludzki gen p53	Leczenie zespołu Li Fraumeni
Portuguese	Vector adenoviral contendo gene p53 humano	Tratamento do síndrome de Li Fraumeni
Slovak	Adenovírusový vektor obsahujúci ľudský gén p53	Liečba Li Fraumeniho syndrómu
Slovenian	Adenovirusni vektor, ki vsebuje človeški gen p53	Zdravljenje sindroma Li Fraumeni
Spanish	Vector adenovírico portador del gen humano p53	Tratamiento del síndrome de Li Fraumeni
Swedish	Adenovirusvektor som innehåller mänsklig p53-gen	Behandling av Li Fraumeni-syndrom
Norwegian	Adenovirusvektor med humant p53 gen	Behandling av Li Fraumeni-syndrom
Icelandic	Adenoveiru ferja sem inniheldur p53 erfðavísi manna	Meðferð á Li Fraumeni heilkenni