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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF enzastraurin hydrochloride for the treatment of diffuse large B cell lymphoma

On 20 March 2007, orphan designation (EU/3/07/442) was granted by the European Commission to Eli Lilly Nederland B.V., The Netherlands, for enzastraurin hydrochloride for the diffuse large B cell lymphoma.

What is diffuse large B cell lymphoma?

Diffuse large B-cell lymphoma (DLBCL) is the most common cancer of the lymphatic system. The lymphatic system is part of the body's immune system and helps fight infections. It is a complex system made up of organs such as bone marrow, thymus (a gland behind the breast bone), spleen (an organ in the abdomen near the stomach), and the lymph nodes (or lymph glands, located throughout the body), which are connected by a network of tiny lymphatic vessels. In addition, there are isolated lymphatic cells in most tissues of the body, including the skin. The main cells of the lymphatic system are the lymphocytes that belong to the group of white blood cells. There are two main types of lymphocytes: B-lymphocytes (B cells) and T-lymphocytes (T cells). DLBCL is characterised by uncontrolled growth of the B-lymphocytes and mainly affects the lymph nodes. DLBCL is life-threatening.

What are the methods of treatment available?

At the time of submission of the application for orphan drug designation, treatments included medicines such as cytotoxic agents (medicines that kill cells). One monoclonal antibody was authorised for the treatment of DLBCL within the Community at the time of submission of the application for orphan drug designation.

Enzastraurin hydrochloride might be of potential significant benefit for the treatment of DLBCL because 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*?

Based on the information provided by the sponsor and previous knowledge of the Committee, DLBCL was considered to affect less than 2 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 100,000 persons.

How is this medicinal product expected to act?

Cancer cells need to produce a network of new blood vessels in order to grow. Enzastraurin hydrochloride blocks (inhibits) the function of certain proteins such as protein kinases that are involved in cell growth and multiplication and in the progression of some types of cancer, including DLBCL. The theory is that enzastraurin hydrochloride, through its interference with the function of

*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 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

these proteins, will prevent the DLBCL from growing by preventing tumour cell replication and development of new blood vessels.

What is the stage of development of this medicinal product?

The evaluation of the effects of enzastaurin hydrochloride in experimental models is ongoing.

At the time of submission of the application for orphan designation, clinical trials in patients with DLBCL were ongoing.

Enzastaurin hydrochloride was not authorised anywhere worldwide for DLBCL 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 7 February 2007 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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**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Enzastaurin hydrochloride	Treatment of diffuse large B cell lymphoma
Bulgarian	Ензастауринов хидрохлорид	Лечение на дифузен В-едроклетъчен лимфом
Czech	Hydrochlorid enzastaurinum	Léčba velkobuněčného difuzního B-lymfomu.
Danish	Enzastaurin hydrochlorid	Behandling af diffust storcellet B-celle lymfom
Dutch	Enzastaurine hydrochloride	Behandeling van diffuus grootcellig B-cel-lymfoom.
Estonian	Entsastauriinhüdrokloriid	Diffuusse suure β-rakulise lümfoomi ravi
Finnish	Entsastauriinin hydrokloridi	Diffuusin suurisoluisen B-solulymfooman hoito
French	Chlorhydrate d' enzastaurine	Traitement du lymphome diffus à grandes cellules B
German	Enzastaurinhydrochlorid	Behandlung von diffusem großzelligem B-Zell-Lymphom
Greek	Ενζασταυρίνη υδροχλωρική	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)..
Hungarian	Enzastaurin hidroklorid	Diffúz nagy B-sejtes lymphoma kezelése
Italian	Enzastaurina cloridrato	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	Enzastaurīns hidrohlorīds	Difūzas lielo B šūnu limfomas ārstēšana
Lithuanian	Enzastaurinas hidrochloridas	Difuzinės stambių B ląstelių limfomos gydymas
Polish	Enzastauryny chlorowodorek	leczenie rozlanego chłoniaka z dużych limfocytów B.
Portuguese	Cloridrato de enzastaurina	Tratamento do linfoma difuso de grandes células B.
Romanian	Clorhidrat de enzastaurină	Tratamentul limfomului difuz cu celule B mari
Slovak	Enzastaurin hydrochlorid	Liečba difúzneho veľkobunkového lymfómu z B-buniek
Slovenian	Enzastaurin hidroklorid	Zdravljenje razširjenega limfoma velikih B celic
Spanish	Clorhidrato de enzastaurina	Tratamiento del linfoma difuso de células B grandes
Swedish	Enzastaurin hydroklorid	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	Enzastaurinhydroklorid	Behandling av diffust storcellet B-celle lymfom..
Icelandic	Enzastaurin hýdróklóríð	. Til meðferðar á stórfrumu B frumu eitlakraðbameini