



Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of anagrelide hydrochloride for the treatment of essential thrombocythaemia

On 29 December 2000, orphan designation (EU/3/00/010) was granted by the European Commission to Shire Pharmaceutical Development Ltd, United Kingdom, for anagrelide hydrochloride for the treatment of essential thrombocythaemia.

The sponsorship was transferred to Shire Pharmaceuticals Contracts Ltd, United Kingdom, in December 2001.

What is essential thrombocythaemia?

Thrombocytes (also called platelets) are small cell fragments that circulate in the blood and are important in the blood clotting process. Essential thrombocythaemia is a blood disorder characterised by elevated levels of platelets in the blood. This can be caused by either an increased production of platelets in the bone marrow or by decreased clearance of platelets in the spleen. Symptoms include headaches, dizziness, tinnitus, visual disturbances and leg pain. More serious symptoms or the so-called major events include cerebral, myocardial, and peripheral thromboses (blood clots in the brain, heart, arms or legs) and haemorrhages (bleedings). Essential thrombocythaemia can be chronically debilitating and it is life threatening.

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

At the time of designation essential thrombocythaemia affected not more than 2 to 3 in 10,000 people in the European Union (EU)*. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around about 75,000 - 113,000 people.

What treatments are available?

The condition is treated with general anti-coagulants (drugs that reduce the ability of the blood to form clots). Also, drugs that target cells that divide rapidly, such as the cells that produce platelets are commonly used. Patients can also be treated with plateletpheresis which is a way to filter platelets from the blood in order to reduce the abnormally high numbers of platelets.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that anagrelide hydrochloride might be of potential significant benefit for the treatment of essential thrombocythaemia mainly because it might cause less side-effects than current 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 based on data from the European Union. This represents a population of 377,000,000 (Eurostat 2001).

How is this medicine expected to work?

Anagrelide hydrochloride inhibits the activity of cells called megakaryocytes which produce platelets in the bone marrow. The exact mechanism of action is not understood.

What is the stage of development of this medicine?

The effects of anagrelide hydrochloride were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with essential thrombocythaemia were completed.

At the time of submission of the application for orphan drug designation, anagrelide hydrochloride was authorised in several countries worldwide for the treatment of essential thrombocythaemia and related diseases. Orphan designation of the anagrelide hydrochloride was granted in the United States for this condition.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 27 October 2000 a positive opinion recommending the grant of the above-mentioned designation.

Update: anagrelide hydrochloride (Xagrid) has been authorised in the EU since 16 November 2004 for the reduction of elevated platelet counts in at risk essential thrombocythaemia (ET) patients who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.

An at risk patient

An at risk essential thrombocythaemia patient is defined by one or more of the following features:

>60 years of age or

A platelet count $>1000 \times 10^9/l$ or

A history of thrombo-haemorrhagic events.

For more information: www.emea.europa.eu/htms/human/epar/a.htm

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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a 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	Anagrelide Hydrochloride	Treatment of essential thrombocythaemia.
Danish	Anagrelidhydrochlorid	Behandling af essentiel thrombocythaemia
Dutch	Anagrelidehydrochloride	Behandeling van essentiële trombocytemie.
Finnish	Anagrelidihydrokloridi	Essentiaalisen trombosytämian hoito
French	Chlorhydrate d'anagrelide	Traitement de la thrombocytémie essentielle
German	Anagrelidhydrochlorid	Behandlung von essentieller Thrombozythämie
Greek	Αναγκρελίδη Υδροχλωρική	Θεραπεία της θρομβοκυτταραιμίας
Italian	Anagrelide Cloridrato	Trattamento della trombocitemia essenziale.
Portuguese	Cloridrato de anagrelida	Tratamento de trombocitemia essencial
Spanish	Clorhidrato de anagrelida	Tratamiento de la trombocitemia esencial.
Swedish	Anagrelidhydroklorid	Behandling av essentiell trombocytemi.