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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Carboxypeptidase G_2 for the adjunctive treatment in patients at risk of methotrexate toxicity

First publication	17 February 2003
Rev.1: transfer of sponsorship	12 December 2005
Rev.2: sponsor's name and address change	24 April 2015

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 3 February 2003, orphan designation (EU/3/02/128) was granted by the European Commission to Enact Pharma plc, United Kingdom, for carboxypeptidase G_2 for the adjunctive treatment in patients at risk of methotrexate toxicity.

The sponsorship was transferred to Protherics PLC, United Kingdom, in December 2004.

What is methotrexate toxicity?

Cancer occurs when cells grow too rapidly and in an uncontrolled way. For cancer cells to grow, new DNA needs to be made. Methotrexate is a drug that is used to treat certain cancers. With methotrexate, cancer cells can no longer make DNA. This kills cancer cells. However, methotrexate can also be harmful to other normal cells and organs in the body. This harmful effect is called methotrexate toxicity. The longer methotrexate stays in the body, the higher the risk of toxicity. Kidneys are organs in the body that filter waste matters from the blood and produce urine. Methotrexate is normally filtered by the kidney. However, if the kidney is damaged, then methotrexate may concentrate in the blood and in the whole body. This leads to further general toxicity, and further damage to the kidney, in a vicious cycle. Methotrexate toxicity is a life-threatening condition.

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

At the time of designation, methotrexate toxicity affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 11,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

There are already methods of treatment available for methotrexate toxicity. The drug folinic acid is one of these. Folinic acid has been authorised in the Community for the treatment of the condition. Many patients improve with the available treatments. However, these are not sufficient for some patients. In that case, complex medical procedures, called haemodialysis, become necessary. These very heavy procedures aim to filter methotrexate from the blood. Carboxypeptidase G_2 might be an additional treatment in patients at risk of methotrexate toxicity. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that carboxypeptidase G_2 might be of potential significant benefit for the adjunctive treatment in patients at risk of methotrexate toxicity, particularly based on the novel mechanism of action. The assumption of benefit is yet to be validated and the benefit of carboxypeptidase G_2 will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Carboxypeptidase G_2 is a protein that can transform methotrexate into harmless substances. Thus, the amount of methotrexate in blood is lowered, and the risk of toxicity is reduced.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, clinical trials in patients at risk of methotrexate toxicity were ongoing.

Carboxipeptidase G_2 was not marketed anywhere worldwide for methotrexate toxicity or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 December 2002 recommending the granting of this designation.

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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 EU) or insufficient returns on investment.

*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.
At the time of designation, this represented a population of 382,800,000 (Eurostat 2003).

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.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Carboxypeptidase G_2	Adjunctive treatment in patients at risk of methotrexate toxicity.
Czech	Carboxypeptidasa G2	Podpůrná léčba u nemocných s rizikem vzniku methotrexátové toxicity
Danish	Carboxypeptidase G_2	Supplementær behandling til patienter med risiko for methotrexattoksicitet
Dutch	Carboxypeptidase G_2	Adjuvans behandeling bij patiënten met methotrexaattoxiciteit risico .
Estonian	Karboksüpeptidaas G_2	Metotreksaadi toksilisusest tingitud kõrgenenud riskiga patsientide täiendav ravi.
Finnish	Karboksipeptidaasi G_2	Lisähoidoksi potilaille, joilla on uhkaava metotreksaattimyrkytys
French	Carboxypeptidase G_2	Traitement adjuvant chez les patients exposés au risque de toxicité au méthotrexate
German	Carboxypeptidase G_2	Ergänzende Behandlung der bei Patienten unter Risiko von Methotrexattoxizität
Greek	Καρβοξυπεπτιδάση G_2	Επικουρική θεραπεία για ασθενείς σε κίνδυνο τοξικότητας από μεθοτρεξάτη.
Hungarian	Karboxipeptidáz G_2	Methotrexat kezelés veszélyének kitett betegek adjuváns kezelése
Italian	Carboxypeptidase G_2	Trattamento aggiuntivo in pazienti a rischio di tossicità da metotrexato
Latvian	Karboksipeptidāze G_2	Pacientu ar metotreksāta toksicitātes risku papildārstēšana
Lithuanian	Karboksipeptidazė G_2	Papildomas pacientų, kuriems yra metotreksato toksinio poveikio rizika, gydymas
Polish	Karboksypeptydaza G2	Leczenie wspomagające u pacjentów ze zwiększonym zagrożeniem toksycznością metotreksatu
Portuguese	Carboxipeptidase G_2	Tratamento adjuvante de doentes em risco de toxicidade pelo metotrexato.
Slovak	Karboxypeptidáza G_2	Adjuvantná terapia u pacientov s rizikom metotrexátovej toxicity
Slovenian	Karboksipeptidaza G_2	Dodatno zdravljenje bolnikov z zvečanim tveganjem toksičnosti metotreksata
Spanish	Carboxipeptidasa G_2	Tratamiento adyuvante en pacientes con riesgo de sufrir toxicidad por metotrexato.
Swedish	Karboxipeptidas G_2	Komplement behandling till patienter med risk för metotrexattoxicitet

[1] At the time of transfer of sponsorship