30 January 2015
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

4-(3,5-bis-(hydroxy-phenyl)-1,2,4) triazol-1-yl)-benzoic acid for the treatment of chronic iron overload requiring chelation therapy

First publication	6 January 2003
Rev.1: administrative update	8 January 2003
Rev.2: information about Marketing Authorisation	28 February 2007
Rev.3: sponsor's change of address	30 January 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 13 March 2002, orphan designation (EU/3/02/092) was granted by the European Commission to Novartis Europharm Limited, United Kingdom, for 4-(3,5-bis-(hydroxy-phenyl)-1,2,4)triazol-1-yl)-benzoic acid (proposed non proprietary name: deferasirox) for the treatment of chronic iron overload requiring chelation therapy.

What is chronic iron overload requiring chelation therapy?

Chronic iron overload is a condition due to man's inability to actively eliminate iron from the body. Chronic iron accumulation is mainly consecutive to either excess intestinal absorption (hemochromatosis) or excess administration through repetitive transfusions (iron contained in red blood cells). Repeated transfusions can be necessary in patients presenting chronic anaemias (e.g. thalassemia, sickle cell anaemia).

Chronic iron overload is a serious condition. Complications are related to iron deposits in tissues which can induce organ failure. This condition is life-threatening when the heart or the liver is affected.

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

At the time of designation, chronic iron overload requiring chelation therapy affected approximately 2.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000

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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?

Phlebotomy (blood removal by venipuncture) is the first-choice therapy for haemochromatosis, except when blood removal is impossible. For such patients, or for patients with transfusion-dependent anaemias, iron overload can be treated by administration of iron chelators.Two medicinal products which chelate iron had been authorised in the Community at the time of submission of the application for orphan designation. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that deferasirox might be of potential significant benefit for the treatment of chronic iron overload, particularly in terms of its pharmacological properties.

How is this medicine expected to work?

Deferasirox is an iron chelator. Iron chelators are molecules binding to iron in the body, allowing it to then be eliminated through urinary or intestinal routes at a higher rate than the natural very low iron elimination rate (through shedding of skin and mucosal cells, menstruation or other blood loss).

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, clinical trials were ongoing in patients presenting iron overload after repeated transfusions for chronic anaemias.

Deferasirox had not been marketed anywhere worldwide or designated as an 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 23 January 2002 recommending the granting of this designation.

Update: 4-(3,5-Bis(hdroxy-phenyl)-1,2,4) triazol-1-yl) benzoic acid (Exjade) has been authorised in the EU since 28 August 2006 for treatment of chronic iron overload due to frequent blood transfusions (>/= 7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older.

Treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups:

- in patients with other anaemias,
- in patients aged 2 to 5 years,
- in patients with beta thalassaemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells).

*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 380,600,000 (Eurostat 2002).

More information on Exjade can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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.

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	4-(3,5-bis-(hydroxy-phenyl)-1,2,4) triazol-1-yl)-benzoic acid	Treatment of chronic iron overload requiring chelation therapy
Danish	4-(3,5-bis-(hydroxy-phenyl)-1,2,4)triazol-1-yl)benzoe syre	Behandling af kronisk jern overskud, der nødvendiggør chelat behandling
Dutch	4-(3,5- Bis-(hydroxy-fenyl)-1,2,4) triazol-1-yl)-benzoëzuur	Behandeling van chronische ijzerstapeling welke chelatie therapie vergt
Finnish	4-(3,5-Bis-(hydroksifenyyli)-1,2,4) triatsoli-1-yyli)-bentsoehappo	Kroonisen, kelatointihoitoa vaativan raudan liikavarastoitumisen hoito
French	acide 4-(3,5-bis-(hydroxy-phenyl)-1,2,4) triazol-1-yl)-benzoique	Traitement de la surcharge férique chronique nécessitant un traitement chélateur
German	4-(3,5-Bis-(hydroxy-phenyl)-1,2,4) triazol-1-yl)-benzoesäure	Behandlung der Eisenüberladung welche Chelattherapie benötigt
Greek	4-(3,5-Δις-(υδροξυ-φαινύλ)-1,2,4) τριαζόλ-1-υλ)-βενζοϊκό οξύ	θεραπεία της χρόνιας υπερφόρτωσης σιδήρου με χηλικούς παράγοντες
Italian	Acido 4-[3,5-bis-(idrossifenil)-[1,2,4]-triazol-1-il] benzoico	Trattamento dell'accumulo cronico di ferro che necessita di terapia chelante
Portuguese	ácido 4-(3,5-bis-(fenil-hidroxi)-1,2,4) triazol-1-il)-benzóico	Tratamento da sobrecarga crónica de ferro que necessita uma terapia quelante
Spanish	Ácido 4-(3,5 bis-(hidroxi-fenil)-1,2,4)triazol-1-il) benzoico	Tratamiento de la sobrecarga crónica de hierro que necesita de terapia quelante.
Swedish	4-(3,5-bis-(hydroxi-fenyl)-1,2,4)-triazol-1-yl)-bensoesyra	Behandling av kronisk järnupplagring som kräver kelatterapi

[1] At the time of designation