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EMA/COMP/388/2004 Rev.4
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione for the treatment of multiple myeloma

On 12 December 2003, orphan designation (EU/3/03/177) was granted by the European Commission to Gregory Fryer Associates Ltd, United Kingdom, for 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione for the treatment of multiple myeloma.

The sponsorship was transferred to Celgene Europe Limited in July 2005.

What is multiple myeloma?

Multiple myeloma is a cancer of a type of white blood cell called a plasma cell. Plasma cells are found in the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally, the bone marrow makes cells called “blasts” that mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets. Red blood cells carry oxygen and other materials to all tissues of the body. Platelets make the blood clot, and white blood cells fight infection. In multiple myeloma an excessive number of plasma cells are produced. Normally, the division of cells takes place in a controlled manner but with multiple myeloma, the process gets out of control and abnormal plasma cells multiply, producing many myeloma cells. These fill up the bone marrow and interfere with production of the normal white cells, red cells and platelets. This leads to a number of possible complications, which include anaemia, bone pain and fractures, raised levels of calcium in the blood and kidney disease. Multiple myeloma is life-threatening.

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

At the time of designation, multiple myeloma affected approximately 1.3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 50,000 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).

*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 385,000,000 (Eurostat 2002) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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What treatments are available?

The main treatment of multiple myeloma is chemotherapy (using drugs to kill cancer cells) usually combined with steroids (a group of chemical substances, the so-called hormones, which have an effect on the activity of certain organs). Other types of treatment for multiple myeloma are radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) and immunotherapy (using drugs that stimulate the body's own immune system to kill cancer cells). Radiotherapy can be useful to treat painful areas and weakened bones. Several products were authorised for the condition in the Community at the time of submission of the application for orphan drug designation.

3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione could be of potential significant benefit for the treatment of multiple myeloma because it may act in a different way than other available medicines. This assumption 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?

Cancers need to produce a network of new blood vessels in order to grow. Without forming these blood vessels cancers cannot grow. The theory is that 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione will prevent the myeloma from growing by preventing the development of new blood vessels and possibly also reducing the supply of oxygen and nutrients to the cancer cells. 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione is probably also an immunomodulator, in other words it acts by inhibiting the cells from the defence system involved in the inflammation process. This might result in an effect on the tumour growth and survival of the tumour cells.

What is the stage of development of this medicine?

The effects of 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione were evaluated in experimental models.

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

3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione was not marketed anywhere worldwide for multiple myeloma, at the time of submission.

Orphan designation of 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione was granted in the United States for treatment of multiple myeloma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 November 2003 recommending the granting of this designation.

Update: 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione (Revlimid) has been authorised in the EU since 14 June 2007. Revlimid in combination with dexamethasone is indicated for the treatment of multiple myeloma patients who have received at least one prior therapy.

More information on Revlimid 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	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Treatment of multiple myeloma
Czech	3-(4'aminoisoindoline-1'-jedna)-1-piperidine-2,6-dione	Léčba mnohočetného myelomu
Danish	3-(4'aminoisoindolin-1'-1)-1-piperidin-2,6-dion	Behandling af multipelt myelom
Dutch	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Behandeling van multipel myeloom
Estonian	3-(4'aminoisoindoliin-1'-üks)-1-piperidiin-2,6-dioon	Multiibelse imüeloomi ravi
Finnish	3-(4'aminoisoindoliini-1'-oni)-1-piperidiini-2,6-dioni	Multippelin myelooman hoito
French	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Traitement du myélome multiple
German	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Behandlung des multiplen Myeloms
Greek	3-(4'-αμινο-ισοϊνδολινο-1-ονη)-πιπεριδινο-2,6-διόνη	Θεραπεία του πολλαπλού μυελώματος
Hungarian	3-(4'-aminoizoindolin-1'-on)-1-piperidin-2,6-dion	Myeloma multiplex kezelése
Italian	3-(4'amminoisoindoline-1'-one)-1-piperidina-2,6-dione	Trattamento del mieloma multiplo
Latvian	3-(4'aminoizoindolīn-1'-on)-1-piperidīn-2,6-dions	Multiplās mielomas ārstēšana
Lithuanian	3-(4' aminoizoindolino-1'-vienas)-1-piperidino-2,6-dionas	Dauginės mielomos gydymas
Polish	3-(4'aminoizoindolin-1'-on)-1-piperydyno-2,6-dion	Leczenie szpiczaka mnogiego
Portuguese	3-(4'aminoisoindolina-1'-ona)-1-piperidina-2,6-diona	Tratamento do mieloma múltiplo
Slovak	3-(4´aminoizoindolín-1´-ón)-1-piperidín-2,6-dión	Liečba mnohopočetného myelómu
Slovenian	3-(4'aminoizoindolin-1'on)-1-piperidin-2,6-dion	Zdravljenje multiplega mieloma
Spanish	3-(4'aminoisoindolina-1'-ona)-1-piperidina-2,6-diona	Tratamiento del mieloma múltiple
Swedish	3-(4'aminoisoindolin-1'-1)-1-piperidin-2,6-dion	Behandling av multipelt myelom

[1] At the time of transfer of sponsorship