EMA/COMP/81/2004 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 myelodysplastic syndromes

First publication	16 March 2005
Rev.1: transfer of sponsorship	13 October 2005
Rev.2: sponsor's change of address	29 July 2008
Rev.3 sponsor's change of address	20 June 2011
Rev.4 information about Marketing Authorisation	11 September 2013
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 8 March 2004, orphan designation (EU/3/04/192) was granted by the European Commission to Gregory Fryer Associates Limited, United Kingdom, for 3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione for the treatment of myelodysplastic syndromes.

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

What are myelodysplastic syndromes?

Myelodysplastic syndromes are a distinct group of disorders in which the production of blood cells by the bone marrow is abnormal. The bone marrow is the spongy tissue found in the large bones. It has the function of producing red cells (which are the main carriers of oxygen to body tissues), white blood cells (which fight infection), and platelets (which make the blood clot). In myelodysplastic syndromes these cells do not grow and maturate normally. Consequently several symptoms can develop: fatigue or weakness (due to anaemia, the red cells deficit), infections (due to decrease in white blood cells) or easy bruising or abnormal bleeding (platelets deficit). Myelodysplastic syndromes are life threatening because it can result in severe anaemia, infections or haemorrhages and it can progress to acute leukaemia.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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

At the time of designation, myelodysplastic syndromes affected between 1 and 3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 46,000 to 139,000 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?

At the time of submission of the application for the orphan drug designation there was no treatment authorised in the European Union. Available therapeutic options for myelodysplastic syndromes included supportive care methods (e.g. antibiotics to treat infections, blood or platelet transfusions for anaemia or bleeding respectively), the use of products such as erythropoietin (a substance that stimulates the bone marrow to produce red cells), chemotherapy (using drugs that can kill the abnormal cells), and bone-marrow transplantation.

How is this medicine expected to work?

3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione mechanism of action is quite complex and only partly understood.

This substance acts at different levels: by modulating the immune system activity, by stimulating the growth of red blood cells (thus reducing the anaemia), and by inhibiting the growth of new blood vessels.

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 myelodysplastic syndromes were ongoing.

The medicinal product was not marketed anywhere worldwide for myelodysplastic syndromes 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 5 February 2004 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 13 June 2013 for the treatment of patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.

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

*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 (EU 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 464,200,000 (Eurostat 2004)

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:

Celgene Europe Limited
1 Longwalk Road
Stockley Park
Uxbridge
Middlesex UB11 1DB
United Kingdom
Telephone: +44 208 831 83 00
Telefax: +44 208 831 83 01
E-mail: medinfo.uk.ire@celgene.com

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 myelodysplastic syndromes
Czech	3-(4'aminoisoindoline-1'-jedna)-1-piperidine-2,6-dione	Léčba myelodysplastického syndromu
Danish	3-(4'aminoisoindolin-1'-1)-1-piperidin-2,6-dion	Behandling af myelodysplastiske syndromer
Dutch	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Behandeling van myelodysplastische syndromen
Estonian	3-(4’aminoisoindoliin-1’-üks)-1-piperidiin-2,6-dioon	Müelodüsplastiliste sündroomide ravi
Finnish	3-(4'aminoisoindoliini-1'-oni)-1-piperidiini-2,6-dioni	Myelodysplastisten syndroomien hoito
French	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Traitement des syndromes myélodysplasiques
German	3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione	Behandlung der myelodysplastischen Syndrome
Greek	3-(4’-αμινο-ισοϊνδολινο-1-ονη)-πιπεριδινο-2,6-διόνη	Θεραπεία των μυελοδυσπλαστικών συνδρόμων
Hungarian	3-(4’-aminoizoindolin-1’-on)-1-piperidin-2,6-dion	Myelodysplasias syndromák kezelése
Italian	3-(4'amminoisoindoline-1'-one)-1-piperidina-2,6-dione	Trattamento delle sindromi mielodisplastiche
Latvian	3-(4’aminoizoindolīn-1’-on)-1-piperidīn-2,6-dions	Mielodisplastiskā sindroma ārstēšana
Lithuanian	3-(4’ aminoizoindolino-1’-vienas)-1-piperidino-2,6-dionas	Mielodisplastinių sindromų gydymas
Polish	3-(4’aminoizoindolin-1’-on)-1-piperydyno-2,6-dion	Leczenie zespołu mielodysplastycznego
Portuguese	3-(4'aminoisoindolina-1'-ona)-1-piperidina-2,6-diona	Tratamento dos síndromes mielodisplásticos
Slovak	3-(4´aminoizoindolín-1´-ón)-1-piperidín-2,6-dión	Liečba myelodysplastického syndrómu
Slovenian	3-(4’aminoizoindolin-1’on)-1-piperidin-2,6-dion	Zdravljenje mielodisplastičnega sindroma
Spanish	3-(4'aminoisoindolina-1'-ona)-1-piperidina-2,6-diona	Tratamiento de los síndromes mielodisplásicos
Swedish	3-(4'aminoisoindolin-1'-1)-1-piperidin-2,6-dion	Behandling av myelodysplastiska syndrom

[1] At the time of transfer of sponsorship