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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(1-Methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl) diamidophosphate for the treatment of soft tissue sarcoma

First publication	4 April 2012
Rev.1: sponsor's name change	5 June 2013
Rev.2: transfer of sponsorship	12 March 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 5 March 2012, orphan designation (EU/3/12/966) was granted by the European Commission to Nexus Oncology Ltd, United Kingdom, for (1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl) diamidophosphate for the treatment of soft tissue sarcoma.

In February 2013, Nexus Oncology Ltd changed name to Ockham Europe Limited.

The sponsorship was transferred to Merck KGaA, Germany, in March 2015.

What is soft tissue sarcoma?

Soft tissue sarcoma is a type of cancer that affects the soft, supportive tissues of the body. It can occur in muscles, blood vessels, fat tissue or in other tissues that support, surround and protect organs. Patients with soft tissue sarcoma do not usually have symptoms in the early stages of the disease. First symptoms appear when the tumour grows large enough to cause swelling and pain.

Soft tissue sarcoma is a serious and life-threatening disease particularly when the cancer has spread to other parts of the body.

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

At the time of designation, soft tissue sarcoma affected approximately 2.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 122,000 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 designation, the main treatment for early-stage soft tissue sarcoma was surgery. For large sarcomas, surgery was usually followed by radiotherapy (treatment with radiation) and chemotherapy (medicines to treat cancer) to kill any cancerous cells that were left behind. Several medicines were authorised in the EU for the treatment of soft tissue sarcoma.

The sponsor has provided sufficient information to show that (1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl) diamidophosphate might be of significant benefit for patients with soft tissue sarcoma because early studies show that it might improve the treatment of patients when used in combination with doxorubicin (a chemotherapy medicine). This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Soft tissue sarcomas, like most solid tumours, have areas with poor blood supply and therefore low levels of oxygen. The low level of oxygen in these areas is known to make tumour cells more resistant to standard chemotherapy. This medicine is a prodrug which is expected to be 'activated' when it enters these low oxygen regions by converting into a substance called bromo-isophosphoramide mustard, which is toxic to cells. This medicine is intended to be given with standard chemotherapy medicines and this is expected to help kill the tumour cells in low oxygen areas as well as other areas of the tumours.

What is the stage of development of this medicine?

The effects of the medicinal product have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicinal product in patients with soft tissue sarcoma were ongoing.

At the time of submission, the medicinal product was not authorised anywhere in the EU for soft tissue sarcoma or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 January 2011 recommending the granting of this designation.

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*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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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	(1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl) diamidophosphate	Treatment of soft tissue sarcoma
Bulgarian	(1-метил-2-нитро-1H-имидазол-5-ил)метил N,N'-бис(2-бромоетил) диамидофосфат	Лечение на сарком на меките тъкани
Croatian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfat	Liječenje sarkoma mekih tkiva
Czech	(1-methyl-2-nitro-1H-imidazol-5-yl)methyl-N,N'-bis(2-bromoethyl)diamidofosfát	Léčba sarkomu měkkých tkání
Danish	(1-methyl-2-nitro-1H-imidazol-5-yl)methyl N,N'-bis(2-bromoethyl) diamidphosphat	Behandling af bløddelssarkom
Dutch	(1-methyl-2-nitro-1H-imidazool-5-yl)methyl N,N'-bis(2-bromoethyl) diamidofosfaat	Behandeling weke delen sarcoom
Estonian	(1-metüül-2-nitro-1H-imidasool-5-üül)metüül N,N'-bis(2-bromoetüül) diamidofosfaat	Pehmete kudede sarkoomi ravi
Finnish	(1-metyyli-2-nitro-1H-imidatsoli-5-yl)metyyli N,N'-bis(2-bromietyyli) diamidifosfaatti	Pehmytkudossarkooman hoito
French	(1-méthyl-2-nitro-1H-imidazole-5-yl)méthyl N,N'-bis(2-bromoéthyl) diamidophosphate	Traitement des sarcomes des tissus mous
German	(1-Methyl-2-Nitro-1H-Imidazol-5-yl)Methyl N,N'-bis(2-Bromoethyl) Diamidophosphat	Behandlung des Weichteilsarkoms
Greek	φωσφορικό (1-μεθυλο-2-νιτρο-1Η-ιμιδαζολ-5-υλο)μεθυλο Ν,Ν'-δις(2-βρωμοαιθυλο) διαμίδιο	Θεραπεία του σαρκώματος των μαλακών ιστών
Hungarian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bisz(2-bromoetil) diamidfoszfát	Lágy szöveti sarcoma kezelése
Italian	(1-metil-2-nitro-1H-imidazolo-5-il)metil N,N'-bis(2-bromoetil) diamido fosfato	Trattamento dei sarcomi dei tessuti molli
Latvian	(1-metil-2-nitro-1H-imidazol-5-il)metil-N,N'-bis(2-brometil)-diamidofosfāts	Mīksto audu sarkomas ārstēšana
Lithuanian	(1-metil-2-nitro-1H-imidazolo-5-il)metil N,N'-bis(2-bromoetil) diamidofosfatas	Minkštųjų audinių sarkomos gydymas
Maltese	(1-methyl-2-nitro-1H-imidazole-5-yl)methyl N,N'-bis(2-bromoethyl) diamidophosphate	Kura tas-sarkoma tat-tessuti rotob
Polish	N,N'-bis(2-bromoetylo)diamidofosforan (1-metylo-2-nitro-1H-imidazol-5-yl)metylu	Leczenie mięsaków tkanek miękkich
Portuguese	(1-metil-2-nitro-1H-imidazole-5-il)metil N,N'-bis(2-brometil) fosfato de diamido	Tratamento do sarcoma dos tecidos moles
Romanian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil) diamidofosfat	Tratamentul sarcomului ţesuturilor moi
Slovak	(1-metyl-2-nitro-1H-imidazol-5-yl)metyl N,N'-bis(2-brómetyl) diamidofosfát	Liečba sarkómu mäkkých tkanív
Slovenian	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfat	Zdravljenje sarkoma mehkih tkiv

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Spanish	(1-metil-2-nitro-1H-imidazol-5-il)metil N,N'-bis(2-bromoetil)diamidofosfato	Tratamiento del sarcoma de tejidos blandos
Swedish	(1-metyl-2-nitro-1H-imidazol-5-yl)metyl N,N'-bis(2-bromoetyl)diamidofosfat	Behandling av mjukdelssarkom
Norwegian	(1-metyl-2-nitro-1H-imidazol-5-yl)metyl N,N'-bis(2-bromoetyl) diamidofosfat	Behandling av bløtvevssarkom
Icelandic	(1-metýl-2-nítro-1H-imídasól-5-ýl)metýl N,N'-bis(2-brómetýl) díamíðfosfat	Meðferð við mjúkvefjasarkmeini