European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Document Date: London, 19 August 2009
Doc.Ref.: EMEA/COMP/373/04 Rev.1

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of muramyl tripeptide phosphatidyl ethanolamine for the treatment of osteosarcoma

On 21 June 2004, orphan designation (EU/3/04/206) was granted by the European Commission to Immuno-Designed Molecules, SA, France, for muramyl tripeptide phosphatidyl ethanolamine for the treatment of osteosarcoma.
Immuno-Designed Molecules, SA changed its name to IDM Pharma, SA in January 2009.

What is osteosarcoma?
Tumours that begin in the bone tissue are known as primary bone tumours. Osteosarcoma is the most common type of primary bone tumour and occurs mainly during childhood and adolescence. It derives from the primitive bone-forming cells, the so-called mesenchymal stem-cells or osteoblasts. Osteosarcoma can develop in any bone in the body. Most often it starts in the bones around the knee joint or in the upper or lower leg next to the knee in the area of bone with the fastest growth. The second most common place to develop is in the upper arm close to the shoulder. Osteosarcoma is a serious condition, potentially debilitating and life-threatening.

What is the estimated number of patients affected by the condition*?
At the time of designation, osteosarcoma affected approximately 0.5 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 19,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?
Surgery is currently the therapy of choice for early stage osteosarcomas. Though complete surgical resection is critical, the disease can reappear in more than 80% of patients. The addition of chemotherapy (using drugs to kill cancer cells) before or after the operation, improves the outcome of the patients. Several products for treatment of osteosarcoma were authorised for the condition in the Community at the time of submission of the application for orphan drug designation.
Muramyl tripeptide phosphatidyl ethanolamine as an add-on treatment to the existing chemotherapy might be of potential significant benefit for the treatment of osteosarcoma, because it might improve the long-term outcome of the patients. 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?
Muramyl tripeptide phosphatidyl ethanolamine helps to activate a certain type of white blood cells, the so-called macrophages. The main role of macrophages is to take-up foreign or waste material

*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.

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(such as bacteria, cancer cells or cell fragments). For example in the case of cancer, following the uptake of cancer cells or cell fragments, macrophages degrade (digest) the cells and present parts of them to the immune system of the body. As these fragments are presented by the macrophages, the immune system reacts against them but also against the other cancer cells that have not been up-taken by the macrophages. Muramyl tripeptide phosphatidyl ethanolamine might help the macrophages to increase the uptake of tumour cells and thereby may help to accelerate the destruction process of tumour cells by the patient immune system.

What is the stage of development of this medicine?
The effects of muramyl tripeptide phosphatidyl ethanolamine were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with osteosarcoma were completed.

Muramyl tripeptide phosphatidyl ethanolamine was not marketed anywhere worldwide for osteosarcoma, at the time of submission. Orphan designation of muramyl tripeptide phosphatidyl ethanolamine was granted in the United States for the treatment of children and adolescents with osteosarcoma.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 14 May 2004 a positive opinion recommending the grant of the above-mentioned designation.

Update: muramyl tripeptide phosphatidyl (Mepact) has been authorised in the EU since 6 March 2009. Mepact is indicated in children, adolescents and young adults for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection. It is used in combination with post-operative multi-agent chemotherapy. Safety and efficacy have been assessed in studies of patients 2 to 30 years of age at initial diagnosis.
For more information on Mepact, see:
www.emea.europa.eu/humandocs/Humans/EPAR/mepact/mepact.htm

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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 Community) 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.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Muramyl tripeptide phosphatidyl ethanolamine	Treatment of osteosarcoma
Czech	Muramyl Tripeptid Fosfatidyl Etanolamin	Léčba osteosarkomu
Danish	Muramyl Tripeptid Phosphatidyl Etanolamin	Behandling af osteosarcoma
Dutch	Muramyl-tripeptide-fosfatidylethanolamine	Behandeling van osteosarcoma
Estonian	Muramüültripeptiid-fosfatidüületanoolamiin	Osteosarkoomi ravi
Finnish	Muramyyli Tripeptidi Fosfaattidyyli Etanolamiini	Osteosarkoman hoito
French	Muramyl Tripeptide Phosphatidyl Ethanolamine	Traitement des ostéosarcomes
German	Muramyl-Tripeptid Phosphatidyl-Äthanolamin	Behandlung von Osteosarkom
Greek	Μουραμυλικό τριπεπτίδιο φωσφατιδυλο-αιθανολαμίνης	Θεραπεία του οστεοσαρκώματος
Hungarian	Muramil Tripeptid Foszfatidil Etanolamin	Osteosarcoma kezelése
Italian	Muramil Tripeptide Fosfatidil Etanolammina	Trattamento dell’osteosarcoma
Latvian	Muramiltripeptīdfosfatidiletanolamīns	Osteosarkomas ārstēšana
Lithuanian	Muramiltripeptido fosfatidiletanolaminas	Osteosarkomos gydymas
Maltese	Muramyl tripeptide phosphatidyl ethanolamine	Treatment of osteosarcoma
Polish	Muramylotripeptyd fosfatydyloetanoloaminy –	Leczenie mięsaka kościopochodnego (osteosarcoma)
Portuguese	Muramil tripéptido fosfatidil etanolamina	Tratamento do osteosarcoma
Slovak	Muramyl tripeptid fosfatidyletanolamín	Liečba osteosarkómu
Slovenian	Muramil tripeptid fosfatidil etanolamin	Zdravljenje osteosarkoma
Spanish	Muramil tripéptido fosfatidil etanolamina	Tratamiento del osteosarcoma
Swedish	Muramyl tripeptid fosfatidyl etanolamin	Behandling av osteosarkom
Norwegian	Muramyltripeptidfosfatidyl etanolamin	Behandling av osteosarkom
Icelandic	Múramíl þrípeptíð fosfatídýl etanólamín	Meðferð við beinsarkmeini