



Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of metastable technetium 99 [⁹⁹mTc] demogastrin 2 for the diagnosis of medullary thyroid carcinoma

On 28 August 2006, orphan designation (EU/3/06/400) was granted by the European Commission to Biomedica Life Sciences S.A., Greece, for metastable technetium 99 [⁹⁹mTc] demogastrin 2 for the diagnosis of medullary thyroid carcinoma.

What is medullary thyroid carcinoma?

Thyroid cancer is a disease in which cancer (malignant) cells are found in certain tissues of the thyroid. The thyroid is a gland in the neck that is composed of mainly two different cell types: the follicular and parafollicular cells. The so-called follicular cells help to concentrate iodine and produce thyroid hormones. These hormones are important for the body growth and metabolism. The parafollicular cells produce a hormone called calcitonin that diminishes the calcium level in the blood. Depending on the type of cell in which the cancer cells originate, different types of thyroid cancer exist.

Medullary thyroid carcinoma is originating from the parafollicular cells (also called C cells), and represents only 5-9% of all thyroid cancers. Signs of cancer are difficult to detect in early stages of the disease and is often limited to a single local swelling of the thyroid gland which is not painful but can be felt by touching. Patients are frequently diagnosed when the disease has spread locally giving symptoms such as shortness of breath, difficulties in swallowing or changes in the voice. Some patients may have severe diarrhoea as a first sign of the disease.

Medullary thyroid carcinoma is a life-threatening disease.

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

At the time of designation medullary thyroid carcinoma affected approximately 0.7 in 10,000 people in the European Union (EU)*. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 32,000 people.

What methods of diagnosis are available?

Medullary thyroid carcinoma is diagnosed by elevated levels of calcitonin in the blood and fine needle aspiration of the tumour (cells are sucked out of the tumour through a fine needle to be studied under a microscope). Sometimes magnetic resonance imaging (MRI) and computer tomography (CT) are used to visualise the location of the tumour or tumours, if the disease has spread.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that metastable technetium 99 [⁹⁹mTc] demogastrin 2 might be of potential significant benefit for the diagnosis of medullary thyroid carcinoma, mainly because it may provide a tool to detect micrometastases (tiny

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

tumours that have spread to other parts of the body). 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?

Metastable technetium 99 [⁹⁹mTc] demogastrin 2 is structurally similar to a part of an endogenous (naturally occurring in the body) protein called gastrin. On the surface of medullary thyroid carcinoma cells there are specific structures (receptors) that bind gastrin. Metastable technetium 99 [⁹⁹mTc] demogastrin 2 binds to these structures and, because this product has a radioactive part ([⁹⁹mTc]), its spreading in the body can be detected by imaging methods from the outside. By doing this, it is hoped that small metastases can be found.

What is the stage of development of this medicine?

The effects of metastable technetium 99 [⁹⁹mTc] demogastrin 2 were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with medullary thyroid carcinoma were ongoing.

Metastable technetium 99 [⁹⁹mTc] demogastrin 2 was not authorised anywhere worldwide for the diagnosis of medullary thyroid carcinoma, nor designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 12 July 2006 a positive opinion recommending the grant of the above-mentioned designation.

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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the 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 | Metastable technetium 99 [^{99m} Tc] Demogastrin 2 | Diagnosis of medullary thyroid carcinoma |
| Czech | Demogastrin 2 s metastabilním techneciem [^{99m} Tc] | Diagnóza medulárního karcinomu štítné žlázy |
| Danish | Demogastrin 2 mærket med metastabil technetium 99 (^{99m} Tc-mærket Demogastrin 2) | Diagnose af medullært thyreoideakarcinom |
| Dutch | Metastabel technetium 99- [^{99m} Tc]- Demogastrine 2 | Diagnose van medullair schilkkliercarcinoom |
| Estonian | Metastabiilne tehneetsium 99 [^{99m} Tc] Demogastrin 2 | Medullaarse kilpnäärmevähi diagnoosimiseks |
| Finnish | Metastabiililla teknetiumilla 99 [^{99m} Tc] leimattu demogastrini 2 | Medullaarisen kilpirauhaskarsinooman diagnosointi |
| French | Démogastrine 2 marquée au technétium 99 métastable [^{99m} Tc] | Diagnostic du cancer médullaire de la thyroïde |
| German | Metastabiles technetium 99 [^{99m} Tc] Demogastrin 2 | Diagnose des medullären Schilddrüsenkarzinoms |
| Greek | μετασταθερό τεχνήτιο 99 [^{99m} Tc] Demogastrin 2 | διάγνωση του μυελοειδούς καρκινώματος του θυρεοειδούς. |
| Hungarian | Metastabil technetium [^{99m} Tc] Demogastrin 2 | Medulláris pajzsmirigy carcinoma diagnosztizálása |
| Italian | Tecnezio 99 metastabile [^{99m} Tc] Demogastrin 2 | Diagnosi del carcinoma midollare della tiroide |
| Latvian | Metastabilo tehnciiju 99 [^{99m} Tc] saturošs demogastrīns 2 | Medulāras vairogdziedzera karcinomas diagnostika |
| Lithuanian | Metastabilus technecis [^{99m} Tc] Demogastrinas 2 | Medulinės skydliaukės karcinomos diagnozė |
| Polish | Demogastryna 2 znakowana metastabilnym izotopem technetu 99 [^{99m} Tc] | Rozpoznanie raka rdzeniastego tarczycy |
| Portuguese | Demogastrin 2 marcado com tecnécio 99 metaestável [^{99m} Tc] | Diagnóstico do carcinoma medular da tiroide |
| Slovak | Metastabilné technécium [^{99m} Tc] Demogastrin 2 | Diagnóza medulárneho karcinómu štítnej žľazy |
| Slovenian | Metastabilni tehnecij [^{99m} Tc] Demogastrin 2 | Diagnosticiranje medularnega karcinoma ščitnice |
| Spanish | Demogastrina 2 marcada con tecnecio metaestable 99 [^{99m} Tc] | Diagnóstico del cáncer medular de tiroides |
| Swedish | Demogastrin 2 märkt med metastabil teknetium 99 (^{99m} Tc-Demogastrin 2) | Diagnos av medullär thyreoideacancer |
| Norwegian | Metastabil technetium 99 [^{99m} Tc] Demogastrin 2 | Diagnose av medullært thyreoideacarcinom |
| Icelandic | Hálfstöðugt teknetíum 99 [^{99m} Tc] Demogastrin 2 | Til greiningar á merggerðarkrabbameini í skjaldkirtli |