EMA/COMP/136/2004 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-Methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl) ethenyl]-phenol for the treatment of anaplastic thyroid cancer

First publication	5 November 2004
Rev.1: transfer of sponsorship	3 May 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 14 April 2004, orphan designation (EU/3/04/195) was granted by the European Commission to David Chaplin, United Kingdom, for 2-Methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl) ethenyl]-phenol (combretastatin A4 phosphate) for the treatment of anaplastic thyroid cancer.

The sponsorship was transferred to Diamond BioPharm Limited, United Kingdom, in January 2013.

What is anaplastic thyroid cancer?

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.

Anaplastic thyroid cancer is most likely originating from the follicular cells, and represents only 1-3% of all thyroid cancers. Signs of cancer are difficult to detect in early stages of the disease, and 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. In 25 to 50% of the patients, the disease has spread to distant parts of the body, such as the lungs, at the moment of diagnosis. Anaplastic thyroid cancer is a life-threatening disease.

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

At the time of designation, anaplastic thyroid cancer affected approximately 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of around 500 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?

There are no treatments available for anaplastic thyroid cancer. Surgery, if possible, is mainly done to control the local symptoms. Only in case of early diagnosis, extensive surgery followed by some local radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) or chemotherapy (using drugs to kill cancer cells) is considered the most appropriate treatment.

How is this medicine expected to work?

Combretastatin A4 phosphate is a substance that was originally isolated from the bark of the South African willow tree, *Combretum caffrum*. It is thought that combretastatin A4 phosphate acts on the cells of the vessels that bring blood to the tumour, blocking the normal flow of the blood. Cancer cells grow rapidly and thus require a large amount of blood. By blocking blood vessels combretastatin A4 phosphate might stop the tumour growth and might even help to kill the tumour cells.

What is the stage of development of this medicine?

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

Combretastatin A4 phosphate was not marketed anywhere worldwide for anaplastic thyroid cancer, at the time of submission.

Orphan designation of Combretastatin A4 phosphate was granted in the United States for the treatment of anaplastic thyroid cancer, medullary thyroid cancer, stage IV papillary and stage IV follicular thyroid cancer.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 March 2004 recommending the granting of this designation.

*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:

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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	2-Methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-phenol	Treatment of anaplastic thyroid cancer
Bulgarian	2-Метокси-5-[(1Z)-2-(3,4,5-триметоксифенил)етенил]-фенол	Лечение на анапластичен карцином на щитовидната жлеза
Czech	2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyfenyl)ethenyl]-fenol	Léčba anaplastického karcinomu štítné žlázy
Danish	2-Methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-phenol	Behandling af anaplastisk thyroideacancer
Dutch	2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyfenyl)ethenyl]-fenol	Behandeling van anaplastisch schildklierkanker
Estonian	2-Metoksü-5-[(1Z)-2-(3,4,5-trimetoksüfenüül)etenüül]-fenool	Anaplastilise kilpnäärmevähi ravi
Finnish	2-metoksi-5-[(1Z)-2-(3,4,5-trimetoksifenyyli)etenyyli]-fenoli	Anaplastisen kilpirauhassyövän hoito
French	2-Méthoxy-5-[(1Z)-2-(3,4,5-triméthoxyphényl)éthényl]-phénol	Traitement du cancer anaplastique de la thyroïde
German	2-Methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-phenol	Behandlung von anaplastischem Schilddrüsenkrebs
Greek	2-Μεθοξυ-5-[(1Z)-2-(3,4,5-τριμεθοξυφαινυλο)αιθυνυλο]-φαινόλη	Θεραπεία του αναπλαστικού θυρεοειδικού καρκίνου
Hungarian	2-metoxi-5[(1Z)-2(3,4,5-trimetoxifenil)etenil]-fenol	Anaplasztikus pajzsmirigyrák kezelése
Italian	2-Metoxi-5-[(1Z)-2-(3,4,5-trimetoxifenile)etenile]-fenolo	Trattamento del carcinoma anaplastico della tiroide
Latvian	2-metoksi-5-[(1Z)-2-(3,4,5-trimetoksifenil)etenil]-fenols	Vairogdziedzera anaplastiskā vēža ārstēšana
Lithuanian	2-metoksi-5-[(1Z)-2-(3,4,5-trimetoksifenil)etenil]-fenolis	Anaplastinio skydliaukės vėžio gydymas
Maltese	2-Methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-phenol	Kura tal-kanċer tat-tirojde anaplastiku
Polish	2-Metoksy-5-[(1Z)-2-(3,4,5-trimetoksyfenyl)etenyl]-fenol	Leczenie anaplastycznego raka tarczycy
Portuguese	2-metoxi-5-[(1Z)-2-(3,4,5-trimetoxifenil)etenil]-fenol	Tratamento do cancro anaplástico da tiróide
Romanian	2-metoxi-5-[(1Z)-2-(3,4,5-trimetoxifenil)etenil]-fenol	Tratamentul cancerului tiroidian anaplazic
Slovak	2-metoxy-5-[(1Z)-2-(3,4,5-trimetoxyfenyl)etenyl]-fenol	Liečba anaplastickej rakoviny štítnej žľazy
Slovenian	2-metoksi-5-[(1Z)-2-(3,4,5-trimetoksifenil)etenil]-fenol	Zdravljenje anaplastičnega raka ščitnice

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Spanish	2-metoxi-5-[(1Z)-2-(3,4,5-trimetoxifenil)etenil]-fenol	Tratamiento del cáncer anaplástico de tiroides
Swedish	2-metoxi-5-[(1Z)-2-(3,4,5-trimetoxifenyl)etenyl]-fenol	Behandling av anaplastisk thyreoideacancer