15 January 2019
EMA/776179/2018

Public summary of opinion on orphan designation

Larotrectinib for treatment of papillary thyroid cancer

On 19 November 2018, orphan designation (EU/3/18/2098) was granted by the European Commission to Bayer AG, Germany, for larotrectinib for the treatment of papillary thyroid cancer.

What is papillary thyroid cancer?

Papillary thyroid cancer is a type of cancer affecting the thyroid, a small gland at the base of the neck that produces thyroid hormones.

The thyroid has two main cell types: follicular cells, which produce hormones that help regulate growth and metabolism (the process of breaking down substances in the body), and parafollicular cells, which produce calcitonin, a hormone that helps to regulate calcium levels in the blood.

Papillary thyroid cancer starts in the follicular cells and it can spread to other parts of the body. Signs of papillary thyroid cancer are difficult to detect in the early stages of the disease and are usually limited to local swelling of the thyroid gland. Patients are often diagnosed when the disease has spread locally giving symptoms such as shortness of breath, difficulties in swallowing or changes in the voice.

Papillary thyroid cancer is a long-term debilitating disease which is life-threatening if it does not respond to treatment and if the cancer spreads to other parts of the body.

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

At the time of designation, papillary thyroid cancer affected approximately 3.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 171,000 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 papillary thyroid cancer in the EU was surgery to remove the thyroid. Therapy using radioactive iodine (131I) to destroy thyroid cells was also used.

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 517,400,000 (Eurostat 2018).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Hormonal therapy was used as an additional treatment for preventing recurrence of the disease. In addition, the medicines Nexavar (sorafenib), Lenvima (lenvatinib), Thyrogen (thyrotropin alfa) and doxorubicin were authorised for the treatment of papillary thyroid cancer.

The sponsor has provided sufficient information to show that larotrectinib might be of significant benefit for patients with papillary thyroid cancer. Early data indicate that patients in whom other treatments had failed responded to treatment with this 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?

Some patients with papillary thyroid cancer have genetic mutations (changes) called *NTRK* gene fusions which result in the production of altered TRK proteins that can cause cancer.

Larotrectinib blocks the activity of the altered TRK proteins, thus preventing or slowing down the growth of papillary thyroid cancer.

What is the stage of development of this medicine?

The effects of larotrectinib have been evaluated in experimental models.

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

At the time of submission, larotrectinib was not authorised anywhere in the EU for papillary thyroid cancer. Orphan designation of the medicine had been granted in the United States for soft tissue sarcoma, solid tumors with NTRK-fusion proteins and infantile fibrosarcoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 October 2018 recommending the granting of this designation.

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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 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Larotrectinib	Treatment of papillary thyroid cancer
Bulgarian	Ларотректиниб	Лечение на папиларен тироиден карцином
Croatian	Larotrectinib	Liječenje papilarnog raka štitnjače
Czech	Larotrectinib	Léčba papilárního karcinomu štítné žlázy
Danish	Larotrectinib	Behandling af papillær tyreoideacancer
Dutch	Larotrectinib	Behandeling van papillaire schildklierkanker
Estonian	Larotrektiniib	Papillaarse kilpnäärmevähi ravi
Finnish	Larotrektinibi	Papillaarisen kilpirauhassyövän hoito
French	Larotrectinib	Traitement du cancer thyroïdien papillaire
German	Larotrectinib	Behandlung des papillären Schilddrüsenkarzinoms
Greek	Λαροτρεκτινίμπη	Θεραπεία του θηλώδους καρκινώματος του θυρεοειδούς
Hungarian	Larotrectinib	Papillaris pajzsmirigyrák kezelése
Italian	Larotrectinib	Trattamento del carcinoma papillare della tiroide
Latvian	Larotrektinibs	Papillāra vairogdziedzera vēža ārstēšana
Lithuanian	Larotrektinibas	Papilinio skydliaukės vėžio gydymas
Maltese	Larotrektinib	Kura ta' kanċer papillari tat-tirojde
Polish	Larotrektynib	Leczenie raka brodawkowatego tarczycy
Portuguese	Larotrectinib	Tratamento do carcinoma papilar da tiroide
Romanian	Larotrectinib	Tratamentul cancerului tiroidian papilar
Slovak	Larotrektinib	Liečba papilárneho karcinómu štítnej žľazy
Slovenian	Larotrektinib	Zdravljenje papilarnega raka ščitnice
Spanish	Larotrectinib	Tratamiento del carcinoma papilar de tiroides
Swedish	Larotrektinib	Behandling av papillär sköldkörtelcancer
Norwegian	Larotrektinib	Behandling av papillær thyreoideacancer
Icelandic	Larótrektíníb	Meðferð totukrabbameins í skjaldkirtli

[1] At the time of designation