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Public summary of opinion on orphan designation

1-[[[4-(4-fluoro-2-methyl-1H-indol-5-yloxy)-6-methoxyquinolin-7-yl]oxy]methyl]cyclopropanamine-dihydrochloride for the treatment of soft tissue sarcoma

On 22 February 2018, orphan designation (EU/3/18/1972) was granted by the European Commission to CATS Consultants GmbH, Germany, for 1-[[[4-(4-fluoro-2-methyl-1H-indol-5-yloxy)-6-methoxyquinolin-7-yl]oxy]methyl]cyclopropanamine-dihydrochloride (also known as AL3818 and anlotinib) for the treatment of soft tissue sarcoma.

What is soft tissue sarcoma?

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

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

At the time of designation, soft tissue sarcoma affected approximately 3.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 191,000 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 treatments for soft tissue sarcoma were surgery and chemotherapy (medicines to treat cancer). Radiotherapy (treatment with radiation) was also used. Several medicines have been authorised in the EU for the treatment of soft tissue sarcoma.

*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).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with soft tissue sarcoma because early studies in some types of advanced sarcoma suggest improved effects with this medicine compared with authorised medicines. 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?

The medicine belongs to a class of cancer medicines called tyrosine kinase inhibitors, and blocks targets called VEGF receptors on the cancer cells. These receptors are very important for the development of new blood vessels that supply blood to the cancer. By blocking VEGF receptors, it is expected that the medicine will reduce the supply of blood to the cancer and stop it from growing and spreading.

What is the stage of development of this medicine?

The effects of the medicine 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 soft tissue sarcoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for soft tissue sarcoma. Orphan designation of the medicine had been granted in the United States for soft tissue sarcomas.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 January 2018 recommending the granting of this 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;
- 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	1-[[[4-(4-fluoro-2-methyl-1H-indol-5-yloxy)-6-methoxyquinolin-7-yl]oxy)methyl]cyclopropanamine-dihydrochloride	Treatment of soft tissue sarcoma
Bulgarian	1-[[[4-(4-флуоро-2-метил-1H-индол-5-илокси)-6-метоксихинолин-7-ил]окси]метил]циклопропанамин дихидрохлорид	Лечение на сарком на меките тъкани
Croatian	1-[[[4-(4-fluoro-2-metil-1H-indol-5-iloksi)-6-metoksikinolin-7-il]oksi]metil]ciklopropanamin –dihidroklorid	Liječenje sarkoma mekih tkiva
Czech	1-[[[4-(4-fluor-2-methyl-1H-indol-5-yloxy)-6-methoxychinolin-7-yl]oxy)methyl]cyklopropylamin dihydrochlorid	Léčba sarkomu měkkých tkání
Danish	1-[[[4-(4-fluor-2-methyl-1H-indol-5-yloxy)-6-methoxyquinolin-7-yl]oxy)methyl]cyclopropanamindihydrochlorid	Behandling af bløddelsarkom
Dutch	1-[[[4-(4-fluor-2-methyl-1H-indool-5-yloxy)-6-methoxyquinoline-7-yl]oxy)methyl]cyclopropanaminedihydrochloride	Behandeling weke delen sarcoom
Estonian	1-[[[4-(4-fluoro-2-metüül-1H-indool-5-üüloksi)-6-metoksükinoliin-7-üül]oksü]metüül]tsüklopropanamiindivesinikkloriid	Pehmele kudede sarkoomi ravi
Finnish	1-[[[4-(4-fluori-2-metyyli-1H-indol-5-yylioksi)-6-metoksikinolin-7-yyli]oksi]metyyli]syklopropanaamiinidihydrokloridi	Pehmytkudossarkoo man hoito
French	dichlorhydrate de 1-[[[4-(4-fluoro-2-méthyl-1H-indol-5-yloxy)-6-méthoxyquinoléin-7-yl]oxy]méthyl]cyclopropanamine	Traitement des sarcomes des tissus mous
German	1-[[[4-(4-Fluor-2-methyl-1H-indol-5-yloxy)-6-methoxychinolin-7-yl]oxy)methyl]cyclopropanamindihydrochlorid	Behandlung des Weichteilsarkoms
Greek	Διυδροχλωριούχος 1-[[[4-(4-φθορο-2-μεθυλο-1H-ινδολ-5-υλοξυ)-6-μεθοξικινολιν-7-υλο]οξύ]μεθυλο]κυκλοπροπαναμίνη	Θεραπεία του σαρρώματος των μαλακών ιστών
Hungarian	1-[[[4-(4-fluor-2-metil-1H-indol-5-iloxi)-6-metoxikinolin-7-il]oxi]metil]ciklopropánamin-dihidroklorid	Lágy szöveti sarcoma kezelése
Italian	1-[[[4-(4-fluoro-2-metil-1H-indol-5-ilossi)-6-metossichinolin-7-il]ossi]metil]ciclopropanamina dicloridrato	Trattamento dei sarcomi dei tessuti molli
Latvian	1-[[[4-(4-fluoro-2-metil-1H-indol-5-iloksi)-6-metoksihinolīn-7-il]oksi] metil] ciklopropānamīna dihidrohlorīds	Mīksto audu sarkomas ārstēšana
Lithuanian	1-[[[4-(4-fluor-2-metil-1H-indol-5-iloksi)-6-metoksikvinolin-7-il]oksi]metil]ciklopropanaminodihidrochloridas	Minkštųjų audinių sarkomos gydymas
Maltese	1-[[[4-(4-fluwor-2-metil-1H-indol-5-ilossi)-6-metossikwinolin-7-yl]ossi]metil]ċiklopropanamina-diidroklorur	Kura tas-sarkoma tat-tessuti rotob
Polish	Dichlorowodorek 1-[[[4-(4-fluoro-2-metylo-1 H-indol-5-iloksy)-6-metoksychinolin-7-ylo]oksy]metylo]cyklopropanoaminy	Leczenie mięsaków tkanek miękkich

¹ At the time of designation

Language	Active ingredient	Indication
Portuguese	Dicloridrato de 1-[[[4-(4-fluoro-2-metil-1H-indol-5-iloxi)-6-metoxiquinolin-7-il]oxi]metil]ciclopropanamina	Tratamento do sarcoma dos tecidos moles
Romanian	Diclorhidrat de 1-[[[4-(4-fluor-2-metil-1H-indol-5-iloxi)-6-metoxichinolin-7-yl]oxi]metil]ciclopropanamină	Tratamentul sarcomului țesuturilor moi
Slovak	1-[[[4-(4-fluór-2-metyl-1H-indol-5-yloxy)-6-metoxychinolín-7-yl]oxy]metyl]cyklopropánamíndihydrochlorid	Liečba sarkómu mäkkých tkanív
Slovenian	1-[[[4-(4-fluoro-2-metil-1H-indol-5-iloksi)-6-metoksikinolin-7-il]oksi]metil]ciklopropanamin dihidroklorid	Zdravljenje sarkoma mehkih tkiv
Spanish	diclorhidrato de 1-[[[4-(4-fluoro-2-metil-1H-indol-5-iloxi)-6-metoxiquinolin-7-il]oxi]metil]ciclopropanamina	Tratamiento del sarcoma de tejidos blandos
Swedish	1-[[[4-(4-fluoro-2-metyl-1H-indol-5-yloxi)-6-metoxikinolin-7-Yl]oxi]metyl]cyklopropanamin-dihydroklorid	Behandling av mjukdelssarkom
Norwegian	1-[[[4-(4-fluor-2-metyl-1H-indol-5-yloxy)-6-metoksykinolin-7-yl]oksy]metyl]syklopropanamindihydroklorid	Behandling av bløtvevssarkom
Icelandic	1-[[[4-(4-flúor-2-metýl-1H-indól-5-ýloxý)-6-metoxýkínólín-7-ýl]oxý]metýl]sýklóprópanamíndíhýdróklóríð	Meðferð við mjúkvefjasarkmeini