



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(-)-*trans*-3-(5,6-dihydro-4H-pyrrolo[3,2,1-*ij*]quinolin-1-yl)-4-(1H-indol-3-yl)pyrrolidine-2, 5-dione for the treatment of soft tissue sarcoma

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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.	

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in January 2012 on request of the Sponsor.

On 8 October 2009, orphan designation (EU/3/09/678) was granted by the European Commission to Gregory Fryer Associates Ltd, United Kingdom, for (-)-*trans*-3-(5,6-dihydro-4H-pyrrolo[3,2,1-*ij*]quinolin-1-yl)-4-(1H-indol-3-yl)pyrrolidine-2, 5-dione for the treatment of soft tissue sarcoma.

What is soft tissue sarcoma?

Soft tissue sarcoma is a type of cancer that affects the supportive tissues of the body. It can occur in muscles, blood vessels, fat tissue or in other tissues that support, surround and protect organs. The cause of soft tissue sarcoma is largely unknown.

Soft tissue sarcoma is a serious 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 2.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 121,000 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?

At the time of designation, the main treatment for early-stage soft tissue sarcoma was surgery. For large sarcomas, surgery was usually followed by radiotherapy (treatment with radiation) and chemotherapy (medicines to treat cancer) to kill any cancerous cells that were left behind. Several medicines were authorised in the EU for the treatment of soft tissue sarcoma.

The sponsor has provided sufficient information to show that (-)-*trans*-3-(5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidine-2, 5-dione might be of significant benefit for patients with soft tissue sarcoma because it works in a different way to existing medicines and it might improve the treatment of patients with particular subtypes of the disease. It is also being developed as capsules to be taken by mouth, whereas the existing medicines are given by injection. These assumptions 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?

This medicine is expected to work by blocking enzymes known as tyrosine kinases that are found in some receptors called c-Met on the surface of cancer cells. c-Met is involved in stimulating the cells to divide uncontrollably. By blocking these enzymes, this medicine is expected to control cell division and slow down the growth of the cancer.

What is the stage of development of this medicine?

The effects of (-)-*trans*-3-(5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidine-2, 5-dione have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with soft tissue sarcoma were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for soft tissue sarcoma or designated as orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 July 2009 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 27), Norway, Iceland and Liechtenstein. This represents a population of 504,800,000 (Eurostat 2009).

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidine-2, 5-dione	Treatment of soft tissue sarcoma
Bulgarian	(-)- <i>trans</i> -3-(5,6-дихидро-4Н-пироло[3,2,1- <i>ij</i>]квинолин-1-yl)-4-(1Н-индол-3-yl) пиролдин-2, 5-дион	Лечение на сарком на меките тъкани
Czech	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidin-2, 5-dion	Léčba sarkomu měkkých tkání
Danish	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidin-2, 5-dion	Behandling af bløddelssarkom
Dutch	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]chinoline-1-yl)-4-(1H-indol-3-yl) pyrrolidine-2, 5-dione	Behandeling weke delen sarcoom
Estonian	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pürrolo[3,2,1- <i>i,j</i>]kinoliin-1-üül)-4-(1H-indol-3-üül)pürrolidiin-2,5-dioon	Pehmele kudede sarkoomi ravi
Finnish	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]kinoliini-1-yyli)-4-(1H-indol-3-yyli) pyrrolidiini-2, 5-dioni	Pehmytkudossarkooman hoito
French	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinoline-1-yl)-4-(1H-indol-3-yl) pyrrolidine-2, 5-dione	Traitement des sarcomes des tissus mous
German	(-)- <i>trans</i> -3-(5,6-Dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidin-2, 5-dion	Behandlung des Weichteilsarkoms
Greek	(-)- <i>trans</i> -3-(5,6-δι-υδρο-4Η-πυρρολο[3,2,1- <i>ij</i>]κινολινο-1-υλ)-4-(1Η-ινδολ-3-υλ) πυρρολιδινο-2, 5-διόνη	Θεραπεία του σαρκώματος των μαλακών ιστών
Hungarian	(-)- <i>transz</i> -3-(5,6-dihidro-4H-pirrollo[3,2,1- <i>i ij</i>]kinolin-1-il)-4-(1H-indol-3-il) pirrolidin 2,5-dion	Lágy szöveti sarcoma kezelése
Italian	(-)- <i>trans</i> -3-(5,6-diidro-4H-pirrollo[3,2,1- <i>ij</i>]chinolin-1-il)-4-(1H-indol-3-il) pirrolidina-2, 5-dione	Trattamento dei sarcomi dei tessuti molli
Latvian	(-)- <i>trans</i> -3-(5,6-dihidro-4H-pirrollo[3,2,1- <i>ij</i>]kvinolīn-1-il)-4-(1H-indol-3-il) pirrolidīna-2, 5-dions	Mīksto audu sarkomas ārstēšana
Lithuanian	(-)- <i>trans</i> -3-(5,6-dihidro-4H-pirollo[3,2,1- <i>ij</i>]kvinolin-1-il)-4-(1H-indol-3-il) pirolidino-2, 5-dionas	Minkštųjų audinių sarkomos gydymas

¹ At the time of designation

Language	Active ingredient	Indication
Maltese	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidine-2, 5-dione	Kura tas-sarkoma tat-tessuti rotob
Polish	(-)- <i>trans</i> -3-(5,6- dihydro-4H-pirololo[3,2,1- <i>ij</i>]chinolino-1-yl)-4-(1H-indol-3-yl) pirolidyno-2, 5-dion	Leczenie mięsaków tkanek miękkich
Portuguese	(-)- <i>trans</i> -3-(5,6-di-hidro-4H-pirrololo[3,2,1- <i>ij</i>]quinolina-1-ilo)-4-(1H-indol-3-ilo) pirrolidina-2, 5-diona	Tratamento do sarcoma dos tecidos moles
Romanian	(-)- <i>trans</i> -3-(5,6-dihidro-4H-pirol[3,2,1- <i>ij</i>]chinolină-1-il)-4-(1H-indol-3-il) pirolidină-2, 5-dionă	Tratamentul sarcomului țesuturilor moi
Slovak	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrolo[3,2,1- <i>ij</i>]chinolín-1-yl)-4-(1H-indol-3-yl) pyrolidín-2, 5-dión	Liečba sarkómu mäkkých tkanív
Slovenian	(-)- <i>trans</i> -3-(5,6-dihidro-4H-pirololo[3,2,1- <i>ij</i>]kinolin-1-il)-4-(1H-indol-3-il) pirolidin-2, 5-dion	Zdravljenje sarkoma mehkih tkiv
Spanish	(-)- <i>trans</i> -3-(5,6-dihidro-4H-pirrololo[3,2,1- <i>ij</i>]quinolina-1-il)-4-(1H-indol-3-il) pirrolidina-2, 5-diona	Tratamiento del sarcoma de tejidos blandos
Swedish	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]kinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidin-2, 5-dion	Behandling av mjukdelssarkom
Norwegian	(-)- <i>trans</i> -3-(5,6-dihydro-4H-pyrrolo[3,2,1- <i>ij</i>]quinolin-1-yl)-4-(1H-indol-3-yl) pyrrolidin-2, 5-dion	Behandling av bløtvevssarkom
Icelandic	(-)- <i>trans</i> -3-(5,6-díhýdró-4H-pýrróló[3,2,1- <i>ij</i>]kínólín-1-ýl)-4-(1H-indól-3-ýl) pýrrólídín-2, 5-díón	Meðferð við mjúkvefjasarkmeini