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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pralatrexate for the treatment of non-papillary transitional cell carcinoma of the urinary bladder

On 19 January 2009, orphan designation (EU/3/08/603) was granted by the European Commission to European Medical Advisory Services Limited, United Kingdom, for pralatrexate for the treatment of non-papillary transitional cell carcinoma of the urinary bladder.

The sponsorship was transferred to Allos Therapeutics Limited, United Kingdom, in February 2010.

What is non-papillary transitional cell carcinoma of the urinary bladder?

A carcinoma is any cancer that arises from epithelial cells. These cells line cavities and structures throughout the body, such as the bladder. Transitional epithelial cells surround organs that can stretch. For example, the urothelium is the cell layer that lines the bladder and ureter in the human body. Non-papillary transitional cell carcinoma is a carcinoma of this type of cells that line the urinary bladder. This cancer is also called urothelial carcinoma and it accounts for more than 90% of all bladder cancers.

There are two distinct transitional cell carcinomas of the urinary bladder called papillary and non-papillary depending on their aspect (raised or flat). While papillary carcinomas do not invade tissues around or disseminate through the body (metastasize), non-papillary carcinomas can aggressively invade the bladder wall (they are usually invasive at the time of diagnosis) and often disseminate quickly during the course of the disease. Non-papillary transitional cell carcinoma of the urinary bladder is a life-threatening condition.

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

At the time of designation non-papillary transitional cell carcinoma of the urinary bladder affected approximately 3.7 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 186,000 people.

[*]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 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

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What treatments are available?

The choice of treatment for non-papillary cell carcinoma of the urinary bladder depends on the extent of the disease. Treatment for the condition includes surgery to remove the cancer (transurethral resection), immunotherapy, interferon therapy, radiation therapy, and chemotherapy (using drugs to kill cancer cells).

Pralatrexate might be of potential significant benefit for the treatment of non-papillary transitional cell carcinoma of the urinary bladder because it is expected to improve the overall outcome of patients with the condition particularly due to its expected activity against the cancer cells. 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?

Enzymes are proteins produced by the cells of the body that speed up (catalyse) the conversion of certain substances into others. Pralatrexate inhibits (blocks) the activity of the enzyme dihydrofolate reductase, which is necessary for cell growth and multiplication. As the function of dihydrofolate reductase is inhibited, cell growth can be arrested. Since non-papillary transitional cell carcinoma of the urinary bladder is caused by the uncontrolled growth of the bladder transitional epithelial cells, pralatrexate might help in slowing down or stopping this uncontrolled cell growth.

What is the stage of development of this medicine?

The effects of pralatrexate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial in patients with non-papillary transitional cell carcinoma of the urinary bladder was ongoing.

At the time of submission, pralatrexate was not authorised anywhere in the world for non-papillary transitional cell carcinoma of the urinary bladder 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 5 November 2008 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 European Union) 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	Pralatrexate	Treatment of non-papillary transitional cell carcinoma of the urinary bladder
Bulgarian	Пралатрексат	Лечение на пациенти с непапиларен преходноклетъчен карцином на пикочния мехур
Czech	Pralatrexat	Léčba nepapilárního karcinomu močového měchýře z přechodného epitelu.
Danish	Pralatrexat	Behandling af patienter med nonpapillært transitionalcellekarcinom i urinblæren
Dutch	Pralatrexate	Behandeling van niet-papillair overgangsepitheelcarcinoom van de urineblaas
Estonian	Pralatreksaat	Kusepõie mittepapillaarse üleminekurakk-kartsinoomi ravi.
Finnish	Pralatreksaatti	Virtsarakon ei-papillaarisen välimuotoisen karsinooman hoito
French	Pralatrexate	Traitement des patients atteints de carcinome vésjcal à cellules transitionnelles non papillaire
German	Pralatrexat	Behandlung des nicht-papillären Übergangszellkarzinoms der Harnblase
Greek	Πραλατρεξάτη	Θεραπεία ασθενών με μη θηλώδες καρκίνωμα από μεταβατικό επιθήλιο της ουροδόχου κύστης
Hungarian	Pralatrexat	Nem-papilláris átmeneti sejtes húgyhólyag-carcinoma kezelése
Italian	Pralatrexato	Trattamento del carcinoma transizionale (non papillare) della vescica
Latvian	Pralatreksāts	Urīnpūšļa nepapilāras epitēlija pārejas šūnu karcinomas ārstēšanai
Lithuanian	Pralatreksatas	Šlapimo pūslės nepapilinės pereinamojo epitelio ląstelių karcinomos gydymas
Maltese	Pralatrexate	Kura tal-karċinoma taċ-ċelloli transizzjonali mhux papillari tal-bużżieqa ta' l-awrina
Polish	Pralatreksat	Leczenie niepapilarnego,raka nabłonka przejściowo komórkowego pęcherza moczowego
Portuguese	Pralatrexato	Tratamento de doentes com carcinoma não papilar de células de transicão da bexiga, avançado ou com metástases
Romanian	Pralatrexat	Tratamentul carcinomului de vezică urinară, non-papilar cu celule tranziţionale
Slovak	Pralatrexát	Liečba nepapilárneho karcinómu močového mechúra z prechodných buniek
Slovenian	Pralatreksat	Zdravljenje nepapilarnega prehodnoceličnega karcinoma sečnega mehurja
Spanish	Pralatrexato	Tratamiento del carcinoma de células transicionales no papilar de vejiga urinaria

[1] At the time of designation

Language	Active Ingredient	Indication
Swedish	Pralatrexat	Behandling av icke-papillärt övergångsepitelkarcinom i urinblåsan
Norwegian	Pralatreksat	Behandling av ikke-papillært fovergangscellekarsinom i urinblæren.
Icelandic	Pralatrexat	Meðferð við umskiptaþekjukrabbameini í þvagblöðru sem ekki er totumyndandi