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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Mercaptopurine (oral liquid) for the treatment of acute lymphoblastic leukaemia

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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.	

On 22 October 2007, orphan designation (EU/3/07/496) was granted by the European Commission to Only for Children Pharmaceuticals, France, for mercaptopurine (oral liquid) for the treatment of acute lymphoblastic leukaemia.

The sponsorship was transferred to Orbona Pharma Ltd, United Kingdom, in October 2013.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic leukaemia is a disease in which cancer cells are found in the blood and the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally, the bone marrow makes cells called "blasts" that mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets. Red blood cells carry oxygen and other materials to all tissues of the body. White blood cells fight infection. Platelets make the blood clot. When leukaemia develops, the bone marrow produces large numbers of abnormal blood cells. There are several types of leukaemias. Acute lymphoblastic leukaemia is a cancer of certain white blood cells called lymphocytes. In this disease the lymphocytes multiply continuously and live too long, so there are too many of them circulating in the blood. These leukaemic lymphocytes look normal, but they are not fully developed and do not work properly. Over a period of time, these abnormal cells also replace the normal white cells, red cells and platelets in the bone marrow, which causes anaemia, easy bleeding and bruising, and infections. It is the most common type of leukaemia in young children. This disease also affects adults, especially those aged 65 years and older. Many



people with acute leukaemia can be cured; however, despite the available treatments, acute lymphoblastic leukaemia remains a serious and life threatening condition in a subgroup of patients.

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

At the time of designation, acute lymphoblastic leukaemia affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 30,000 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?

Treatment for leukaemia is complex and depends on a number of factors including the type of leukaemia, the extent of the disease and whether the leukaemia has been treated before. It also depends on the patient's age, symptoms, and general health. The primary treatment of acute lymphoblastic leukaemia is chemotherapy (using drugs to kill cancer cells) followed or combined with radiotherapy (using high-energy x-rays or other types of high-energy rays to kill cancer cells). Bone marrow transplantation is also available.

Mercaptopurine is already authorised in the European Union for the treatment of this condition, in a different pharmaceutical form.

The sponsor has submitted satisfactory argumentation to justify the assumption that mercaptopurine (oral liquid) might be of potential significant benefit for the treatment of acute lymphoblastic leukaemia, mainly because its administration in children will be easier and more precise dosing could be achieved. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain orphan status.

How is this medicine expected to work?

Mercaptopurine is a drug that decreases the action of an enzyme (a protein, called HGPRTase, which speeds up a specific chemical reaction in the cells). This enzyme is necessary for cell growth and replication. There are many biochemical effects of mercaptopurine, and although it is not known which of these mechanisms is more important, mercaptopurine is particularly toxic to cells that are rapidly dividing, such as cancer cells (including leukaemia cells).

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, no clinical trials in patients with acute lymphoblastic leukaemia had been initiated.

Mercaptopurine was authorised in the European Union, in different pharmaceutical forms from mercaptopurine (oral liquid), for the treatment of acute lymphoblastic leukaemia at the time of submission of the application.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 September 2007 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. At the time of designation, this represented a population of 500,300,000 (Eurostat 2007).

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

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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	Mercaptopurine (oral liquid)	Treatment of acute lymphoblastic leukaemia
Bulgarian	Меркаптопурин (перорална течност)	Лечение на остра лимфобластна левкемия
Croatian	Merkaptopurin (oralna tekućina)	Liječenje akutne limfoblastične leukemije
Czech	Mercaptopurine (perorální tekutina)	Léčba akutní lymfoblastické leukémie
Danish	Mercaptopurine (oral væske)	Behandling af akut lymfoblastær leukæmi
Dutch	Mercaptopurine (vloeistof voor oraal gebruik)	Behandeling van acute lymfoblastaire leukemie
Estonian	Merkaptopuriin (suukaudne vedelik)	Ägeda lümfoblastilise leukeemia ravi
Finnish	Merkaptopuriini (oraalineneste)	Akuutin lymfoblastileukemian hoito
French	Mercaptopurine (liquide oral)	Traitement de la leucémie lymphoblastique aiguë
German	Mercaptopurin (Lösung zum Einnehmen)	Behandlung der akuten lymphatischen Leukämie
Greek	Μερκατοπούρινη (στοματικό υγρό)	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	Mercaptopurine (orális oldat)	Akut lymphoblastos leukaemia kezelése
Italian	Mercaptopurina (liquido orale)	Trattamento della leucemia linfoblastica acuta
Latvian	Merkaptopurīns (šķidrums iekšķīgai lietošanai)	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	Merkaptopurinas (geriamasis skystis)	Ūmios limfoblastinės leukemijos gydymas
Maltese	Mercaptopurine (likwidu orali)	Kura tal-lewkimja limfoblastika akuta
Polish	Mercaptopurine (płyn do ust)	Leczenie ostrej białaczki limfoblastycznej
Portuguese	Mercaptopurina (líquido oral)	Tratamento da leucemia linfoblástica aguda
Romanian	Mercaptopurină (lichid oral)	Tratamentul leucemiei limfoblastice acute
Slovak	Merkaptopurín (perorálna kvapalina)	Liečba akútnej lymfoblastickej leukémie
Slovenian	Merkaptopurine (peroralna tekočina)	Zdravljenje akutne limfoblastne levkemije
Spanish	Mercaptopurina (líquido oral)	Tratamiento de la leucemia linfoblástica aguda
Swedish	Mercaptopurin (oral vätska)	Behandling av akut lymfatisk leukemi
Norwegian	Merkaptopurin (mikstur)	Behandling av akutt lymfoblastisk leukemi
Icelandic	Mercaptópúrín (lausn til inntöku)	Meðferð við bráðu eitlifrúmuhvítblæði

¹ At the time of transfer of sponsorship