European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole for the treatment of mastocytosis

On 16 November 2004, orphan designation (EU/3/04/242) was granted by the European Commission to AB Science, France, for N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole for the treatment of mastocytosis.

What is mastocytosis?

Mastocytosis is a disease in which cancer cells (so-called mast cells) are found in the bone marrow and in the organs where they accumulate. 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 mastocytosis develops, large numbers of a certain white blood cell called "mast cells" are produced. In normal circumstances these cells are mainly located in the skin and in the linings of the intestine. Their role is two-fold: they take part in the defence of these tissues against diseases and they contribute in the development of allergic reactions.

The manifestation of the disease is variable. In most of the patients, mainly in children, only the skin is involved and these lesions may spontaneously disappear (cutaneous mastocytosis). In some patients, more often occurring in adults, the cancer cells become aggressive tumours infiltrating organs (systemic mastocytosis) leading to organ failure and poor long-term outcome.

What are the methods of treatment available?

No satisfactory methods exist that were authorised at the time of application.

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

According to the information provided by the sponsor, mastocytosis was considered to affect about 14,000 persons in the European Union.

How is this medicinal product expected to act?

Enzymes are proteins produced by the human body that speed up the conversion of certain substances into other substances. N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole blocks (inhibits) the enzyme "tyrosine kinase", that is involved in the cell growth and proliferation. In cancer cells, the function of this enzyme is disturbed causing uncontrolled growth and multiplication of the cancer cells. N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole might, by inhibition of this tyrosine kinase, help in slowing down or stopping the further growth of the cancercells.

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What is the stage of development of this medicinal product?
The effects of N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole were evaluated in experimental models.

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

The medicinal product was not marketed anywhere worldwide for mastocytosis or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 7 October 2004 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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*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 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole	Treatment of mastocytosis
Czech	N-(metyl-diazacyklohexyl-metylbenzamid)-azafenyl-aminotiopyrol	Léčba mastocytózy
Danish	N-(methyldiazacyclohexyl-methylbenzamid)-azaphenyl-aminothiopyrrol	Behandling af mastocytose
Dutch	N-(methyl-diazacyclohexyl-methylbenzamide)-azafenyl-aminothiopyrrol	Behandeling van mastocytose
Estonian	N-(metüül-diasatsükloheksüül-metüülbensamiid)-asafenüül-aminotiopürrol	Mastotsüstoosi ravi
Finnish	N-(metyyli-diatsasykloheksyyli-metyylibentsamidi)-atsafenyyli-aminotiopyrroli	Mastosytoosin hoito
French	N-(méthyle-diazacyclohexyl-méthylbenzamide)-azaphényl-aminothiopyrrole	Traitement de la mastocytose
German	N-(Methyl-diazacyclohexyl-methylbenzamid)-azaphenyl-aminothiopyrrol	Behandlung von Mastozytose
Greek	Ν-(μέθυλο-διαζακυκλοεξυλενική-μεθυλοβενζοαμίδη) αζαφαινυλική-αμινοθειοπυρρόλη	Θεραπευτική αγωγή της Μαστοκύττωσης
Hungarian	N-(metil-diaza-ciklohexil-metilbenzamid)-aza-fenil-amino-tio-pirrol	Mastocytosis kezelése
Italian	N-(metil-diazacicloesil-metilbenzamide)-azafenil-aminotiopirrolo	Trattamento della mastocitosi
Latvian	N-(metil-diazacikloheksil-metilbenzamīds)-azafenil-aminotiopirols	Mastocitozes terapija
Lithuanian	N-(metil-diazacikloheksil-metilbenzamidas)-azafenil-aminotiopirolas	Mastocitozės gydymas
Maltese	N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole	Treatment of mastocytosis
Polish	N-(metylo-diazacykloheksylo-metylobenzamid)-azafenylo-aminotiopyrol	Leczenie mastocytozy
Portuguese	N-(metil-diazaciclohexil-metilbenzamida)-azafenil-	Tratamento da mastocitose

	aminotiopirrol	
Slovak	N-(metyl-diazacyklohexyl-metylbenzamid)-azafenyl-aminotiopyrol	Liečba mastocytózy
Slovenian	N-(metil-diazacikloheksil-metilbenzamid)-azafenil-aminotiopirol	Zdravljenje mastocitoze
Spanish	N-(metil-diazaciclohexil-metilbenzamida)-azafenil-aminotiopirrol	Tratamiento de la mastocitosis
Swedish	N-(metyl-diazacyklohexyl-metylbenzamid)-azafenyl-aminotiopyrrol	Behandling av mastocytos
Norwegian	N-(metyl-diazacykloheksyl-metylbenzamid)-azafenyl-aminotiopyrrol	Behandling av mastocytose
Icelandic	N-(metýl-díazacýklóhexýl-metýlbenzamíð)-azafenýl-amínótíópyrról)	Til meðferðar við mastfrumnageri