



Document Date: London, 6 January 2006
Doc.Ref.: EMEA/COMP/155795/2004

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF

N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole for the treatment of malignant gastro intestinal stromal tumours

On 21 December 2004, orphan designation (EU/3/04/251) was granted by the European Commission to AB Science, France, for N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole for the treatment of malignant gastro intestinal stromal tumours.

What are malignant gastro intestinal stromal tumours?

Malignant gastrointestinal stromal tumours (GIST) are the most common subtype of gastro-intestinal sarcomas, which belong to the group of soft tissue sarcomas. Soft tissue sarcomas are cancers of the tissues that support, surround and protect the organs of the body, such as muscle tissue and fat tissue. The cause of gastrointestinal stromal tumours is largely unknown. Gastrointestinal stromal tumours are most common in the stomach (60-70%), followed by small intestine (20-30%), and colon and rectum (5%). Gastrointestinal stromal tumours occur predominantly in middle-aged and older persons and are considered as a life-threatening condition.

What are the methods of treatment available?

The current methods of treatment are surgical removal of the tumour and treatment with a medicinal product, which belongs to the same group of substances called tyrosine kinase inhibitors, aimed to slow down and potentially stop the tumour growth.

N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole could be of potential significant benefit for the treatment of malignant GIST, because it could act in a different way and thereby might improve the long-term outcome of the patients. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

According to the information provided by the sponsor, malignant GIST 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 transformation of certain substances into other substances. N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole blocks (inhibits) the enzyme tyrosine kinase. This enzyme plays a role in a cascade of molecular reactions to bring a certain signal from outside the cell into the cell thereby controlling the growth of cells. In GIST, 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 enzyme activity at a certain level in the cascade, help in slowing down or stopping the further growth of the cancer cells.

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 malignant GIST were ongoing.

The medicinal product was not marketed anywhere worldwide for malignant GIST 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 16 November 2004 a positive opinion recommending the grant of the above-mentioned designation.

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.

For more information:

Sponsor's contact details:

AB Science

3, avenue Gerorge

F-75008 Paris

France

Telephone: + 33 1 47 20 10 35

Telefax: + 33 1 47 20 24 11

E-mail: contact@ab-science.com

Patients' associations contact points:

The Association of European Cancer Leagues (ECL)

c/o Belgian Federation against Cancer

Chaussée de Louvain, 479

B-1030 Brussels

Belgium

Telephone: +32 2 743 3705

Telefax: +32 2 734 9250

E-mail: chartmann@cancer.be

*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.

Ligue Nationale Contre le Cancer

13 Av. de la Grande Armée

75116 Paris

France

Telephone: +33 1 45 00 00 17

Tefefax: +33 1 45 00 63 06

E-mail: ligue@ligue-cancer.net

Deutsche Krebshilfe e.V.

Buschstrasse 32

53113 Bonn

Postfach 1467

53004 Bonn

Germany

Telephone: +49 2 28 72 99 00

Telefax: +49 22 87 29 90 11

E-mail: deutsche@krebshilfe.de

**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 malignant gastro intestinal stromal tumours
Czech	N-(metyl-diazacyklohexyl-metylbenzamid)-azafenyl-aminotiopyrol	Léčba gastrointestinálních stromálních tumorů
Danish	N-(methyldiazacyclohexyl-methylbenzamid)-azaphenyl-aminothiopyrrol	Behandling af malign gastrointestinal stromal tumor
Dutch	N-(methyl-diazacyclohexyl-methylbenzamide)-azafenyl-aminothiopyrrol	Behandeling van kwaadaardige gastro-intestinale stromale tumoren
Estonian	N-(metüül-diasatsükloheksüül-metüülbensamiid)-asafenüül-aminotiopürrol	Pahaloomuliste seedetrakti stroomaalsete kasvajate ravi.
Finnish	N-(metyyli-diatsasykloheksyyli-metyyllibentsamidi)-atsafenyli-aminotiopyrroli	Ruusuansulatuskanavan pahanlaatuisten stroomatumorien hoito
French	N-(méthyle-diazacyclohexyl-méthylbenzamide)-azaphényl-aminothiopyrrole	Traitement des tumeurs malignes stromales gastrointestinales
German	N-(Methyl-diazacyclohexyl-methylbenzamid)-azaphenyl-aminothiopyrrol	Behandlung von bösartigen gastrointestinalen Stromatumoren
Greek	N-(μέθυλο-διαζακυκλοεξυλενική-μεθυλοβενζοαμίδη) αζαφαινυλική-αμινοθειοπυρρόλη	Θεραπευτική αγωγή των κακοήθων γαστρεντερικών στρωματικών όγκων
Hungarian	N-(metil-diaza-ciklohexil-metilbenzamid)-aza-fenil-amino-tio-pirrol	Roszzindulatú gasztrointesztinális stromalis tumorok kezelése
Italian	N-(metil-diazacicloesil-metilbenzamide)-azafenil-aminotiopirrol	Trattamento dei tumori stromali gastrointestinali maligni
Latvian	N-(metil-diazacikloheksil-metilbenzamīds)-azafenil-aminotiopīrōls	Ļaundabīga kuņģa-zarnu trakta stromas audzēju terapija
Lithuanian	N-(metil-diazacikloheksil-metilbenzamid)-azafenil-aminotiopīrolas	Skrandžio ir žarnyno stromos piktybinių auglių gydymas
Polish	N-(metylo-diazacykloheksylo-metylobenzamid)-azafenylo-aminotiopyrol	Leczenie złośliwych nowotworów podścieliska przewodu pokarmowego
Portuguese	N-(metil-diazaciclohexil-metilbenzamida)-azafenil-aminotiopirrol	Tratamento de tumores estromais gastrintestinais malignos
Slovak	N-(metyl-diazacyklohexyl-metylbenzamid)-azafenyl-aminotiopyrol	Liečba malígnych gastrointestinálnych stromatóznych nádorov
Slovenian	N-(metil-diazacikloheksil-metilbenzamid)-azafenil-aminotiopirrol	Zdravljenje malignih gastrointestinalnih stromalnih tumorjev
Spanish	N-(metil-diazaciclohexil-metilbenzamida)-azafenil-aminotiopirrol	Tratamiento de los tumores malignos del estroma gastrointestinal
Swedish	N-(metyl-diazacyklohexyl-metylbenzamid)-azafenyl-aminotiopyrrol	Behandling av maligna gastrointestinala stromala tumörer

Norwegian	N-(metyl-diazacykloheksyl-metylbenzamid)-azafenyl-aminotiopyrrol	Behandling av maligne gastrointestinale stromale tumorer
Icelandic	N-(metýl-díazacyklóhexýl-metýlbenzamíð)-azafenýl-amínótíópyrról	Til meðferðar við grunnfrumuæxlum í meltingarfærum