

London, 7 December 2009

Doc.Ref.: EMA/COMP/662971/2009

## Committee for Orphan Medicinal Products

### Public summary of positive opinion for orphan designation of

### 8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)- one mono-hydrochloride for the treatment of ovarian cancer

On 30 November 2009, orphan designation (EU/3/09/695) was granted by the European Commission to Merck Sharp & Dohme Limited, United Kingdom, for 8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)-one mono-hydrochloride for the treatment of ovarian cancer.

#### What is ovarian cancer?

Ovarian cancer is cancer of the ovaries (two organs in the female reproductive system that produce eggs). Most ovarian cancers occur in women over the age of 50 years. Due to the absence of symptoms in the early stages of the disease, the majority of patients are diagnosed when the cancer has spread locally or to other parts of the body.

Ovarian cancer is a life-threatening disease that leads to poor long-term survival.

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

At the time of designation, ovarian cancer affected approximately 3 in 10,000 people in the European Union (EU)<sup>\*</sup>. This is equivalent to a total of around 151,000 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, several medicines were authorised in the EU for the treatment of ovarian cancer. The choice of treatment depended mainly on how advanced the disease is. Treatments included surgery and chemotherapy (medicines to treat cancer).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with ovarian cancer because it works in a different way to existing medicines and because early studies in experimental models indicate that it might improve the treatment of patients with this condition. 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?

8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)-one mono-hydrochloride is expected to work by blocking types of enzymes called AKT. These enzymes are protein kinases which are involved in cell survival and growth. In ovarian cancer, AKT enzymes are

<sup>\*</sup>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).

often activated, enabling cancer cells to survive and multiply. By blocking AKT, this medicine is expected to control cell survival and slow down the growth of cancer cells.

**What is the stage of development of this medicine?**

The effects of 8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-*f*][1,6]naphthyridin-3(2*H*)-one mono-hydrochloride have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the designated product including patients with ovarian cancer were ongoing.

At the time of submission, 8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-*f*][1,6]naphthyridin-3(2*H*)-one mono-hydrochloride was not authorised anywhere in the EU for ovarian cancer. Orphan designation of this medicine had been granted in the United States of America for ovarian cancer.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 October 2009 recommending the granting of this designation.

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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 Community) 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.

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

Language	Active ingredient	Indication
English	8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)-one mono-hydrochloride	Treatment of ovarian cancer
Bulgarian	8-[4-(1-аминоцикобутил)фенил]-9-фенил-1,2,4-триазоло[3,4-f][1,6]нафтиридин-3(2H)- едно моно - хидрохлорид	Лечение на рак на яйчниците
Czech	8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)-on monohydrochlorid	Léčba karcinomu vaječníků
Danish	8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)-on monohydrochlorid	Behandling af ovarie cancer
Dutch	8-[4-(1-aminocyclobutyl)fenyl]-9-fenyl-1,2,4-triazolo[3,4-f][1,6]naftyridine-3(2H)-on-mono-hydrochloride	Behandeling van ovariumkanker
Estonian	8-[4-(1-aminotsüklobutüül)fenüül]-9-fenüül-1,2,4-triasolo[3,4-f][1,6]naftüridiin-3(2H)- üks hüdrokloriid	Munasarjavähi ravi
Finnish	8-[4-(1-aminosyklobutyli)fenyli]-9-fenyli-1,2,4-triatsolo[3,4-f][1,6]naftyridin-3(2H)-oni mono-hydrokloridi	Munasarjasyövän hoito
French	Monochlorhydrate de 8-[4-(1-aminocyclobutyl)phényl]-9-phényl-1,2,4-triazolo[3,4-f][1,6]naphthyridine-3(2H)- one	Traitemet du cancer de l'ovaire
German	8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)- on Mono-Hydrochlorid	Behandlung des Ovarialkarzinoms
Greek	8-[4-(1-αμινοκυκλοβουτυλο)φαινυλο]-9-φαινυλο-1,2,4-τριαζολο[3,4-f][1,6]ναφθυριδιν-3(2H)-όνη μονο-ϋδροχλωρική	Θεραπεία του καρκίνου των ωοθηκών
Hungarian	8-[4-(1-aminociklobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridin-3(2H)-on mono-hidroklorid	Peteſszekrák kezelése
Italian	8-[4-(1-aminociclobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridin-3(2H)-one monocloridrato	Trattamento del carcinoma dell'ovaio
Latvian	8-[4-(1-aminociklobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridīn-3(2H)- viens monohidrohlorīds	Olnīcu vēža ārstēšanai
Lithuanian	8-[4-(1-aminociklobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridin-3(2H)- vienas monohidrochloridas	Kiaušidžių vėžio gydymas
Maltese	8-[4-(1-aminocyclobutyl)phenyl]-9-phenyl-1,2,4-triazolo[3,4-f][1,6]naphthyridin-3(2H)- one mono-hydrochloride	Kura tal-kanċer ta' l-ovarji
Polish	8-[4-(1-aminocyklobutylo)fenylo]-9-fenylo-1,2,4-triazolo[3,4-f][1,6]naftyrydyn-3(2H)onu chlorowodorek	Leczenie raka jajnika

Portuguese	8-[4-(1-aminociclobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridina-3(2H)- um monocloridrato	Tratamento do carcinoma do ovário
Romanian	8-[4-(1-aminociclobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridin-3(2H)- onă monoclorhidrat	Tratamentul cancerului ovarian
Slovak	8-[4-(1-aminocyklobutyl)fenyl]-9-fenyl-1,2,4-triazolo[3,4-f][1,6]naftyridin-3(2H)-ón monohydrochlorid	Liečba rakoviny vaječníkov
Slovenian	8-[4-(1-aminociklobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridin-3(2H)- on monoklorid	Zdravljenje raka na jajčnikih
Spanish	Monoclorhidrato de 8-[4-(1-aminociclobutil)fenil]-9-fenil-1,2,4-triazolo[3,4-f][1,6]naftiridin-3(2H)- ona	Tratamiento del cáncer de ovario
Swedish	8-[4-(1-aminocyklobutyl)fenyl]-9-fenyl-1,2,4-triazolo[3,4-f][1,6]naftyridin-3(2H)-on- monohydroklorid	Behandling av ovarialcancer
Norwegian	8-[4-(1-aminocyklobutyl)fenyl]-9-fenyl-1,2,4-triazolo[3,4-f][1,6]naftyridin-3(2H)- on monohydroklorid	Behandling av eggstokkrekf
Icelandic	8-[4-(1-amínócyklóbútyl) fenyl] - 9- fenyl – 1,2,4-trázóló [3,4 -f][1,6] naftýridín – 3 (2H) – eitt einhyðróklóríð	Meðferð eggjastokkakrabba meins