21 May 2015
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-Allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one for the treatment of ovarian cancer

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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 26 April 2012, orphan designation (EU/3/12/989) was granted by the European Commission to Merck Sharp & Dohme Limited, United Kingdom, for 2-Allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one for the treatment of ovarian cancer.

The sponsorship was transferred to AstraZeneca UK Limited, United Kingdom, in May 2015.

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 to other parts of the body.

Ovarian cancer is a life-threatening disease that is associated with poor long-term survival.

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

At the time of designation, ovarian cancer affected not more than 3 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 153,000 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?

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 was. 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 early studies show that it might improve the outcome of patients by further reducing the size of the tumour when used in combination with chemotherapy. This assumption 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?

This medicine is expected to work by blocking an enzyme called Wee1. Wee1 plays an important role in regulating cell growth and repairing DNA. However, in ovarian cancer the Wee1 enzyme has the effect of helping the cancer cells resist chemotherapy - firstly, by slowing down the rate at which the cancer cells divide (which makes them resistant to chemotherapy because chemotherapy works more effectively against rapidly dividing cells) and secondly, by repairing the DNA damage caused by the chemotherapy itself. As ovarian cancer cells commonly lack p53, another main protein involved in DNA repair, the cells rely on Wee1 for their survival.

By inhibiting Wee1, the medicine is therefore expected to make chemotherapy more effective at killing cancer cells and at slowing down or curing the disease.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with ovarian cancer were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for ovarian cancer or designated as an 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 8 March 2012 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 509,000,000 (Eurostat 2012).

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

Sponsor's contact details:

AstraZeneca UK Limited
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Cheshire SK10 4TG
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E-mail: medical.informationuk@astrazeneca.com

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	2-Allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one	Treatment of ovarian cancer
Bulgarian	2-алил-1-[6-(1-хидрокси-1-метилетил)пиридин-2-ил]-6-{[4-(4-метилпиперазин-1-ил)фенил]амино}-1,2-дихидро-3H-пиразоло [3,4-о]пиримидин-3-он	Лечение на рак на яйчниците
Croatian	2-alil-1-[6-(1-hidroksi-1-metiletil)piridin-2-il]-6-{[4-(4-metilpiperazin-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo[3,4-d]pirimidin-3-on	Liječenje raka jajnika
Czech	2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazol [3,4-d]pyrimidin-3-on	Léčba karcinomu vaječníků
Danish	2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-on	Behandling af ovarie cancer
Dutch	2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridine-2-yl]-6-{[4-(4-methylpiperazine-1-yl)fenyl]amino}-1,2-dihydro-3H-pyrazolo [3,4-d]pyrimidine-3-on	Behandeling van ovariumkanker
Estonian	2-allüül-1-[6-(1-hüdroksü-1-metüületüül)püridiin-2-üül]-6-{[4-(4-metüülpiperasiin-1-üül)fenüül]amino}-1,2-dihüdro-3H-pürasolo [3,4-d]pürimidiin-3-oon	Munasarjavähi ravi
Finnish	2-allyyli-1-[6-(1-hydroksi-1-metyylietyyli)pyridin-2-yyli]-6-{[4-(4-metyylipiperatsin-1-yyli)fenyyli]amino}-1,2-dihydro-3H-pyratsolo [3,4-d]pyrimidin-3-oni	Munasarjasyövän hoito
French	2-allyl-1-[6-(1-hydroxy-1-méthyléthyl)pyridine-2-yl]-6-{[4-(4-méthylpiperazine-1-yl)phényl]amino}-1,2-dihydro-3H-pyrazolo [3,4-d]pyrimidine-3-one	Traitement du cancer de l'ovaire
German	2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo [3,4-d]pyrimidin-3-on	Behandlung des Ovarialkarzinoms
Greek	2-αλλυλο-1-[6-(1-υδροξυ-μεθυλεθυλο)πυριδινο-2-υλ]-6-{[4-(4-μεθυλπιπεραζίνο--1-υλ)φαινυλ]άμινο}-1,2-διυδρο-3 Η- πυράζολο[3,4-d]πυριμιδίν-3-όνη	Θεραπεία του καρκίνου των ωοθηκών
Hungarian	2-allil-1-[6-(1-hidroxi-1-metiletil)piridin-2-il]-6-{[4-(4-metilpiperazin-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo [3,4-d]pirimidin-3-on	Petefészekrák kezelése
Italian	2-allil-1-[6-(1-idrossi-1-metiletil)piridin-2-il]-6-{[4-	Trattamento del carcinoma

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
	(4-metilpiperazin-1-il)fenil]amino}-1,2-diidro-3H-pirazolo [3,4-d]pirimidin-3-one	dell'ovaio
Latvian	2-alil-1-[6-(1-hidroksi-1-metiletil)piridīn-2-il]-6-{[4-(4-metilpiperazīn-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo [3,4-d]pirimidīn-3-ons	Olnīcu vēža ārstēšanai
Lithuanian	2-alil-1-[6-(1-hidroksi-1-metiletil)piridin-2-il]-6-{[4-(4-metilpiperazin-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo [3,4-d]pirimidin-3-onas	Kiaušidžių vėžio gydymas
Maltese	2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo [3,4-d]pyrimidin-3-one	Kura għal kanċer tal-ovarji
Polish	2-allilo-1-[6-(1-hydroksy-1-metyloetylo)pirydyn-2-ylo]-6-{[4-(4-metylopiperazyn-1-ylo)fenylo]amino}-1,2-dihydro-3H-pirazolo[3,4-d]pirymidyn-3-on	Leczenie raka jajnika
Portuguese	2-alil-1-[6-(1-hidroxi-1-metiletil)piridina-2-il]-6-{[4-(4-metilpiperazina-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo [3,4-d]pirimidina-3-ona	Tratamento do carcinoma do ovário
Romanian	2-alil-1-[6-(1-hidroxi-1-metiletil)piridin-2-il]-6-{[4-(4-metilpiperazin-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo [3,4-d]pirimidin-3-onă	Tratamentul cancerului ovarian
Slovak	2-alyl-1-[6-(1-hydroxy-1-metyletyl)pyridín-2-yl]-6-{[4-(4-metylpiperazín-1-yl)fenyl]amino}-1,2-dihydro-3H-pyrazolo [3,4-d]pyrimidín-3-ón	Liečba rakoviny vaječníkov
Slovenian	2-alil-1-[6-(1-hidroksi-1-metiletil)piridin-2-il]-6-{[4-(4-metilpiperazin-1-il)fenil]amino}-1,2-dihidro-3H-pirazolo [3,4-d]pirimidin-3-on	Zdravljenje raka na jajčnikih
Spanish	2-alil-1-[6-(1-hidroxi-1-metiletil)piridin-2-il]-6-{[4-(4-metilpiperazin-1-il)fenil]amino}-1,2-dihidro-3H-pirazol [3,4-d]pirimidin-3-ona	Tratamiento del cáncer de ovario
Swedish	2-allyl-1-[6-(1-hydroxi-1-metyletyl)pyridin-2-yl]-6-{[4-(4-metylpiperazin-1-yl)fenyl]amino}-1,2-dihydro-3H-pyrazol [3,4-d]pyrimidin-3-on	Behandling av ovarialcancer
Norwegian	2-allyl-1-[6-(1-hydroksy-1-metyletyl)pyridin-2-yl]-6-{[4-(4-metylpiperazin-1-yl)fenyl]amino}-1,2-dihydro-3H-pyrazolo [3,4-d]pyrimidin-3-on	Behandling av eggstokkreft
Icelandic	2-allýl-1-[6-(1-hýdroxý-1-metýletýl)pýrídín-2-ýl]-6-{[4-(4-metýlpíperazín-1-ýl)fenýl]amínó}-1,2-díhýdró-3H-pýrazóló [3,4-d]pýrimídín-3-ón	Meðferð eggjastokkakrabbameins