



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

7 March 2013
EMA/COMP/476246/2010 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl] phenyl} piperidine tosylate monohydrate salt for the treatment of mantle cell lymphoma

On 1 October 2010, orphan designation (EU/3/10/787) was granted by the European Commission to Merck Sharp & Dohme Limited, United Kingdom, for (3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl] phenyl} piperidine tosylate monohydrate salt for the treatment of mantle cell lymphoma.

The sponsorship was transferred to TESARO U.K. Limited, United Kingdom, in December 2012.

What is mantle cell lymphoma?

Mantle cell lymphoma is an aggressive cancer of a type of white blood cell called B-lymphocytes, or B cells. In mantle cell lymphoma, the B cells multiply too quickly and live for too long, so there are too many of them in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin area, caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats.

Mantle cell lymphoma is usually diagnosed in people aged over 50 years. It is more common in men than women. Mantle cell lymphoma is a severe and life-threatening disease that is associated with poor overall survival.

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

At the time of designation, mantle cell lymphoma affected approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 20,000 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, temsirolimus was authorised in the EU for the treatment of mantle cell lymphoma that has come back after previous treatment or has not responded to other treatments. The

*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 506,300,000 (Eurostat 2010).



main treatments for mantle cell lymphoma included chemotherapy (medicines to treat cancer), immunotherapy (medicines that stimulate the body's own immune system to kill the cancer cells) and radiotherapy (treatment with radiation). Haematopoietic (blood) stem cell transplantation was also used. This is a complex procedure where patients receive stem cells to help restore the bone marrow.

The sponsor has provided sufficient information to show that the medicine '(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl] phenyl} piperidine tosylate monohydrate salt' might be of significant benefit for patients with mantle cell lymphoma because it works in a different way to existing treatments, and early studies in experimental models indicate that it might be used in combination with existing treatment to improve the outcome of patients with this condition. 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 the enzymes known as poly(ADP-ribose) polymerase (PARP)-1 and -2. These enzymes are used to repair damaged DNA. By blocking PARP-1 and -2, the medicine prevents cancer cells from repairing their DNA, eventually killing them. It is expected that the medicine will be able to be used on its own in some patients with mantle cell lymphoma whose cancer cells do not have other ways of repairing DNA damage. The medicine is also expected to be used in combination with other cytotoxic (cell-killing) medicines that cause DNA damage, where it is expected to make them more effective by preventing DNA repair.

What is the stage of development of this medicine?

The effects of (3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl] phenyl} piperidine tosylate monohydrate salt 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 mantle cell lymphoma were planned.

At the time of submission, this medicine was not authorised anywhere in the EU for mantle cell lymphoma 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 16 July 2010 recommending the granting of this designation.

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:

TESARO U.K. Limited
c/o Sisec Limited
21 Holborn Viaduct
London, EC1A2DY
United Kingdom
Telephone: +44 20 3300 0105
Telefax: +44 20 3300 0105

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	(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl]phenyl} piperidine tosylate monohydrate salt	Treatment of mantle cell lymphoma
Bulgarian	(3S)-3-{4-[7-(аминокарбонил)-2H-индазол-2-ил] фенил} пиперидин тозилат монохидратна сол	Лечение на мантелно-клетъчна лимфома.
Czech	(3S)-3-{4-[7-(aminokarbonyl)-2H-indazol-2-yl]fenyl}piperidin monohydrát soli tosylátu	Léčba lymfomu z plášťové zóny
Danish	(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl]phenyl} piperidin tosylat monohydrat salt	Behandling af mantelcellelymfom
Dutch	(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl]fenyl} piperidine tosylaat monohydraat	Behandeling van mantelcellymfoom
Estonian	(3S)-3-{4-[7-(aminokarbonüül)-2H-indasool-2-üül]fenüül}piperidiin tosulaatmonohüdraadi sool	Mantelrakulise lümfoomi ravi
Finnish	(3S)-3-{4-[7-(aminokarbonyyli)-2H-indatsoli-2-yyli] fenyyl}piperidiini tosylaatmonohydraattisuola	Manttelisolu-lymfooman hoito
French	(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl]phényl} piperidine sel de tosylate monohydrate	Traitement des lymphomes du manteau
German	(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl]phenyl} piperidin Tosylat monohydrat Salz	Behandlung von Mantelzelllymphom
Greek	(3S)-3-{4-[7-(αμινοκαρβονυλο)-2H-ινδαζολο-2-] φαινυλο} πιπεριδίνη μονοϋδρικό τοζυλικό άλας	Θεραπεία του λεμφώματος μανδυκών κυττάρων
Hungarian	(3S)-3-{4-[7-(aminokarbonil)-2H-indazol-2-il]fenil} piperidin tozilát monohidrát só	Köpenysejtes lymphoma kezelése
Italian	(3S)-3-{4-[7-(aminocarbonil)-2H-indazol-2-il]fenil} piperidina sale tosilato monoidrato	Trattamento del linfoma con cellule a mantello
Latvian	(3S)-3-{4-[7-(aminokarbonil)-2H-indazol-2-il]fenil} piperidīna tozīlāta monohidrāta sāls	Mantijšūnu limfomas ārstēšana
Lithuanian	(3S)-3-{4-[7-(aminokarbonil)-2H-indazol-2-il]fenil} piperidin tosilato monohidrato druska	Mantijos ląstelių limfomos gydymas
Maltese	(3S)-3-{4-[7-(aminocarbonyl)-2H-indazol-2-yl]phenyl} piperidine tosylate monohydrate salt	Kura tal-limfoma taċ-ċelloli tal-mantell
Polish	Tosylan (3S)-3-{4-[7-(aminokarbonylo)-2H-indazolo-2-ylo]fenylo}piperydyny jednowodny	Leczenie chłoniaków z komórek płaszczowych
Portuguese	(3S)-3-{4-[7-(aminocarbonil)-2H-indazole-2-il]fenil} piperidina sal tosilato monohidratado	Tratamento de linfoma de células do manto
Romanian	(3S)-3-{4-[7-(aminocarbonil)-2H-indazol-2-il]fenil} piperidină sare tosilat monohidrat	Tratamentul limfomului cu celule în manta
Slovak	(3S)-3-{4-[7-(aminokarbonyl)-2H-indazol-2-yl]fenyl}piperidín monohydrát tosylát	Liečba lymfómu plášťovej zóny

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	(3S)-3-{4-[7-(aminokarbonil)-2H-indazol-2-il] fenil} piperidin tozilat monohidrat	Zdravljenje limfoma plaščnih celic
Spanish	Monohidrato de sal de (3S)-3-{4-[7-(aminocarbonil)-2H-indazol-2-il] fenil} piperidina tosilato	Tratamiento del linfoma de células del manto
Swedish	(3S)-3-{4-[7-(aminokarbonyl)-2H-indazol-2-yl] fenyl} piperidin tosylatmonohyratsalt	Behandling av mantelcellslymfom
Norwegian	(3S)-3-{4-[7-(aminokarbonyl)-2H-indazol-2-yl] fenyl}piperidin tosylatmonohydrat salt	Behandling av mantelcelle-lymfom
Icelandic	(3S)-3-{4-[7-(amínókarbónýl)-2H-indazól-2-ýl] fenýl} píperidín tosýlateinhýdrat salt	Meðferð möttulfrumu eitlakraðbameins