



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

2-(2-phenylvinyl)-4-[4- methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidine L(+) tartrate salt for the treatment of hepatocellular carcinoma

On 10 August 2015, orphan designation (EU/3/15/1544) was granted by the European Commission to Dr Ulrich Granzer, Germany, for 2-(2-phenylvinyl)-4-[4- methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidine L(+) tartrate salt for the treatment of hepatocellular carcinoma.

### What is hepatocellular carcinoma?

Hepatocellular carcinoma is a primary cancer of the liver (a cancer that starts in the liver, rather than one that has spread to the liver from elsewhere in the body). It is more common in men than in women, and occurs mostly in people who have liver scarring (cirrhosis) or have had an infection with the hepatitis B or C viruses. Symptoms of the disease include pain and swelling in the abdomen, weight loss, weakness, loss of appetite and nausea.

Hepatocellular carcinoma is a serious disease and is life threatening because it is often diagnosed at an advanced stage.

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

At the time of designation, hepatocellular carcinoma affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 people<sup>\*</sup>, 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, some patients with early stage hepatocellular carcinoma were treated with surgery to remove part of the liver. Chemotherapy (medicines to treat cancer) was generally used after surgery or on its own if surgery was not possible or the disease had spread to other parts of the

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<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 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).



body (metastatic disease). A medicine called sorafenib was authorised in the EU for use in hepatocellular carcinoma.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with hepatocellular carcinoma. Data provided include laboratory data showing improved beneficial effects with this product as compared with authorised treatments and data from one patient whose disease had come back after previous treatment showing a clinical response with this product. This assumption of significant benefit 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 an aurora A kinase inhibitor. This means that it works by blocking the activity of an enzyme known as aurora A kinase, which plays a role in cell division and is found in high amounts in some cancer cells, including hepatocellular carcinoma cells. By blocking this enzyme, the medicine is expected to interfere with the division of cancer cells and thereby slow down or stop the growth of the cancer.

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

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

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

At the time of submission, the medicine was not authorised anywhere in the EU for hepatocellular carcinoma 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 2015 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 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:

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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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-(2-phenylvinyl)-4-[4-methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidine L(+) tartrate salt	Treatment of hepatocellular carcinoma
Bulgarian	2-(2-фенилвинил)-4-[4-метилпиперазин-1-ил]-6-(5-метил-2H-пиразол-3-ил-амино)-пиримидин L(+) тартаратна сол	Лечение на хепатоцелуларен карцином
Croatian	2-(2-fenilvinil)-4-[4-metilpiperazin-1-il]-6-(5-metil-2H-pirazol-3-il-amino)-pirimidin-L(+)-tartarat	Liječenje hepatocelularnog karcinoma
Czech	2-(2-fenylvinyl)-4-[4-methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidin L(+) tartrát	Léčba hepatocelulárního karcinomu
Danish	2-(2-phenylvinyl)-4-[4-methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidin L(+) tartratsalt	Behandling af hepatocellulært karcinom
Dutch	2-(2-fenylvinyl)-4-[4-methylpiperazine-1-yl]-6-(5-methyl-2H-pyrazool-3-yl-amino)-pyrimidine L(+) tartraatzout	Behandeling van hepatocellulair carcinoom
Estonian	2-(2-fenüülviniüül)-4-[4-metüülpiperasiin-1-üül]-6-(5-metüül-2H-pürasool-3-üül-amino) pürimidiin L(+) tartraatsool	Hepatotsellulaarse kartsinoomi ravi
Finnish	2-(2-fenyylivinyyli)-4-[4-metyyilpiperatsin-1-yyli]-6-(5-metyyli-2H-pyratsol-3-yyli-amino)-pyrimidiinin (L +) tartraattisuola	Hepatosellulaarisen karsinooman hoito
French	2-(2-phénylvinyle)-4-[4-méthylpipérazine-1-yl]-6-(5-méthyl-2H-pyrazol-3-yl-amino)-pyrimidine L(+) tartrate	Traitement du cancer hépatocellulaire
German	2-(2-phenylvinyl)-4-[4-Methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidin L(+) Weinsäuresalz	Behandlung des Leberzellkarzinoms
Greek	2-(2-φαινυλοβινύλιο)-4-[4-μεθυλπιπεραζιν-1-υλ]-6-(5-μεθυλ-2H-πυραζολ-3-υλο-αμινο)-πυριμιδίνη L(+) τρυγικού άλατος	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	2-(2-fenil-vinil)-4-[4-metil-piperazin-1-il]-6-(5-metil-2H-pirazol-3-il-amino)-pirimidin-L(+)-tartarát	Hepatocelluláris carcinoma kezelése
Italian	2-(2-phenylvinyl)-4-[1-il-metilpiperazin]4]-6-(5-metil-2H-pirazol-3-il-ammino)-pirimidina L(+) tartrato	Trattamento del carcinoma epatocellulare
Latvian	2-(2-fenilvinil)-4-[4-metilpiperazīn-1-il]-6-(5-metil-2H-pirazol-3-il-amino)-pirimidīna L(+) tartrāta sāls	Hepatocellulāras karcinomas ārstēšana

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Lithuanian	2-(2-fenilvinil)-4-[4-metilpiperazin-1-il]-6-(5-metil-2H-pirazol-3-il-amino)-pirimidino L(+) tartrato druska	Hepatoceliulinės karcinomos gydymas
Maltese	2-(2-phenylvinil)-4-[4-methylpiperazin-1-yl]-6-(5-methyl-2H-pyrazol-3-yl-amino)-pyrimidine L(+) tartrate salt	Kura tal-karċinoma epatoċellulari
Polish	2-(2-fenylowinylo)-4-[4-metylopiperazyn-1-ylo]-6-(5-metylo-2H-pirazol-3-ilo-amino)pirymidyno L(+) winian	Leczenie raka wątrobowokomórkowego
Portuguese	2-(2-fenilvinil)-4-[1-il-metilpiperazin]4]-6-(5-metil-2H-pirazol-3-il-amino)-pirimidina L(+) tartarato	Tratamento do carcinoma hepatocelular
Romanian	Tartrat L(+) de 2-(2-fenilvinil)-4-[4-metilpiperazin-1-il]-6-(5-metil-2H-pirazol-3-il-amino)pirimidină	Tratamentul carcinomului hepatocelular
Slovak	2-(2-fenylvinil)-4-[4-Metylpipezazín-1-yl]-6-(5-metyl-2H-pyrazol-3-yl-amino)pyrimidín L(+) tartrát	Liečba hepatocelulárneho karcinómu
Slovenian	2-(2-feni)-4-[4-metilpiperazin-1-il]-6-(5-metil-2H-pirazol-3-il-amino)pirimidin L(+) tartratna sol	Zdravljenje hepatocelularnega karcinoma
Spanish	2-(2-fenilvinilo)-4-[1-il-metilpiperazin]4]-6-(5-metil-2H-pirazol-3-il-amino)-pirimidin L(+) tartrate	Tratamiento del carcinoma hepatocelular
Swedish	2-(2-fenylvinyl)-4-[4-metylpipezazín-1-yl]-6-(5-metyl-2H-pyrazol-3-yl-amino)-pyrimidin-L(+) tartratsaltt	Behandling av hepatocellulärt karcinom
Norwegian	2-(2-fenylvinyl)-4-[4-metylpipezazín-1-yl]-6-(5-metyl-2H-pyrazol-3-yl-amino)-pyrimidin L(+) tartratsalt	Behandling av hepatocellulært karsinom
Icelandic	2-(2-phenýlvínýl)-4-[4-metýlpíperasín-1-ýl]-6-(5-metýl-2H-pýrasól-3-ýl-amínó)pýrimn L(+) tartrat salt	Meðferð við lifrarfrumukrabbameini