



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

### Tirapazamine for the treatment of hepatocellular carcinoma

On 17 July 2017, orphan designation (EU/3/17/1897) was granted by the European Commission to PhaRA bvba, Belgium, for tirapazamine 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 after hepatitis B or C infection. Features of the disease include yellow skin, pain and swelling in the abdomen, easy bruising, weight loss, weakness, loss of appetite and nausea.

Hepatocellular carcinoma is long-term debilitating and life threatening, with patients surviving on average for a few months or years after diagnosis.

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

At the time of designation, hepatocellular carcinoma affected approximately 1.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 77,000 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, some patients with early stage hepatocellular carcinoma were treated with surgery to remove part of the liver, liver transplantation or radiofrequency ablation (directing heat and electricity through a needle to destroy cancer cells). Chemotherapy (medicines to treat cancer) was used if surgery was not possible or the disease had spread to other parts of the body (metastatic disease). Nexavar (sorafenib) was authorised in the EU for use in hepatocellular carcinoma.

The sponsor has provided sufficient information to show that tirapazamine might be of significant benefit for patients with hepatocellular carcinoma, with early studies indicating that it can improve

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\*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 515,700,000 (Eurostat 2017).



treatment outcomes when compared with current treatments. 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?**

Tirapazamine damages the DNA strands in cells, which stops the cells from multiplying. However, the medicine only works in an environment with little or no oxygen. In order for the medicine to work against liver cancer cells, patients will undergo a surgical procedure known as transarterial embolisation, which blocks off part of the tumour's blood supply, creating a low-oxygen environment. Tirapazamine is to be injected first into the patient followed by embolisation. In this way, the medicine is expected to damage the DNA of cancer cells and help slow down the progression of the disease.

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

The effects of tirapazamine have been evaluated in experimental models.

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

At the time of submission, the medicine was not authorised anywhere in the EU for hepatocellular carcinoma. Orphan designation had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 June 2017 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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	Tirapazamine	Treatment of hepatocellular carcinoma
Bulgarian	Тирапазамин	Лечение на хепатоцелуларен карцином
Croatian	Tirapazamin	Liječenje hepatocelularnog karcinoma
Czech	Tirapazamin	Léčba hepatocelulárního karcinomu
Danish	Tirapazamin	Behandling af hepatocellulært karcinom
Dutch	Tirapazamine	Behandeling van hepatocellulair carcinoom
Estonian	Tirapasamiin	Hepatosellulaarse kartsinoomi ravi
Finnish	Tirapatsamiini	Hepatosellulaarisen karsinooman hoito
French	Tirapazamine	Traitement du cancer hépatocellulaire
German	Tirapazamin	Behandlung des Leberzellkarzinoms
Greek	Τιραπαζαμίνη	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Tirapazamin	Hepatocelluláris carcinoma kezelése
Italian	Tirapazamina	Trattamento del carcinoma epatozellulare
Latvian	Tirapazamīns	Hepatocelulāras karcinomas ārstēšana
Lithuanian	Tirapazaminas	Hepatoceliulinės karcinomos gydymas
Maltese	Tirapazamine	Kura tal-karcinoma epatoċellulari
Polish	Tirapazamina	Leczenie raka wątrobowokomórkowego
Portuguese	Tirapazamina	Tratamento do carcinoma hepatocelular
Romanian	Tirapazamină	Tratamentul carcinomului hepatocelular
Slovak	Tirapazamín	Liečba hepatocelulárneho karcinómu
Slovenian	Tirapazamin	Zdravljenje hepatocelularnega karcinoma
Spanish	Tirapazamina	Tratamiento del carcinoma hepatocelular
Swedish	Tirapazamin	Behandling av hepatocellulärt karcinom
Norwegian	Tirapazamin	Behandling av hepatocellulært karsinom
Icelandic	Tírapazamín	Meðferð við lífrarfrumukrabbameini

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