



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate for the treatment of renal cell carcinoma

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in August 2010 on request of the sponsor.

On 29 July 2004, orphan designation (EU/3/04/218) was granted by the European Commission to Innate Pharma SAS, France, for (R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate for the treatment of renal cell carcinoma.

The sponsor's name changed from Innate Pharma SAS to Innate Pharma S.A. in March 2006.

What is renal cell carcinoma?

Renal cell carcinoma (also called cancer of the kidney or renal adenocarcinoma) is a disease in which cancer (malignant) cells are found in certain tissues of the kidney. Inside each kidney are tiny tubules that filter and clean the blood, taking out waste products, and making urine. Renal cell carcinoma is a cancer of the lining of the tubules in the kidney. Renal cell carcinoma accounts for approximately 85% of all kidney cancers. Signs of cancer are difficult to detect in early stages of the disease, and about half of the patients are diagnosed when the disease has spread around the kidney or to distant parts of the body. Surgery is a common treatment of renal cell cancer, and allows taking out the cancer in an operation, although the cancer may appear again. Renal cell carcinoma is life-threatening.

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

At the time of designation, renal cell carcinoma affected approximately 3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 138,000 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).

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.



What treatments are available?

There are treatments for most patients with renal cell cancer. These may include surgery (taking out the cancer in an operation), chemotherapy (using drugs to kill cancer cells), radiation therapy (using high-dose x-rays or other high-energy rays to kill cancer cells), hormone therapy (using hormones to stop cancer cells from growing), and biological therapy (using the body's immune system to fight cancer). The primary therapies for advanced cancer are biologic agents, such as interleukin-2 (IL-2) and interferon- α (IFN- α). Other anticancer agents had also been authorised in the Community for treatment of renal cell carcinoma at the time of submission of the application for orphan designation.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that (R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate might be of potential significant benefit for the treatment of renal cell carcinoma. The potential significant benefit is mainly due to the fact that it may act in a different way than other available medicines. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

The body's immune system is a complex system made up of organs such as the bone marrow, the thymus (a gland behind the breast bone), the spleen (an organ in the abdomen, near the stomach), and the lymph nodes (or lymph glands, located throughout the body), which are connected by a network of tiny lymphatic vessels. There are two main types of cells, which make up the lymphatic tissue. These cells are called lymphocytes and belong to the group of white blood cells. The two types are called B lymphocytes (B cells) and T lymphocytes (T cells). T lymphocytes can carry different types of receptors (proteins found on the surface of the cell, with a specific shape on which another, free, specific protein can bind in order to activate certain biologic reactions of that cell). Depending on the type of receptor the T lymphocyte is carrying, they are subdivided in different types of T cells. In healthy human blood, one of these subtype T cells, the so-called gamma δ 2 T cells, are only represented in small amounts. This subtype T cell seems to play a role in the control and destruction of tumour cells, as shown in experimental studies. (R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate can specifically increase the amount of this T cell subset; this may result in stimulation of both T and B cell immunity and therefore might have a role in helping the immune system to destroy the cancer cells. The overall expected outcome is the destruction of cancer cells.

What is the stage of development of this medicine?

The effects of (R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with renal cell carcinoma were ongoing.

(R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate was not marketed anywhere worldwide for renal cell carcinoma or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 June 2004 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:

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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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	(R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate	Treatment of renal cell carcinoma
Czech	(R, S)-3-(bromometyl)-3-butanol-1-yl-difosfát	Léčba renálního karcinomu
Danish	(R, S)-3-(bromomethyl)-3-butanol-1-yl-difosfat	Behandling af renalcellekarcinom
Dutch	(R, S)-3-(broommethyl)-3-butanol-1-yl-difosfaat	Behandeling van renaal celcarcinoom
Estonian	(R, S)-3-(broommetüül)-3-butanol-1-üül-difosfaat	Neeruvähi ravi
Finnish	(R, S) -3-(bromimetyyli)-3-butanoli-1-yl-difosfaatti	Munuaissolukarsinooman hoito
French	(R, S)-3-(bromométhyl)-3-butanol-1-yl-diphosphate	Traitement du carcinome rénal
German	(R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphat	Behandlung von Nierenzellkarzinom
Greek	(R, S)-3-(βρωμομεθύλιο)-3- βουτανόλη -1-υλ-διφωσφορικό	Θεραπεία του νεφροκυτταρικού καρκινώματος.
Hungarian	(R, S)-3-(brom-metil)-3-butanol-1-il-difoszfát	Vesesejtes carcinoma kezelése
Italian	(R, S)-3-(bromometil)-3-butanol-1-yl-difosfato	Trattamento del carcinoma a cellule renali
Latvian	(R, S)-3-bromometils-3-butanols-1-yl-difosfāts	Nieru karcinomas ārtēšana
Lithuanian	(R, S)-3-(bromometil)-3-butanol-1-il-difosfatas	Inkstų ląstelių karcinomos gydymas
Maltese	(R, S)-3-(bromomethyl)-3-butanol-1-yl-diphosphate	Treatment of renal cell carcinoma
Polish	(R, S)-3-(bromometylo)-3-butanolo-1-yl-difosfat	Leczenie raka nerki
Portuguese	(R, S)-3-(bromometil)-3-butanol-1-il-difosfato	Tratamento do carcinoma das células renais
Slovak	(R,S) – 3 (brómometyl) – 3 – butanol – 1 –yl difosfát	Liečba karcinómu obličky
Slovenian	(R, S)-3-(brommetil)-3-butanol-1-yl-difosfat	Zdravljenje karcinoma ledvičnih celic
Spanish	(R, S)-3-(bromometil)-3-butanol-1-il-difosfato	Tratamiento del carcinoma de células renales
Swedish	(R, S)-3-(bromometyl)-3-butanol-1-yl-difosfat	Behandling av njurcellskarcinom
Norwegian	(R,S)-3-(bromometyl)-3-butanol-1-yl-difosfat	Behandling av nyrecellekarsinom
Icelandic	(R,S)-3-(brómómetýl)-3-bútanól-1-yl-tvífosfat	Meðferð á nýrafrumukrabbameini

¹ At the time of designation