



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

(S)-3-((3-(1-((6-(3,4-Dimethoxyphenyl)pyrazin-2-yl)amino)ethyl)phenyl)carbamoyl)-5-methylpidin-1-ium for the treatment of pulmonary arterial hypertension

On 29 May 2019, orphan designation (EU/3/19/2158) was granted by the European Commission to MWB Consulting S.A.R.L., France, for (S)-3-((3-(1-((6-(3,4-dimethoxyphenyl)pyrazin-2-yl)amino)ethyl)phenyl)carbamoyl)-5-methylpidin-1-ium (also known as GB002) for the treatment of pulmonary arterial hypertension.

### What is pulmonary arterial hypertension?

Pulmonary arterial hypertension is a condition in which patients have abnormally high blood pressure in the arteries in the lungs. In patients with this condition, the walls of the arteries that carry blood to the lungs become thick and stiff. This narrows the space through which the blood flows, making it harder for the heart to pump blood into the lungs.

Pulmonary arterial hypertension is a long-term debilitating and life-threatening condition that shortens patients' life expectancy because it may lead to difficulty breathing and heart failure.

### What is the estimated number of patients' pulmonary arterial hypertension?

At the time of designation, pulmonary arterial hypertension affected approximately 1.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 78,000 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).

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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 518,400,000 (Eurostat 2019).

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## **What treatments are available?**

Several medicines were authorised for the treatment of pulmonary arterial hypertension in the EU at the time of designation. They included ambrisentan, bosentan, epoprostenol, iloprost, macitentan, riociguat, selexipag, sildenafil, tadalafil and treprostinil. Some patients also underwent lung transplantation or atrial septostomy (an operation to create a small hole between the upper two chambers of the heart, the atria).

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with pulmonary arterial hypertension. Early data from laboratory studies indicate that adding the medicine to standard treatment could further reduce high blood pressure in the lung vessels. 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 blocks a receptor (target) called platelet-derived growth factor receptor (PDGFR), which is involved in stimulating the growth of cells that make up the blood vessels. PDGFR is thought to be over-active in patients with pulmonary arterial hypertension. By blocking PDGFR, this medicine is expected to reduce the narrowing and thickening of the blood vessels in patients with this condition, thus improving the symptoms of the disease.

## **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, no clinical trials with the medicine in patients with pulmonary arterial hypertension had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of pulmonary arterial hypertension. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 29 April 2019, 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	(S)-3-((3-(1-((6-(3,4-dimethoxyphenyl)pyrazin-2-yl)amino)ethyl)phenyl)carbamoyl)-5-methylpyridin-1-ium	Treatment of pulmonary arterial hypertension
Bulgarian	(S)-3-((3-(1-((6-(3,4-диметоксифенил)празин-2-ил)амино)етил)фенил)карбамоил)-5-метилпиридин-1-иум	Лечение на белодробна артериална хипертония
Croatian	(S)-3-((3-(1-((6-(3,4-dimetoksifenil)pirazin-2-il)amino)etil)fenil)karbamoil)-5-metilpiridin-1-ium	Liječenje plućne arterijske hipertenzije
Czech	(S)-3-((3-(1-((6-(3,4-dimethoxyfenyl)pyrazin-2-yl)amino)ethyl)fenyl)karbamoyl)-5-methylpyridin-1-ium	Léčba plicní arteriální hypertenze
Danish	(S)-3-((3-(1-((6-(3,4-dimethoxyphenyl)pyrazin-2-yl)amino)ethyl)phenyl)carbamoyl)-5-methylpyridin-1-ium	Behandling af pulmonal arteriel hypertension
Dutch	(S)-3-((3-(1-((6-(3,4-dimethoxyfenyl)pyrazin-2-yl)amino)ethyl)fenyl)carbamoyl)-5-methylpyridin-1-ium	Behandeling van pulmonale arteriële hypertensie
Estonian	(S)-3-((3-(1-((6-(3,4-dimetoksüfenüül)prüasiin-2-üül)amino)etüül)fenüül)karbamoüül)-5-metüülpridiin-1-ium	Arteriaalse pulmonaalhüpertensiooni ravi
Finnish	(S)-3-((3-(1-((6-(3,4-dimetoksifenyyli)pyratsin-2-yyli)amino)etyyli)fenyyli)karbamoyyli)-5-metyylipiridin-1-ium	Keuhkoverenkierron hypertension hoito
French	(S)-3-((3-(1-(6-(3,4-diméthoxyphényl)pyrazin-2-yl)amino)éthyl)phényl)carbamoyl)-5-méthylpyridine-1-ium	Traitement de l'hypertension artérielle pulmonaire

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

Language	Active ingredient	Indication
German	(S)-3-((3-(1-((6-(3,4-dimethoxyphenyl)pyrazin-2-yl)amino)ethyl)phenyl)carbamoil)-5-methylpidin-1-ium	Behandlung der pulmonalen arteriellen Hypertonie
Greek	(S)-3-((3-(1-((6-(3,4-διμεθοξυφαινυλ)προζαζιν-2-υλ)αμινο)αιθυλ)φαινυλ)καρβαμοΐλ)-5-μεθυλπριδιν-1-ιο	Θεραπεία της πνευμονικής αρτηριακής υπέρτασης
Hungarian	(S)-3-((3-(1-((6-(3,4-dimetoxi-fenil)pyrazin-2-il)-amino)-etil)-fenil)-karbamoil)-5-methylpidin-1-ium	Pulmonáris arteriális hipertónia kezelése
Italian	(S)-3-((3-(1-((6-(3,4-dimetossifenil)pirazin-2-il)ammino)etil)fenil)carbamoil)-5-metilpidin-1-io	Trattamento dell'ipertensione arteriosa polmonare
Latvian	(S)-3-((3-(1-((6-(3,4-dimetoksifenil)pirazīn-2-il)amino)etil)fenil)karbamoil)-5-metilpidīn-1-iums	Plaušu arteriālās hipertensijas ārstēšana
Lithuanian	(S)-3-((3-(1-((6-(3,4-dimetoksifenil)pirazin-2-il)amino)etil)fenil)karbamoil)-5-metilpidin-1-iumas	Plaučių arterinės hipertenzijos gydymas
Maltese	(S)-3-((3-(1-((6-(3,4-dimetossifenil)pirazin-2-il)amino)etil)fenil)karbamoil)-5-metilpidin-1-ium	Kura ta' pressjoni arterjali pulmonari għolja
Polish	(S)-3-((3-(1-((6-(3,4-dimetoksyfenylo)pyrazin-2-ylo)amino)etylo)fenylo)karbamoilo)-5-metylopirydyn-1-yl	Leczenie tętniczego nadciśnienia płucnego
Portuguese	S)-3-((3-(1-((6-(3,4-dimetoxifenil)pirazin-2-il)amino)etil)fenil)carbamoil)-5-metilpidin-1-ium	Tratamento da hipertensão arterial pulmonar
Romanian	(S)-3-((3-(1-((6-(3,4-dimetoxifenil)-pirazin 2-il)amino)etil)fenil)carbamoil)-5-metilpidin-1-ium	Tratamentul hipertensiunii arteriale pulmonare
Slovak	(S)-3-((3-(1-((6-(3,4-dimetoxyfenyl)pyrazin-2-yl)amino)etyl)fenyl)karbamoyl)-5-methylpidin-1-ium	Liečba pľúcnej arteriálnej hypertenzie vrátane
Slovenian	(S)-3-((3-(1-((6-(3,4-dimetoksifenil)pirazin-2-il)amino)etil)fenil)karbamoil)-5-metilpidin-1-il	Zdravljenje pljučne arterijske hipertenzije vključno

Language	Active ingredient	Indication
Spanish	(S)-3-((3-(1-((6-(3,4-dimetoxifenil)prazin-2-il)amino)etil)fenil)carbamoil)-5-metilpridin-1-io	Tratamiento de la hipertensión arterial pulmonar
Swedish	(S)-3-((3-(1-((6-(3,4-dimetoxifenyl)pryazin-2-yl)amino)etyl)fenyl)karbamoyl)-5-methylpridin-1-ium	Behandling av pulmonell arteriell hypertension
Norwegian	(S)-3-((3-(1-((6-(3,4-dimetoksyfenyl)pryazin-2-yl)amino)etyl)fenyl)karbamoyl)-5-metylpyridin-1-ium	Behandling av pulmonal arteriell hypertensjon
Icelandic	(S)-3-((3-(1-((6-(3,4-dímetoxýfenýl)prýazín-2-ýl)amínó)etýl)fenýl)karbamóýl)-5-metýlprídín-1-ium	Meðferð við háþrýstingi í lungnablóðrás