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Public summary of opinion on orphan designation

Ralinepag for the treatment of pulmonary arterial hypertension

On 11 January 2019, orphan designation (EU/3/18/2130) was granted by the European Commission to Arena Pharmaceuticals Limited, Ireland, for ralinepag 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 affected by the condition?

At the time of designation, pulmonary arterial hypertension affected less than 1.8 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 93,000 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?

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).

*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 517,400,000 (Eurostat 2018).

The sponsor has provided sufficient information to show that ralinepag might be of significant benefit for patients with pulmonary arterial hypertension. Early data from studies in patients indicate that adding the medicine to standard treatment could reduce resistance to blood flow in the lungs and improve other features of the 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?

The production of a substance called prostacyclin is reduced in patients with pulmonary arterial hypertension. Prostacyclin, which is produced in the cells of blood vessels, causes the blood vessels to expand and slows down the growth of cells that make up the vessels. Ralinepag works in the same way as prostacyclin and is expected to help expand the blood vessels and thereby allow blood to flow more freely and relieve the patient's symptoms.

What is the stage of development of this medicine?

The effects of ralinepag 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 pulmonary arterial hypertension were ongoing.

At the time of submission, ralinepag was not authorised anywhere in the EU for pulmonary arterial hypertension. 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 6 December 2018 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:

Contact details of the current sponsor for this orphan designation can be found on [the EMA website](#).

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 orphan condition in all official EU languages¹, Norwegian and Icelandic

| Language | Active ingredient | Indication |
|------------|-------------------|------------------------------------------------------|
| English | Ralinepag | Treatment of pulmonary arterial hypertension |
| Bulgarian | Ралинепаг | Лечение на белодробна артериална хипертония |
| Croatian | Ralinepag | Liječenje plućne arterijske hipertenzije |
| Czech | Ralinepag | Léčba plicní arteriální hypertenze |
| Danish | Ralinepag | Behandling af pulmonal arteriel hypertension |
| Dutch | Ralinepag | Behandeling van pulmonale arteriële hypertensie |
| Estonian | Ralinepaag | Arteriaalse pulmonaalhüpertensiooni ravi |
| Finnish | Ralinepagi | Keuhkoverenkierron hypertension hoito |
| French | Ralinepag | Traitement de l'hypertension artérielle pulmonaire |
| German | Ralinepag | Behandlung der pulmonalen arteriellen Hypertonie |
| Greek | Ralinepag | Θεραπεία της πνευμονικής αρτηριακής υπέρτασης |
| Hungarian | Ralinepag | Pulmonáris arteriális hipertónia kezelése |
| Italian | Ralinepag | Trattamento dell'ipertensione arteriosa polmonare |
| Latvian | Ralinepags | Plaušu arteriālās hipertensijas ārstēšana |
| Lithuanian | Ralinepagas | Plaučių arterinės hipertenzijos gydymas |
| Maltese | Ralinepag | Kura ta' pressjoni arterjali pulmonari għolja |
| Polish | Ralinepag | Leczenie tętniczego nadciśnienia płucnego |
| Portuguese | Ralinepag | Tratamento da hipertensão arterial pulmonar |
| Romanian | Ralinepag | Tratamentul hipertensiunii arteriale pulmonare |
| Slovak | Ralinepag | Liečba pľúcnej artériovej hypertenzie |
| Slovenian | Ralinepag | Zdravljenje pljučne arterijske hipertenzije vključno |
| Spanish | Ralinepag | Tratamiento de la hipertensión arterial pulmonar |
| Swedish | Ralinepag | Behandling av pulmonell arteriell hypertension |
| Norwegian | Ralinepag | Behandling av pulmonal arteriell hypertensjon |
| Icelandic | Ralinepag | Meðferð við háþrýstingi í lungnablóðrás |

¹ At the time of designation