



EUROPEAN MEDICINES AGENCY
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Public summary of opinion on orphan designation

Propranolol hydrochloride for the treatment of von Hippel-Lindau disease

On 27 February 2017, orphan designation (EU/3/17/1841) was granted by the European Commission to Consejo Superior de Investigaciones Científicas (CSIC), Spain, for propranolol hydrochloride for the treatment of von Hippel-Lindau disease.

What is von Hippel-Lindau disease?

Von Hippel-Lindau disease is a genetic disease characterised by growth of mostly benign but also cancerous tumours in many organs of the body, including in the kidneys, pancreas, adrenal glands and inner ear, as well as abnormal growth of blood vessels in the eye, brain and spinal cord.

The disease is caused by a defect in the *VHL* gene which is responsible for the production of a protein that prevents tumour formation. In patients with von Hippel-Lindau disease, the defective gene cannot produce sufficient protein that works properly, leading to the development of tumours.

Von Hippel-Lindau disease is a long-term debilitating and life-threatening disease due to the complications caused by the various tumours that can have wide-ranging effects on the body.

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

At the time of designation, von Hippel-Lindau disease affected approximately 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 10,000 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, no satisfactory methods were authorised in the EU for the treatment of von Hippel-Lindau disease. Patients were mainly treated with surgery to remove tumours in the affected organs and with laser therapy to treat eye symptoms.

^{*}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).



How is this medicine expected to work?

Propranolol is a type of medicine called a beta blocker, which has been used for many years in the EU to treat a variety of conditions, including diseases of the heart and high blood pressure, and benign tumours of the blood vessels (haemangioma) in children. It blocks receptors in the body called beta adrenoceptors, preventing them from responding to the natural hormones adrenaline and noradrenaline. This leads to a narrowing of blood vessels, reducing the amount of blood flowing through them. The way in which this medicine may work in von Hippel-Lindau disease is not fully understood. It may help to slow growth of tumours by reducing blood supply to tumours.

What is the stage of development of this medicine?

The effects of propranolol hydrochloride 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 von Hippel-Lindau disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for von Hippel-Lindau disease 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 19 January 2017 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 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Propranolol hydrochloride	Treatment of von Hippel-Lindau disease
Bulgarian	Пропранолол хидрохлорид	Лечение на болестта на von Hippel-Lindau
Croatian	Propranolol hidroklorid	Liječenje von Hippel-Lindauove bolesti
Czech	Propranolol hydrochlorid	Léčba von Hippel-Lindau chorobyz
Danish	Propranololhydrochlorid	Behandling af von Hippel-Lindaus sygdom
Dutch	Propranolol hydrochloride	Behandeling van de ziekte von Hippel-Lindau
Estonian	Propranolool hüdrokloriid	Von Hippel-Lindau haiguse ravi
Finnish	Propranololi hydrokloridi	Von Hippel-Lindaun oireyhtymän hoito
French	Propranolol chlorhydrate	Traitement de la maladie de von Hippel-Lindau
German	Propranolol Hydrochlorid	Behandlung des von-Hippel-Lindau-Syndroms
Greek	Προπρανολόλη υδροχλωρική	Θεραπεία της νόσου von Hippel-Lindau
Hungarian	Propranolol hidroklorid	Von Hippel-Lindau betegség kezelése
Italian	Propranololo cloridrato	Trattamento della sindrome di von Hippel-Lindau
Latvian	Propranolola hidrohlorīds	Hipela un Lindava (Von Hippel-Lindau) slimības ārstēšana
Lithuanian	Propranololio hidrochloridas	Von Hippel-Lindau ligos gydymas
Maltese	Propranolol kloridrat	Kura tal-marda von Hippel-Lindau
Polish	Propranolol chlorowodorek	Leczenie choroby von Hippel-Lindau'a
Portuguese	Cloridrato propranolol	Tratamento da doença de von Hippel-Lindau
Romanian	Propranolol clorhidrat	Tratamentul sindromului von Hippel-Lindau
Slovak	Propranolol hydrochlorid	Liečba Von Hippel-Lindau choroba
Slovenian	Propranololijev klorid	Zdravljenje bolezni von Hippel-Lindau
Spanish	Cloridrato de propranolol	Tratamiento del síndrome de von Hippel-Lindau
Swedish	Propranolol hydroklorid	Behandling av von Hippel-Lindaus sjukdom
Norwegian	Propranololhydroklorid	Behandling av von Hippel-Lindaus sykdom
Icelandic	Própranolól hýdróklóríð	Meðferð von Hippel-Lindau sjúkdóms

¹ At the time of designation