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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Tolvaptan for the treatment of autosomal dominant polycystic kidney disease

First publication	12 September 2013
Rev.1: sponsor's change of address	13 January 2014
Rev.2: withdrawal from the Community Register	17 April 2015
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in March 2015 at the request of the sponsor.

On 5 August 2013, orphan designation (EU/3/13/1175) was granted by the European Commission to Otsuka Pharmaceutical Europe Ltd, United Kingdom, for tolvaptan for the treatment of autosomal dominant polycystic kidney disease.

What is autosomal dominant polycystic kidney disease?

Polycystic kidney disease is an inherited condition marked by the growth of numerous fluid-filled cysts in the kidneys. The growth of cysts eventually affects kidney function and can cause the kidneys to fail. Symptoms include abdominal pain, problems with urinating, high blood pressure and infection.

In most cases polycystic kidney disease is 'autosomal dominant', which means that it is caused by gene mutations (defects) that are 'dominant' because a person can have the disease even if they have inherited a defective gene from only one parent. Autosomal dominant polycystic kidney disease is caused by a mutation of either of two genes, PKD1 and PKD2.

Autosomal dominant polycystic kidney disease is debilitating in the long term and life threatening because patients can develop kidney failure and problems with the heart and the gut.

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What is the estimated number of patients?

At the time of designation, autosomal dominant polycystic kidney disease affected approximately 4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 205,000 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, there were no satisfactory treatments authorised for autosomal dominant polycystic kidney disease in the EU. Treatments that were available targeted symptoms of the disease and included antihypertensive medicines (for high blood pressure), pain killers, antibiotics for infection and dialysis and kidney transplantation.

How is this medicine expected to work?

Tolvaptan is already authorised in the EU for treating hyponatraemia (abnormally low sodium levels). It acts by blocking receptors in the kidney to which the hormone vasopressin attaches, which regulates the level of water and sodium in the body.

In autosomal dominant polycystic kidney disease, it is thought that the vasopressin receptors do not function as they should, leading to the formation of fluid-filled cysts. By blocking these receptors, tolvaptan is expected to help slow down cyst formation, thereby improving the symptoms of the disease.

What is the stage of development of this medicine?

The effects of tolvaptan have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with autosomal dominant polycystic kidney disease were ongoing.

At the time of submission, tolvaptan was not authorised anywhere in the EU for autosomal dominant polycystic kidney disease. Orphan designation had been granted in the United States and Japan for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 July 2013 recommending the granting of this designation.

[*]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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 512,200,000 (Eurostat 2013).

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Tolvaptan	Treatment of autosomal dominant polycystic kidney disease
Bulgarian	Толваптан	Лечение на автозомно-доминантна поликостозна бъбречна болест
Croatian	Tolvaptan	Liječenje autosomno dominantne policistične bolesti bubrega
Czech	Tolvaptan	Léčba autozomálně dominantní polycystózy ledvin
Danish	Tolvaptan	Behandling af autosomal dominant polycystisk nyresygdom
Dutch	Tolvaptan	Behandeling van autosomale dominante polycystische nierziekte
Estonian	Tolvaptaan	Autosoom-dominantse polütsüstilise neeruhaiguse ravi
Finnish	Tolvaptaani	Autosomaalisen dominantin polykystisen munuaistaudin hoito
French	Tolvaptan	Traitement de la polykystose rénale autosomique dominante
German	Tolvaptan	Behandlung der autosomal-dominanten polyzystischen Nierenerkrankung
Greek	Τολβαπτάνη	Θεραπεία της αυτοσωματικής κυρίαρχης πολυκυστικής νόσου των νεφρών
Hungarian	Tolvaptán	Autoszomális domináns policisztás vesebetegség kezelése
Italian	Tolvaptan	Trattamento della malattia renale policistica autosomica dominante
Latvian	Tolvaptāns	Autosomāli dominantas nieru policistozes ārstēšana
Lithuanian	Tolvaptanas	Autosominės dominantinės policistinės inkstų ligos gydymas
Maltese	Tolvaptan	Kura tal-marda poliċistika tal-kliewi awtosomali dominanti
Polish	Tolwaptan	Leczenie autosomalnie dominującej wielotorbielowatości nerek
Portuguese	Tolvaptan	Tratamento da doença renal poliquística autossómica dominante
Romanian	Tolvaptan	Tratamentul bolii polichistice renale cu transmitere autozomal dominantă
Slovak	Tolvaptan	Liečba autozomálneho dominantného polycystického ochorenia obličiek
Slovenian	Tolvaptan	Zdravljenje avtosomne dominantne policistične bolezni ledvic
Spanish	Tolvaptán	Tratamiento de la poliquistosis renal autosómica dominante
Swedish	Tolvaptan	Behandling av autosomalt dominant polycystisk njursjukdom
Norwegian	Tolvaptan	Behandling av autosomal dominant polycystisk nyresykdom
Icelandic	Tolvaptan	Meðferð við nýrnafjölblöðrusjúkdómi með ríkjandi erfðamáta

[1] At the time of designation