9 February 2015
EMA/COMP/158/2004 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ibuprofen for the treatment of patent ductus arteriosus

First publication	13 May 2009
Rev.1: withdrawal from the Community Register	9 February 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Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in August 2014 at the end of the period of market exclusivity.

On 14 February 2001, orphan designation (EU/3/01/020) was granted by the European Commission to Orphan Europe, France, for ibuprofen for the treatment of patent ductus arteriosus.

What is patent ductus arteriosus?

Patent ductus arteriosus (PDA) is a heart disease where the ductus arteriosus fails to close at birth. The pulmonary artery is a blood vessel that transports blood from the heart to the lungs. The aorta is a blood vessel that transports blood from the heart out to the rest of the body. In the womb, the baby gets its oxygen from the mother across the placenta (organ joining the mother and baby during pregnancy). The ductus arteriosus is the passageway that helps the distribution of oxygen from the mother to the baby's organs and allows blood flow to avoid the lungs.

In most babies, the ductus arteriosus closes within a few hours of birth. When the ductus arteriosus stays open (patent) after birth, blood travels in the wrong direction between the aorta and pulmonary artery. The abnormal blood flow patterns across the ductus may lead to heart failure, pulmonary (lung) hypertension (high blood pressure) and an increased risk of bacterial infection of the heart and ductus itself. The infection, or rupture of the ductus, may be life threatening.

Symptoms vary with the size of the ductus and the amount of blood that flows through it. If the ductus is small, there may be no symptoms. When symptoms occur they include; rapid breathing, increased work to breathe, getting tired quickly, poor growth, respiratory infection (e.g. cold).

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

At the time of designation, patent ductus arteriosus affected approximately 2.13 in 10,000 people in the European Union (EU). This was equivalent to a total of around 81,000 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?

Current treatment of patent ductus arteriosus comprises two steps. The first is medicinal treatment with an anti-inflammatory drug administered intravenously. The second step is surgical ligation (connection) of the ductus, if the medicinal treatment has failed. One product with anti-inflammatory activity was authorised for the condition in several Member States of the Community at the time of submission of the application for orphan drug designation.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that ibuprofen might be of potential significant benefit for the treatment of patent ductus arteriosus. 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?

Ibuprofen is an anti-inflammatory drug which closes the ductus by inhibiting the production of prostaglandin. Prostaglandins are a class of hormone-like (chemical messenger) lipids (fats) present in tissues and bodily fluids. They may be involved in processes such as pain, inflammation and kidney function and affect blood pressure and smooth muscle (muscle that performs automatic tasks such as opening/closing blood vessels) activity.

What is the stage of development of this medicine?

The evaluation of the effects of ibuprofen in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with patent ductus arteriosus were initiated.

Ibuprofen for intravenous formulation was not marketed anywhere worldwide for patent ductus arteriosus, at the time of submission.

Orphan designation of ibuprofen was granted in the United States in 1996 for patent ductus arteriosus.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 December 2000 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.
At the time of designation, this represented a population of 378,800,000 (Eurostat 2001).

Update: Ibuprofen (Pedea) has been authorised in the EU since 29 July 2004 for treatment of a haemodynamically significant patent ductus arteriosus in preterm newborn infants less than 34 weeks of gestational age.

More information on Pedea can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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:

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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	Ibuprofen	Treatment of patent ductus arteriosus
Danish	Ibuprofen	Behandling af åben ductus arteriosus
Dutch	Ibuprofen	Behandeling van ductus arteriosus apertus
Finnish	Ibuprofeeni	Avoimen ductus arteriosuksen hoitoon
French	Ibuprofen	Traitement du canal artériel persistant
German	Ibuprofen	Behandlung des persistierenden Ductus arteriosus
Greek	Ιβουπροφένη	Θεραπεία του Ανοικτού Αρτηριακού Πόρου
Italian	Ibuprofene	Trattamento del dotto arterioso pervio
Portuguese	Ibuprofen	Tratamento de ductus arteriosus persistente
Spanish	Ibuprofeno	Tratamiento del ductus arterioso persistente
Swedish	Ibuprofen	Behandling av öppen ductus arteriosus

[1] At the time of designation