



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in July 2008 on request of the sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of ibuprofen for the prevention of patent ductus arteriosus in premature neonates of less than 34 weeks of gestational age

On 5 March 2001, orphan designation (EU/3/01/027) was granted by the European Commission to Orphan Europe, France, for ibuprofen for the prevention of patent ductus arteriosus in premature neonates of less than 34 weeks of gestational age.

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 normally closes within a few hours of birth. When the ductus arteriosus stays open (patent) after birth, the 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.

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

At the time of designation patent ductus arteriosus in premature neonates of less than 34 weeks of gestational age affected approximately 1.7 in 10,000 people in the European Union (EU) *. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 64,000 people.

* Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition.

What methods of prevention are available?

No medicinal products were authorised for the prevention of patent ductus arteriosus in premature neonates of less than 34 weeks of gestational age in the Community at the time of submission for orphan drug designation.

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 prevention of patent ductus arteriosus, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 15 January 2001 a positive opinion recommending the grant of the above-mentioned 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Ibuprofen	Prevention of patent ductus arteriosus in premature neonates of less than 34 weeks of gestational age
Danish	Ibuprofen	Forebyggelse ved åben ductus arteriosus hos præmature neonatale børn med en gestationsalder mindre end 34 uger
Dutch	Ibuprofen	Preventie van ductus arteriosus apertus bij premature neonaten met een zwangerschapsduur van minder dan 34 weken.
Finnish	Ibuprofeeni	Avoimen ductus arteriosuksen ehkäisy alle 34 raskausviikkoisilla ennenaikaisilla vastasyntyneillä
French	Ibuprofen	Prévention de la persistance du canal artériel chez les prématurés de moins de 34 semaines d'âge gestationnel
German	Ibuprofen	Prävention des persistierenden Ductus arteriosus in unreifen Neugeborenen von weniger als 34 Wochen Tragzeit
Greek	Ιβουπροφένη	Προληπτική Θεραπεία του Ανοικτού Αρτηριακού Πόρου σε πρωίμα βρεφη κατω των 34 εβδομαδων κυοφοριακης ηλικίας
Italian	Ibuprofene	Prevenzione del dotto arterioso pervio in neonati prematuri di età gestazionale inferiore alle 34 settimane
Portuguese	Ibuprofen	Provenção do ductus arteriosus persistente em recém-nascidos prematuros com idade gestacional inferior a 34 semanas.
Spanish	Ibuprofeno	Prevención del ductus arterioso persistente en neonatos prematuros de menos de 34 semanas de edad de gestación
Swedish	Ibuprofen	Profylax vid öppen ductus arteriosus i prematura nyfödda barn med en gestationsålder mindre än 34 veckor