



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

Estradiol hemihydrate and progesterone for the prevention of bronchopulmonary dysplasia in premature neonates of less than 30 weeks of gestational age

On 11 April 2005, orphan designation (EU/3/05/275) was granted by the European Commission to B. Braun Melsungen AG, Germany, for estradiol hemihydrate and progesterone for the prevention of bronchopulmonary dysplasia in premature neonates of less than 30 weeks of gestational age.

The sponsorship was transferred to Dr Frank Pohlandt, Germany, in September 2011.

### What is bronchopulmonary dysplasia?

Bronchopulmonary dysplasia (BPD) is a chronic lung disease that develops in premature neonates and is associated with the infant's low birth weight and gestational age. BPD is caused by several factors such as a lack of the protective coating of the lungs due to immaturity, bacterial infections and artificial oxygen administration to support the breathing. These factors can damage the lungs, which means that the normal functions of the lung tissue (exchange of oxygen and carbon dioxide between air and blood) are impaired. This leads to inflammation (the body's to the injury caused to the tissue) and progressive formation of scar tissue. The patient will develop an increasing shortness of breath. Bronchopulmonary dysplasia is a chronically debilitating and life-threatening condition.

### What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of neonates of less than 30 weeks of gestational age at risk of bronchopulmonary dysplasia was estimated to be approximately 1.3 people in 10,000 in the European Union (EU)\*. This is equivalent to a total of around 60,000 people, which 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).

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.



## **What methods of prevention are available?**

At the time of submission of the application for the orphan drug designation there was no preventive treatment authorised in the European Union. Corticosteroids are commonly used to prevent bronchopulmonary dysplasia in premature neonates of less than 30 weeks of gestational age as they induce maturation of the lungs.

## **How is this medicine expected to work?**

Estradiol hemihydrate and progesterone are able to increase the functional and structural maturation of the lungs. They are expected to prevent the development of the condition in premature neonates of less than 30 weeks of gestational age by substituting the estradiol and progesterone that the neonate would normally receive from the mother if the intrauterine life would continue.

## **What is the stage of development of this medicine?**

The effects of estradiol hemihydrate and progesterone were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with bronchopulmonary dysplasia were ongoing.

Estradiol hemihydrate and progesterone was not authorised anywhere worldwide for bronchopulmonary dysplasia or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 3 March 2005 recommending the granting of this designation.

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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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Estradiol Hemihydrate and Progesterone	Prevention of bronchopulmonary dysplasia in premature neonates of less than 30 weeks of gestational age
Bulgarian	Естрадиол Хемихидрат и Прогестерон	Превенция на бронхопулмонарна дисплазия при недоносени новородени с гестационна възраст под 30 седмици.
Czech	hemihydrát estradiolu a progesteron	Prevence (bronchopulmonální dysplázie - BPD) u předčasně narozených dětí s s věkem nižším než 30 týdnů gestačního věku
Danish	Estradiolhemihydrat og Progesteron	Forebyggende behandling af luggedysplasi hos præmature spædbørn yngre end 30 gestationsuge
Dutch	Estradiolhemihydraat en Progesteron	Preventie van bronchopulmonaire dysplasie bij premature pasgeborenen met een draagtijd van minder dan 30 weken
Estonian	Estradioli hemihüdraat ja progesteron	Bronhopulmonaalse düsplaasia ennetamiseks alla 30. rasedusnädalat sündinud enneaegsetel vastsündinutel
Finnish	Estradiolihemihydraatti ja Progesteroni	Bronkopulmonaalisen dysplasian ehkäiseminen keskosilla, joiden sikiöikä on alle 30 viikkoa
French	Estradiol hémihydraté et Progesterone	Prévention de la dysplasie bronchopulmonaire chez les prématurés âgés de moins de 30 semaines à la naissance
German	Estradiol-Hemihydrat und Progesteron	Zur vorbeugenden Behandlung, um die Entwicklung einer chronischen Lungenerkrankung (BPD) bei Frühgeborenen mit einem Gestationsalter von unter 30 Wochen zu verhindern oder zu verringern
Greek	Ημιένυδρη οιστραδιόλη και Προγεστερόνη	Πρόληψη βρογχοπνευμονικής δυσπλασίας σε βρέφη ηλικίας κύησης μικρότερης των 30 εβδομάδων
Hungarian	Ösztradiol hemihidrát és Progeszteron	Bronchopulmonális dysplasia megelőzése 30 hétnél rövidebb gesztációs időt követően született koraszülötteknél
Italian	Estradiolo emiidrato e Progesterone	Prevenzione della displasia broncopulmonare in neonati prematuri di età gestazionale inferiore alle 30 settimane
Latvian	Estradiola hemihidrāts un progesterons	Bronhopulmonārās displāzijas profilaksei jaundzimušiem ar gestācijas vecumu mazāku par 30 nedēļām

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Lithuanian	Estradiolio hemihidratas ir Progesteronas	Neišnešiotų naujagimių, mažesnių nei 30 gestacijos savaitių amžiaus, bronchopulmoninės displazijos prevencija
Maltese	Estradiol Hemihydrate u Progesterone	Prevenzjoni ta' displasja bronkopulmonari fi trabi tat-twelid prematuri ta' età ta' gestazzjoni inqas minn 30 ġimgħa
Polish	Estradiolu półwodzian i Progesteron	Zapobieganie dysplazji oskrzelowo-płucnej, (BPD) u wcześniaków urodzonych przed 30 tygodniem wieku ciążowego
Portuguese	Estradiol, Hemihidrato e Progesterona	Prevenção de displasia broncopulmonar em recém-nascidos com menos de 30 semanas de idade gestacional
Romanian	Estradiol Hemihidrat și Progesteron	Prevenția displaziei bronhopulmonare la nou-născuții prematuri cu vârsta gestațională mai mică de 30 de săptămâni
Slovak	Hemihydrát estradiolu a Progesterón	Prevenca bronchopulmonárnej dysplázie u predčasne narodených novorodencov s menej ako 30 týždňov gestačného veku
Slovenian	Estradiol hemihidrat in progesteron	Preprečevanje bronhopulmonalne displazije pri nedonošenčkih pod 30 tedni gestacijske starosti
Spanish	Estradiol hemihidrato y progesterona	Prevenición de la displasia broncopulmonar en neonatos prematuros con edad gestacional inferior a 30 semanas
Swedish	Estradiolhemihydrat och Progesteron	Profylax av bronkopulmonell dysplasi hos prematurt nyfödda barn under 30 veckors gestationsålder
Norwegian	Østradiol hemihydrat og Progesteron	Forebygging av bronkopulmonal dysplasi hos premature nyfødte med gestasjonsalder mindre enn 30 uker.
Icelandic	Estradíól-hemíhýdrat og prógesterón	Til að fyrirbyggja berkju-og lungnavanþroska hjá fyrirburum eftir minna en 30 vikna meðgöngu.