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

Document Date: London, 2 September 2009
Doc.Ref.: EMEA/COMP/376/04 Rev.1

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of sinapultide, dipalmitoylphosphatidylcholine, palmitoyl-oleoyl phosphatidylglycerol and palmitic acid for the prevention of respiratory distress syndrome in premature neonates of less than 32 weeks of gestational age

On 29 July 2004, orphan designation (EU/3/04/216) was granted by the European Commission to GMG BioBusiness Ltd., United Kingdom, for sinapultide, dipalmitoylphosphatidylcholine, palmitoyl-oleoyl phosphatidylglycerol and palmitic acid for the prevention of respiratory distress syndrome in premature neonates of less than 32 weeks of gestational age.
The sponsorship was transferred to Pharm Research Associates (UK) Limited, United Kingdom, in May 2009.

What is respiratory distress syndrome?
Respiratory distress syndrome (RDS) is a lung disorder that causes increasing difficulty in breathing. It may occur in adults (adult respiratory distress syndrome) or in newborn children, when it is also known as hyaline membrane disease. RDS in premature, low birth weight infants is characterised by the onset of difficulty in breathing within minutes to a few hours after birth. The condition is associated with the presence of deposits of a dense membrane (called hyaline membrane) in the air sacs (alveoli) of the lung. RDS is a life-threatening condition.

What is the estimated number of patients at risk of developing the condition?
At the time of designation, the number of premature neonates of less than 32 weeks of gestational age at risk of respiratory distress syndrome was estimated to be approximately 1.1 people in 10,000 in the European Union (EU) [*]. This is equivalent to a total of around 51,000 people, which is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of prevention are available?
Several surfactant products (see definition below) were authorised for prevention of the condition in the Community at the time of submission of the application for orphan drug designation. Other methods of prevention include the administration of steroidal medication to the expectant mother to accelerate lung development in the unborn child.
Satisfactory argumentation has been submitted by the sponsor to justify the assumption that Surfaxin might be of potential significant benefit for the prevention of RDS in premature neonates. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

[*]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 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

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How is this medicine expected to work?
Surfaxin is a surfactant agent. Lung surfactant is a protein and fat complex that coat the alveoli of the lung, and keep them open. This ensures a stable alveoli surface for oxygen passage.
Surfactant substances are naturally produced in lungs. In premature neonates the lungs have not fully matured and there may be a deficiency of natural surfactant. Surfaxin is intended to compensate for the lack of natural surfactant in infants with RDS and thus aims to improve the lung function.

What is the stage of development of this medicine?
The effects of sinapultide, dipalmitoylphosphatidylcholine, palmitoyl-oleoyl phosphatidylglycerol and palmitic acid were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in pemature neonates at risk of developing RDS were completed.

This medicinal product was not marketed anywhere worldwide for RDS at the time of submission. Orphan designation of Surfaxin has previously been granted in the European Union for treatment of meconium aspiration syndrome (EU/3/01/054) and treatment of acute lung injury (EU/3/01/079).

In the United States orphan drug status has been granted for: treatment of acute respiratory distress syndrome in adults, treatment of respiratory distress syndrome in premature infants, and treatment of meconium aspiration syndrome in newborn infants.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 16 June 2004 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;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the Community) 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.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Sinapultide, dipalmitoylphosphatidylcholine, palmitoyloleoylphosphatidylglycerol and palmitic acid	Prevention of respiratory distress syndrome in premature neonates of less than 32 weeks of gestational age
Czech	Sinapultid, Dipalmitoylfosfatidylcholin, Palmitoyloleoyl fosfatidylglycerol a kyselina palmitová	Prevence syndromu dechové tísně u předčasně narozených novorozenců před 32.týdnem gestačního věku
Danish	Sinapultid, dipalmitoylfosfatidylcholin, palmitoyloleoyl phosphatidylglycerol og palmitinsyre	Forebyggelse af Respiratorisk Distress Syndrom hos for tidligt fødte med en gestationsalder mindre end 32 uger
Dutch	Sinapultide, dipalmitoylphosphatidylcholine, palmitoyloleoyl phosphatidylglycerol en palmitinezuur	Preventie van Respiratoir Distress Syndroom in premature pasgeborenen met een draagtijd van minder dan 32 weken
Estonian	Sinapultide, dipalmitoüülfosfatidüülkoliin, palmitoüüloleoüülfostatidüülglütserool ja palmitiinhape	Enne 32 rasedusnädalat sündinud enneagse vastsündinu respiratoorse distress sündroomi ärahoidmine
Finnish	Sinapultiidi Dipalmitolifosfatidylkoliini, palmitolioleoli fosfatidylglyseroli ja palmitiinihappo	Hengitysvaikeusoireyhtymän esto alle 32 viikkoisilla keskosilla
French	Sinapultide, dipalmitoylfosfatidylcholine, palmitoyloleoylfosfatidylglycerol et acide palmitique	Prévention du syndrome de détresse respiratoire du nouveau-né prématuré âgé de moins de 32 semaines.
German	Sinapultide Dipalmitoylfosfatidylcholin, Palmitoyloleoylfosfatidylglycerol und Palmitinsäure	Vorbeugung des respiratorischen Stress Syndroms in Frühgeborenen mit einem Gestationsalter unter 32 Wochen
Greek	Σιναπουλτιδη, διπαλμιτοϋλοφωσφατιδυλοχολίνη, παλμιτοϋλική-ελαιοϋλική φωσφατιδυλογλυκερόλη και παλμιτικό οξύ	Πρόληψη του Συνδρόμου Αναπνευστικής Δυσχέρειας σε πρόωρα νεογνά ηλικίας κύησης μικρότερης από 32 εβδομάδες.
Hungarian	Sinapultide, Dipalmitoil-foszfatidil-kolin, Palmitoil-oleoil-foszfatidil-glicerin és palmitinsav	Respirációs distress szindróma megelőzése koraszülötteknél 32 hétnél rövidebb gesztációs idő esetén
Italian	Sinapultide, dipalmitoilfosfatidilcolina, palmitoiloleoil fosfatidilglicerolo e acido palmitico	Prevenzione della Sindrome da Distress Respiratorio nei neonati prematuri di meno di 32 settimane di eta` gestazionale
Latvian	Sinapultīds, dipalmitoilfosfatidilholīns, palmitoil-oleoil-fosfatidilglicerīns un palmitīnskābe	Respiratorā distresa sindroma profilakse priekšlaicīgi dzimušiem jaundzimušajiem ar gestācijas vecumu mazāku par 32 nedēļām
Lithuanian	Sinapultidas, dipalmitoilfosfatidilcholinas, palmitoiloleoilfosfatidilglicerolis ir palmitino rūgštis	Mažesnių nei 32 gestacijos savaičių neišnešiotų naujagimių respiracinio distreso sindromo prevencija
Maltese	Sinapultide, dipalmitoylphosphatidylcholine,	Prevention of respiratory distress syndrome in premature neonates of less

	palmitoyloleoylphosphatidylglycerol and palmitic acid	than 32 weeks of gestational age
Polish	Synapultyd, dipalmitoilofosfatydylocholina, palmitoilooleilofosfatydyloglicerol i kwas palmitynowy	Zapobieganie zespołowi zaburzeń oddechowych u wcześniaków urodzonych przed 32 tygodniem ciąży
Portuguese	Sinapultide, dipalmitoilfosfatidilcolina, palmitoiloleoilfosfatidilglicerol e ácido palmitico	Prevenção do síndroma de dificuldade respiratória em recem nascidos prematuros com menos de 32 semanas de gestação
Slovak	Sinapultid, dipalmitoylfosfatidylcholín, palmitoyloleoylfosfatidylglycerol a kyselina palmitová	Prevencia syndrómu dychovej tiesne u predčasne narodených novorodencov s gestačným vekom menej ako 32 týždňov
Slovenian	Sinapultid, palmitoil-oleoil fosfatidilglicerol, dipalmitoil fosfatidilholin, palmitinska kislina	Preprečevanje sindroma dihalne stiske novorojenčkov pri nedonošenčkih gestacijske starosti manj kot 32 tednov
Spanish	Sinapultida, dipalmitoilfosfatidilcolina, palmitoiloleoilfosfatidilglicerol y ácido palmítico	Prevención de síndrome de distrés respiratorio en neonatos prematuros de menos de 32 semanas de edad
Swedish	Sinapultid, dipalmitylfosfatidylkolin, palmityloleoylfosfatidylkolin och palmitinsyra	Förebyggande av Respiratoriskt Distress Syndrom hos prematurt nyfödda barn med en fostertidslängd av mindre än 32 veckor
Norwegian	Sinapultid, dipalmitoylfosfatidylcholin, palmitoyloleoylfosfatidylglycerol og palmitinsyre	Forebygging av respiratorisk distress-syndrom hos premature nyfødte med gestasjonsalder under 32 uker
Icelandic	Sínapúltíð, tvípalmítóýlfosfatidýlkólín, palmítóýlfosfatidýlglýseról og palmitínsýra	Til að fyrirbyggjaandnauð hjá fyrirburum eftir minna en 32 vikna meðgöngu