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# EMA Regulatory Decisions in PAH 2011-2012

By:

**Amany Elgazayerly**

Senior clinical assessor, Dutch MEB  
CV-group, Scientific advice group, EMA

Disclaimer: Any viewpoints presented in this talk are not necessarily those of EMA or the Dutch MEB.

All presented data is obtained from public websites

Highlight Important Regulatory variations in the EU labeling of PAH medicinal products.

## Registered PAH products through centralised procedure

Bosentan (Tracleer)	2002
Iloprost (ventavis)	2003
Sildenafil (Revatio)	2005
Ambrisentan (Volibris)	2008
<i>Tadalafil</i> (Adcirca)	2008

National Procedure:

Epoprostenol

Mutual Recognition Procedure : Treprostinil

## Bosentan (Tracleer)

Updated long-term (efficacy and safety) data were generated from 2 open label extension studies (EARLY - OL) and (BREATHE-5 - OL). Preliminary results were already included in the SPC in section 5.1.

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# Iloprost (Ventavis)

Update the labeling e.g delete pregnancy and lactation contraindications.

# Sildenafil (Revatio)

**Paediatric Indication** Treatment of paediatric patients aged 1 year to 17 years old with PAH.

Efficacy in terms of improvement of exercise capacity or pulmonary haemodynamics has been shown in primary pulmonary hypertension and pulmonary hypertension associated with congenital heart disease (see section 5.1).

**Posology** is 10 mg TID (<20 kg) and  
 $\geq 20$  kg 20 mg TID



Supported by

**Study A1481131:** randomised, double-blind, placebo controlled parallel group, dose ranging study.

**Study A1481156:** ongoing, long term non-controlled study.

August 2011: EMA notification DMC discontinuation of high dose treatment arms in the long term extension paediatric study.

40 and 80 mg TID *in line with SPC*

## **Down-titration**

40 mg to 20 mg children >45kg

*in line with SPC*

10-20mg children 20-45 kg

*below SPC*

(depending on investigator judgment)

Further assessment.

Changes in labelling: doses higher than the recommended doses should not be used.

A DHPC.

*August 2012: FDA*

## 2. Revatio

Revatio 10 mg/mL, powder for oral suspension.

## Ambrisentan (Volibris)

A new contraindication:

Idiopathic pulmonary fibrosis (IPF), with or without secondary pulmonary hypertension.

(Pending EC decision)

**Flolan is authorised in the EU via national procedures.**  
This has led to divergences across Member States in the way the medicine can be used (SmPC).

**Harmonisation of labelling.**

- Requirements for products with an established B/R in adults PAH.

Extrapolation of adult to paediatric data.

- Requirements for new medicinal products.

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