ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ventavis 10 microgram/ml nebuliser solution
Ventavis 20 microgram/ml nebuliser solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ventavis 10 microgram/ml nebuliser solution
1 ml solution contains 10 microgram iloprost (as iloprost trometamol).
Each ampoule with 1 ml solution contains 10 microgram iloprost.
Each ampoule with 2 ml solution contains 20 microgram iloprost.

Ventavis 20 microgram/ml nebuliser solution
1 ml solution contains 20 microgram iloprost (as iloprost trometamol).
Each ampoule with 1 ml solution contains 20 microgram iloprost.

Excipient with known effect
- Ventavis 10 microgram/ml:
  Each ml contains 0.81 mg ethanol 96% (equivalent to 0.75 mg ethanol)
- Ventavis 20 microgram/ml:
  Each ml contains 1.62 mg ethanol 96% (equivalent to 1.50 mg ethanol).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nebuliser solution.

Ventavis 10 microgram/ml nebuliser solution
Clear, colourless solution.

Ventavis 20 microgram/ml nebuliser solution
Clear, colourless to slightly yellowish solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of adult patients with primary pulmonary hypertension, classified as NYHA functional class III, to improve exercise capacity and symptoms.

4.2 Posology and method of administration

Drug product	Suitable inhalation device (nebuliser) to be used		
Ventavis 10 microgram/ml	Breelib	I-Neb AAD	Venta-Neb
Ventavis 20 microgram/ml	Breelib	I-Neb AAD	

Ventavis should only be initiated and monitored by a physician experienced in the treatment of pulmonary hypertension.

Posology

Dose per inhalation session
At initiation of Ventavis treatment the first inhaled dose should be 2.5 microgram iloprost as delivered at the mouthpiece of the nebuliser. If this dose is well tolerated, dosing should be increased to 5 microgram iloprost and maintained at that dose. In case of poor tolerability of the 5 microgram dose, the dose should be reduced to 2.5 microgram iloprost.

Daily dose
The dose per inhalation session should be administered 6 to 9 times per day according to the individual need and tolerability.

Duration of treatment
The duration of treatment depends on clinical status and is left to the physician's discretion. Should patients deteriorate on this treatment intravenous prostacyclin treatment should be considered.

Special populations

Hepatic impairment
Iloprost elimination is reduced in patients with hepatic dysfunction (see section 5.2).

To avoid undesired accumulation over the day, special caution has to be exercised with these patients during initial dose titration. Initially, doses of 2.5 microgram iloprost should be administered using Ventavis 10 microgram/ml with dosing intervals of 3-4 hours (corresponds to administration of max. 6 times per day). Thereafter, dosing intervals may be shortened cautiously based on individual tolerability. If a dose up to 5 microgram iloprost is indicated, again dosing intervals of 3-4 hours should be chosen initially and shortened according to individual tolerability. An accumulation of iloprost following treatment over several days is not likely due to the overnight break in administration of the medicinal product.

Renal impairment
There is no need for dose adaptation in patients with a creatinine clearance >30 ml/min (as determined from serum creatinine using the Cockroft and Gault formula). Patients with a creatinine clearance of ≤30 ml/min were not investigated in the clinical trials. Data with intravenously administered iloprost indicated that the elimination is reduced in patients with renal failure requiring dialysis. Therefore, the same dosing recommendations as in patients with hepatic impairment (see above) are to be applied.

Paediatric population
The safety and efficacy of Ventavis in children aged up to 18 years have not been established.
No data from controlled clinical trials are available.

Method of administration

Ventavis is intended for inhalation use by nebulisation.

To minimize accidental exposure it is recommended to keep the room well ventilated.

The ready-to-use Ventavis nebuliser solution is administered with a suitable inhalation device (nebuliser) (see below and section 6.6).
Patients stabilised on one nebuliser should not switch to another nebuliser without supervision by the treating physician as different nebulisers have been shown to produce aerosols with slightly different physical characteristics and delivery of the solution that may be faster (see section 5.2).

- **Breelib**

Breelib is a small handheld, battery-powered, breath activated, vibrating mesh technology system.

Ventavis 10 microgram/ml (1 ml ampoule) and Ventavis 20 microgram/ml nebuliser solution

Ventavis 10 microgram/ml nebuliser solution (1 ml ampoule) delivers 2.5 microgram and Ventavis 20 microgram/ml nebuliser solution delivers 5 microgram at the mouthpiece of the Breelib nebuliser.

At initiation of Ventavis treatment or if the patient is switched from an alternative device, the first inhalation should be made with 1 ml ampoule of Ventavis 10 microgram/ml (see section 4.4). If inhalation with Ventavis 10 microgram/ml is well tolerated, the dose should be increased by using Ventavis 20 microgram/ml. This dose should be maintained. In case of poor tolerability of Ventavis 20 microgram/ml, the dose should be reduced by using 1 ml ampoule of Ventavis 10 microgram/ml (see section 4.4).

The duration of an inhalation session with Breelib nebuliser is approximately 3 minutes, which reflects the higher delivery rate of the Breelib compared to other nebulisers.

Patients initiating Ventavis treatment or switching from an alternative device to Breelib should be closely supervised by the treating physician to ensure that dose and speed of inhalation are well tolerated.

When using the Breelib nebuliser please follow the instructions for use provided with the device. Fill the medication chamber with Ventavis immediately before use.

- **I-Neb AAD**

The I-Neb AAD system is a portable, hand-held, vibrating mesh technology nebuliser system. This system generates droplets by ultrasound, which forces the solution through a mesh. The I-Neb AAD nebuliser has been shown to be suitable for the administration of Ventavis 10 microgram/ml (1 ml ampoule) and 20 microgram/ml nebuliser solution. The Mass Median Aerodynamic Diameter (MMAD) of the aerosol measured using I-Neb nebulising systems equipped with power level 10 disc was similar between Ventavis 20 microgram/ml (golden programme) and Ventavis 10 microgram/ml (purple programme) nebuliser solutions (i.e.: around 2 micrometres) but with faster delivery when using Ventavis 20 microgram/ml.

The dose delivered by the I-Neb AAD system is controlled by the medication chamber in combination with a control disc. Each medication chamber is colour coded and has a corresponding colour coded control disc.

Ventavis 10 microgram/ml nebuliser solution (1 ml ampoule)

At initiation of Ventavis treatment with I-Neb system the first inhaled dose should be 2.5 microgram iloprost as delivered at the mouthpiece of the nebuliser using 1 ml ampoule of Ventavis 10 microgram/ml. If this dose is well tolerated, dosing should be increased to 5 microgram iloprost using 1 ml ampoule of Ventavis 10 microgram/ml and maintained at that dose. In case of poor tolerability of the 5 microgram dose, the dose should be reduced to 2.5 microgram iloprost.

This nebuliser monitors the breathing pattern to determine the aerosol pulse time required to deliver the pre-set dose of 2.5 or 5 microgram iloprost.
For the 2.5 microgram dose of Ventavis 10 microgram/ml the medication chamber with the red coloured latch is used together with the red control disc.
For the 5 microgram dose of Ventavis 10 microgram/ml the medication chamber with the purple coloured latch is used together with the purple control disc.

For each inhalation session with the I-Neb AAD, the content of one 1 ml ampoule of Ventavis 10 microgram/ml, with two coloured rings (white - yellow), is transferred into the medication chamber immediately before use.

Drug product	**Ampoule coloured ring**	**Dosage**	**I-Neb AAD**		**Estimated inhalation time**
			Medication chamber latch	**Control disc**	
Ventavis 10 mcg/ml	1 ml ampoule white - yellow ring	2.5 mcg	red	red	3.2 min
		5 mcg	purple	purple	6.5 min

Ventavis 20 microgram/ml nebuliser solution

Only patients who are maintained at the 5 microgram dose and who have repeatedly experienced extended inhalation times with Ventavis 10 microgram/ml, which could result in incomplete inhalation, may be considered suitable for switching to Ventavis 20 microgram/ml.

Close supervision by the treating physician is necessary if switching from Ventavis 10 microgram/ml to Ventavis 20 microgram/ml to control the acute tolerance relating to faster delivery rate of iloprost with the double concentration.

This nebuliser monitors the breathing pattern to determine the aerosol pulse time required to deliver the pre-set dose of 5 microgram iloprost.
For the 5 microgram dose of Ventavis 20 microgram/ml the medication chamber with the gold coloured latch is used together with the gold control disc.

For each inhalation session with the I-Neb AAD, the content of one 1 ml ampoule of Ventavis 20 microgram/ml with two coloured rings (yellow - red), is transferred into the medication chamber immediately before use.

Drug product	**Ampoule coloured rings**	**Dosage**	**I-Neb AAD**	
			Medication chamber latch	**Control disc**
Ventavis 20 mcg/ml	1 ml ampoule yellow - red ring	5 mcg	golden	golden

- **Venta-Neb**

Venta-Neb, a portable ultrasonic battery-powered nebuliser, has been shown to be suitable for the administration of Ventavis 10 microgram/ml nebuliser solution (2 ml ampoule). The measured MMAD of the aerosol droplets was 2.6 micrometres.

At initiation of Ventavis treatment with Venta-Neb the first inhaled dose should be 2.5 microgram iloprost as delivered at the mouthpiece of the nebuliser using 2 ml ampoule of Ventavis 10 microgram/ml. If this dose is well tolerated, dosing should be increased to 5 microgram iloprost using 2 ml ampoule of Ventavis 10 microgram/ml and maintained at that dose. In case of poor tolerability of the 5 microgram dose, the dose should be reduced to 2.5 microgram iloprost.

For each inhalation session with the Venta-Neb, the content of one 2 ml ampoule of Ventavis 10 microgram/ml with two coloured rings (white – pink) is transferred into the nebuliser medication chamber immediately before use.

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