Due to regulatory changes, the content of the following Patient Information Leaflet may vary from the one found in your medicine pack. Please compare the 'Leaflet prepared/revised date' towards the end of the leaflet to establish if there have been any changes.

If you have any doubts or queries about your medication, please contact your doctor or pharmacist.

Package leaflet: Information for the user

Ventavis 20 microgram/ml nebuliser solution
iloprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ventavis is and what it is used for

What Ventavis is
The active substance of Ventavis is iloprost. It imitates a natural substance in the body called prostacyclin. Ventavis inhibits unwanted blocking or narrowing of blood vessels and allows more blood to flow through the vessels.

What Ventavis is used for
Ventavis is used to treat moderate cases of primary pulmonary hypertension (PPH) in adult patients. PPH is a category of pulmonary hypertension where the cause of the high blood pressure is not known. This is a condition where blood pressure is too high in the blood vessels between the heart and the lungs.
Ventavis is used to improve exercise capacity (the ability to carry out physical activity) and symptoms.

How Ventavis works
Breathing in the mist carries Ventavis to the lungs, where it can work most effectively in the artery between heart and lungs. Improved blood flow leads to a better supply of oxygen to the body and reduced strain on the heart.

2. What you need to know before you use Ventavis

Do not use Ventavis

- **if you are allergic** to iloprost or any of the other ingredients of this medicine (listed in section 6),
- **if you are at risk of bleeding**– for example, if you have an active ulcer of the stomach or of the first part of the small intestine (duodenal ulcers), if you have suffered a physical injury (trauma), if you are at risk of bleeding within the skull,
- **if you have a heart problem**, such as:
  - poor blood flow to the heart muscles (severe coronary heart disease or unstable angina). Symptoms can include chest pain,
  - a heart attack within the last six months,
  - a weak heart (decompensated cardiac failure) which is not under close medical observation,
  - severe unstable heartbeat,
  - a defect of the heart valves (inborn or acquired) that causes the heart to work poorly (not related to pulmonary hypertension),
- **if you have had a stroke within the last 3 months**, or any other occurrence that reduced the blood supply to the brain (e.g. transient ischaemic attack*)*,
- **if your pulmonary hypertension is due to a blocked or narrowed vein** (venous occlusive disease).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Ventavis:

- Inhaling Ventavis might trigger breathing difficulties (see section 4), especially in patients with bronchospasm (sudden constriction of the muscles in the walls of the small airways) and wheezing. Tell your doctor if you have **a lung infection, severe asthma, or chronic lung disease** (chronic obstructive pulmonary disease). Your doctor will monitor you closely.
- **Your blood pressure will be checked before treatment and if it is too low** (less than 85 mmHg for the upper value) then therapy with Ventavis should not be started.
- In general, you will need to **take special care to try and avoid effects of low blood pressure**, such as fainting and dizziness:
  - Tell your doctor if you are taking any other medication because the combined effect with Ventavis may lower your blood pressure further (see below "Other medicines and Ventavis").
  - Stand up slowly when you get out of chairs or bed.
  - If you tend to faint as soon as you get out of bed, it may be helpful to take your first dose of the day while you are still lying down.
  - If you tend to experience fainting episodes, avoid any exceptional straining, for example during physical exertion; it might be useful to inhale Ventavis before.
- Fainting episodes may be due to the underlying disease. Tell your doctor if they get worse. He/she may consider adjusting your dose or changing your treatment.
- **If you suffer from a weak heart condition such as right heart failure, and feel that your disease is worsening,** tell your doctor. Symptoms can include swelling of feet and ankles, shortness of breath, palpitations, urinating more frequently at night or oedema. Your doctor will consider changing your treatment.
- **If you experience difficulty breathing, cough up blood, and/or sweat excessively these may be signs that you have water in the lungs** (lung oedema)**.** Stop using Ventavis and tell your doctor immediately. He/she will look for the cause and take appropriate measures.
- **If you have liver problems or very severe kidney problems, requiring dialysis,** tell your doctor. You may be gradually introduced to the prescribed dose or be prescribed a lower dose of Ventavis than for other patients (see section 3. "How to use Ventavis")**.**

Contact of Ventavis with skin or swallowing Ventavis

- Do NOT let Ventavis solution come into contact with your skin or eyes. If it does, rinse the skin or your eyes immediately with plenty of water.
- Do NOT drink or swallow Ventavis solution. If you swallow it accidentally, drink plenty of water and tell your doctor.

Children and adolescents

The safety and efficacy of Ventavis in children aged up to 18 years have not been established.

Other medicines and Ventavis

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. Ventavis and certain other medicines may affect each other in the way they work in your body.

Tell your doctor if you are taking:

- **Medicines used to treat high blood pressure or heart disease**, such as
  - beta blockers,
  - nitro-vasodilators,
  - ACE inhibitors.

  Your blood pressure may drop much further.

Your doctor may change the dosage.

- **Medicines that thin the blood or inhibit blood clotting,** this includes
  - acetylsalicylic acid (ASA - a compound found in many medicines that lower fever and relieve pain),
  - heparin,
  - coumarin-type anticoagulants such as warfarin or phenprocoumon,
  - non-steroidal anti-inflammatory drugs,
  - non-selective phosphodiesterase inhibitors such as pentoxifylline,
  - selective phosphodiesterase 3 (PDE 3) inhibitors, such as cilostazol or anagrelide
  - ticlopidine,
  - clopidogrel,
  - glycoprotein IIb/IIIa antagonists, such as
    - abciximab,
    - eptifibatide,
    - tirofiban,
  - defibrotide.

  Your doctor will monitor you carefully.

Before taking any medicine ask your doctor or pharmacist, who has more information on medicines to be careful with or avoid when using Ventavis.

Ventavis with food and drink

Food or drink is not expected to affect Ventavis. However, you should avoid taking food or drink during inhalation.

Pregnancy

- **If you suffer from pulmonary hypertension,** avoid getting pregnant as pregnancy may lead to a worsening of your condition and may even endanger your life.
- **If you could get pregnant**, use reliable contraception from the time you start treatment and during treatment.
- **If you are pregnant, think you might be or are planning to have a baby,** tell your doctor straight away. Ventavis should only be used during pregnancy if your doctor decides that the potential benefit outweighs the potential risk to you and the foetus.

Breast-feeding
It is not known whether Ventavis passes into human milk. A potential risk to the breast-feeding child cannot be excluded and it is preferable to avoid breast-feeding during Ventavis therapy.

Ask your doctor or pharmacist for advice before taking any medicine.

Newborns, infants and pregnant women should not be in the same room while you are inhaling Ventavis.

Driving and using machines
Ventavis lowers blood pressure and may cause dizziness or light-headedness in some people.
Do not drive or operate any tools or machines if you feel these effects.

Ventavis contains ethanol
Ventavis 20 microgram/ml contains 1.62 mg alcohol (ethanol) in each ml which is equivalent to 0.162% (w/v). The amount of 1.62 mg of alcohol in 1 ml of this medicine is equivalent to less than 1 ml beer or wine.
The small amount of alcohol in this medicine will not have any noticeable effects.

3. How to use Ventavis

Ventavis therapy should only be initiated by a physician experienced in treatment of pulmonary hypertension.

How much to inhale and for how long

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The dose of Ventavis and the duration of treatment that is right for you depend on your individual condition. Your doctor will advise you. Do not change the recommended dose without consulting your doctor first.

Different nebuliser devices can be used to administer Ventavis 20µg/ml.

- **Breelib nebuliser**

If you are starting Ventavis treatment or if you switch from an alternative device your first inhalation will be with Ventavis 10 microgram/ml (1 ml ampoule with white and yellow rings). If you tolerate this dose well, your next inhalation will be with Ventavis 20 microgram/ml (ampoule with yellow and red rings). You should continue on this dose.

If you cannot tolerate inhalation of Ventavis 20 microgram/ml talk to your doctor who may decide that you should take Ventavis 10 microgram/ml (1 ml ampoule).

Most people will have 6 to 9 inhalation sessions spread throughout the day. One inhalation session with Breelib will usually last about 3 minutes.

Your doctor will supervise your treatment when you start using the Breelib nebuliser to ensure that you tolerate dose and speed of inhalation well.

- **I-Neb nebuliser**

As you repeatedly experience extended inhalation treatment times with Ventavis 10 microgram/ml (1 ml ampoule with white and yellow rings), your doctor decided to switch to Ventavis 20 microgram/ml.

Ventavis 20 microgram/ml is double the concentration of Ventavis 10 microgram/ml. The active substance can be delivered more rapidly to your lungs. Your doctor will supervise your treatment if switching from Ventavis 10 microgram /ml to Ventavis 20 microgram/ml to monitor how well you tolerate the higher concentration.

You should administer the dose 6 to 9 times per day according to individual needs and tolerability.

Depending on your individual needs, Ventavis can be used for long term treatment.

If you have kidney or liver problems

There is no need to alter the dose in patients with mild or moderate kidney problems (patients with a creatinine clearance >30 ml/min).

If you have very severe kidney problems and require dialysis or if you have liver problems, your doctor will introduce you to Ventavis gradually and possibly prescribe fewer daily inhalations. Start therapy by inhaling 2.5 microgram iloprost using Ventavis 10 micrograms/ml (1 ml ampoule with white and yellow rings). Use dosing intervals of 3 – 4 hours (this corresponds to a maximum of 6 administrations per day). Thereafter, your doctor may cautiously shorten the dosing intervals depending on how you tolerate the treatment. If your doctor decides to further increase the dose up to 5 microgram, again dosing intervals of 3 – 4 hours should be chosen initially and shortened depending on how you tolerate the treatment.

If you feel that the effect of Ventavis is too strong or too weak, **talk to your doctor or pharmacist**. Ask your doctor to have someone help you become thoroughly familiar with the use of the nebuliser. You should not switch to another nebuliser without consulting the doctor who is treating you.

How to inhale

For each inhalation session you should use a new ampoule of Ventavis. Just before you start to inhale, break the glass ampoule and pour the solution into the medication chamber following the instructions for use of the nebuliser.

Follow carefully the instructions that come with the nebuliser especially the instructions on hygiene and cleaning of the nebuliser.

Always take Ventavis exactly as your doctor has told you.

- Ventavis 20 microgram/ml nebuliser solution is inhaled using the nebulisers your doctor prescribed (either the Breelib or the I-Neb AAD nebuliser).
- The nebuliser turns Ventavis solution into a mist which you breathe in through your mouth.
- For the inhalation you should use a mouthpiece to prevent Ventavis coming into contact with your skin. Do not use a facial mask.
- Follow carefully any instructions that come with the nebuliser. Check with your doctor or pharmacist if you are unsure.
- Any Ventavis solution remaining in the nebuliser after inhalation must be thrown away (see section 5).

Room ventilation
Be sure to ventilate or air the room in which you have taken your Ventavis treatment. Other people might accidentally be exposed to Ventavis through the room air. In particular, newborns, infants and pregnant women should not be in the same room while you are inhaling Ventavis.

- **Breelib**

Fill the medication chamber with Ventavis immediately before use. For filling please follow the instructions for use of the nebuliser.

Device	**Drug product**	**Dose of iloprost at mouthpiece**	**Estimated inhalation time**
Breelib	Ventavis 20 mcg/ml (1 ml ampoule with yellow and red rings)	5 mcg	3 minutes

I-Neb AAD
1. Just before you start to inhale, take the yellow-red colour coded ampoule of Ventavis 20 microgram/ml, break the glass ampoule and pour the complete contents of 1 ml into the nebuliser medication golden chamber.
2. The pre-set dose provided by the I-Neb AAD nebuliser is controlled by the medication chamber in combination with a control disc.
   For Ventavis **20 microgram/ml (5 microgram dose)**, the medication chamber with **the golden coloured latch is used together with the golden control disc**.
3. To ensure that you receive the prescribed dose, check the colour of the medication chamber and the colour of the control disc.

They should both have the same colour.

Since the I-Neb AAD nebuliser can be used for Ventavis 10 microgram/ml and Ventavis 20 microgram/ml, the table below provides a summary of the user instructions of the I-Neb for the 2 concentrations of Ventavis:

Drug product	**Ampoule / coloured rings**	**Dosage**	**I-Neb AAD**	
			Medication chamber latch	**Control disc**
Ventavis 10 mcg/ml	1 ml ampoule white-yellow ring	2.5 mcg	red	red
		5 mcg	purple	purple
Ventavis 20 mcg/ml	1 ml ampoule yellow-red ring	5 mcg	golden	golden

For further details please refer to the instruction manual of the nebuliser device or ask your doctor.

If you use more Ventavis than you should
Using more Ventavis than you should may lead to dizziness, headache, flushing (reddening of the face), nausea (feeling sick), jaw pain or back pain.
You may also experience a decrease or an increase in blood pressure, bradycardia (reduced heart rate), tachycardia (increased heart rate), vomiting, diarrhoea or limb pain. If any of these happen when you have used more Ventavis than you should:

- stop the inhalation session
- talk to your doctor

Your doctor will monitor you and treat any resulting symptoms. A specific antidote is not known.

If you forget to use Ventavis
Do not take a double dose to make up for a forgotten dose. Please ask your doctor what you should do.

If you stop taking Ventavis
If you stop or wish to stop treatment, discuss it with your doctor first.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following **serious side effects** may occur. In this case talk to your doctor immediately.

Very common (may affect more than 1 in 10 people):
Bleeding events (mostly nosebleed (epistaxis) and coughing up blood (haemoptysis) may very commonly occur, especially if you are also taking blood-thinning medicines (anticoagulants). The risk of bleeding may be increased in patients when inhibitors of platelet aggregation or anticoagulants are given at the same time (see also section 2). Very rarely, fatal cases including bleeding in the brain (cerebral and intracranial haemorrhage) have been reported.

Common (may affect up to 1 in 10 people):

- Fainting (syncope) is a symptom of the illness itself but can also occur during treatment with Ventavis (see also section 2 “Warnings and precautions”, for advice on what you can do to avoid this).
- Low blood pressure (hypotension)

Not known (cannot be estimated from the available data):

- Bronchospasm (sudden constriction of the muscles in the walls of the small airways) and wheezing (see also section 2 “Warnings and precautions”)

Below we list other possible side effects by how likely they are:

Very common: may affect more than 1 in 10 people

- widening of the blood vessels (vasodilatation). Symptoms can be flushing or reddening of the face.
- chest discomfort / chest pain
- coughing
- headache
- nausea
- pain in jaw/spasm of the jaw muscles (trismus)
- swelling of the limbs (peripheral oedema)

Common: may affect up to 1 in 10 people

- breathing difficulties (dyspnoea)
- dizziness
- vomiting
- diarrhoea
- pain when swallowing (pharyngolaryngeal irritation)
- throat irritation
- mouth and tongue irritation including pain
- rash
- fast heartbeat (tachycardia)
- awareness of fast or hard heartbeat (palpitations)

Not known: frequency cannot be estimated from the available data.

- reduction in the number of blood platelets (thrombocytopenia)
- hypersensitivity (i.e. allergy)
- disturbed sense of taste (dysgeusia)

Other possible effects

- Swelling, mainly of the ankles and legs, due to fluid retention (peripheral oedema) is a very common symptom of the illness itself but can also occur during treatment with Ventavis.

Reporting of side effects
If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Ventavis

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the carton and ampoule.
This medicine does not require any special storage conditions.

Any Ventavis solution remaining in the nebuliser must be thrown away.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Ventavis contains:

- **The active substance** is iloprost.

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

- **The other ingredients** are trometamol, ethanol, sodium chloride, hydrochloric acid for pH adjustment, and water for injections.

What Ventavis looks like and content of the pack:

Ventavis is a clear, colourless to slightly yellowish nebuliser solution for inhalation with the Breelib or the I-Neb nebuliser.
Ventavis 20 microgram/ml is provided in colourless ampoules, containing 1 ml nebuliser solution.

Ventavis 20 microgram/ml is available in the following packs:
- Pack containing 30 ampoules or 42 ampoules for use with the Breelib and I-Neb nebuliser.
- Multipack containing 168 (4x42) ampoules for use with the Breelib and I-Neb nebuliser.
- Multipack containing 168 (4x42) ampoules with Breelib consumables set (containing 1 mouthpiece and 1 medication chamber).

The ampoules containing 1 ml are marked with two coloured rings (yellow-red).

Not all pack-sizes may be marketed.

Marketing Authorisation Holder:
Bayer AG
51368 Leverkusen
Germany

Manufacturer:
Berlimed S.A.
Francisco Alonso 7
Polígono Industrial Santa Rosa
28806 Alcala de Henares
Madrid
Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

United Kingdom (Northern Ireland)
Bayer AG
Tel: +44 (0)118 206 3000

This leaflet was last revised in 12/2021.

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

For UK (Great Britain)
Marketing Authorisation Holder:
Bayer plc
400 South Oak Way
Reading
RG2 6AD

<u>The following information is intended for healthcare professionals only:</u>

Instructions for use and handling

Patients stabilised on one nebuliser should not switch to another nebuliser without close supervision by the treating doctor as different nebulisers have been shown to produce aerosols with slightly different

physical characteristics and may have faster delivery of the solution (see section 5.2 of the Summary of Product Characteristics).

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

- **Breelib**

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

Device	**Drug product**	**Dose of iloprost at mouthpiece**	**Estimated inhalation time**
Breelib	Ventavis 20 mcg/ml (1 ml ampoule with yellow and red rings)	5 mcg	3 minutes

- **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 is forcing the solution through a mesh. This nebuliser monitors the breathing pattern to determine the aerosol pulse time required to deliver the pre-set dose of 5 micrograms iloprost of the Ventavis 20 microgram/ml nebuliser solution (1 ml ampoule with yellow and red rings).
The nebulising device delivers 5 microgram iloprost at the mouthpiece. The Mass Median Aerodynamic Diameter (MMAD) of the aerosol is between 1 and 5 micrometers.

When using the I-Neb AAD system the following instructions need to be followed.
The dose delivered by the I-Neb AAD system is controlled by the medication chamber in combination with a control disc. For each medication chamber there is a corresponding colour coded control disc.

For each inhalation session with the I-Neb AAD, the content of one 1-ml ampoule of Ventavis 20 microgram/ml, showing two coloured rings (–yellow-red), will be transferred into the appropriate nebuliser medication chamber with **golden coloured latch together with the golden colour disc** immediately before use.

Since the I-Neb AAD system can be used for Ventavis 10 microgram/ml and Ventavis 20 microgram/ml, the table below provides a summary of the user instructions of the I-Neb for the 2 concentrations of Ventavis:

Drug product	**Ampoule / coloured rings**	**Dosage**	I-Neb AAD	
			Medication chamber latch	**Control disc**
Ventavis 10 mcg/ml	1 ml ampoule white-yellow ring	2.5 mcg	red	red
		5 mcg	purple	purple
Ventavis 20 mcg/ml	1 ml ampoule yellow-red ring	5 mcg	golden	golden

The efficacy and tolerability of inhaled iloprost when administered with other nebulising systems, which provide different nebulisation characteristics of iloprost solution, have not been established.