

Patient Leaflet According to the Pharmacists' Regulations (Preparations) - 1986

This medicine is sold with a doctor's prescription only

Tyvaso

Inhalation Solution

Active ingredient:

Each ampule (2.9 mL) contains 1.74 mg of Treprostinil as sodium salt.

Each mL contains 0.6 mg of Treprostinil.

For the list of the other ingredients, please see section 6.

Read this entire leaflet carefully before using this medicine.

This leaflet contains concise information about the medicine. If you have any further questions, refer to your doctor or pharmacist.

This medicine has been prescribed for treating your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is the medicine intended for?

The medicine is intended for treatment of pulmonary arterial hypertension (PAH - high blood pressure in the arteries of the lungs) and for increasing the distance you can walk.

Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.

Therapeutic group: synthetic analog of prostacyclin, platelet aggregation inhibitor.

2. Before using the medicine

Do not use the medicine if:

Do not use if you are sensitive (allergic) to the active ingredient or to any of the other ingredients the medicine contains (for the list of the other ingredients, please see section 6).

Special warnings regarding the use of this medicine:

- Do not allow the inhalation solution to come into contact with the eyes or skin. If such an accidental contact occurs, rinse the place immediately with water.
- The medicine is intended to be inhaled through the mouth.

Before the treatment with Tyvaso, tell your doctor if:

- You suffer or have suffered in the past from lung diseases (e.g. asthma or COPD) or a lung infection.
- You suffer or have suffered in the past from impaired function of the liver or kidneys.
- You suffer or have suffered in the past from low blood pressure.
- You suffer or have suffered in the past from bleeding problems.

If you are taking or have recently taken any other medicines, including non-prescription medicines and nutrition supplements, please tell your doctor or pharmacist.

Especially inform your doctor or pharmacist if you are taking the following medicines (it should be noted that the following list mentions the active ingredients of the medicines. If you are unsure whether you are using one of these medicines, please consult with your doctor or pharmacist):

- Anticoagulant medicines: concomitant use increases the risk of bleeding.
- Diuretics, medicines for treatment of high blood pressure or heart problems: concomitant use increases the risk of lowering blood pressure.

- Gemfibrozil (for treatment of various disorders related to blood lipids, triglycerides and cholesterol), rifampicin (for treatment of tuberculosis).

Pregnancy and breastfeeding:

- Do not use the medicine without consulting a doctor if you are pregnant, plan to become pregnant, are breastfeeding or plan to breastfeed.

Use in children: The efficacy and safety of the medicine in children and adolescents under 18 years of age has not been tested.

3. How to use this medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure regarding the dosage and manner of treatment with the medicine. The dosage and the manner of treatment will be determined by the doctor only.

Read the instructions for use of the Tyvaso Inhalation System carefully. Use Tyvaso only with the inhalation system, specific to the medicine. Do not mix Tyvaso with other medicines in the Tyvaso Inhalation System. It is recommended that you have an additional inhalation system within reach as a backup.

The medicine is administered via inhalation through the mouth into the lungs. Do not swallow the solution.

The standard dosage is usually: perform 4 inhalation sessions daily, during waking hours, with an interval of about 4 hours between each inhalation session.

The number of breathes in each inhalation session will be determined by the doctor. Your doctor may change the dosage during the treatment, if necessary.

Do not exceed the recommended dosage.

- At the beginning of each day, you should prepare the Tyvaso Inhalation System for use.
- Each inhalation session will take 2 to 3 minutes.
- Use the Treatment Tracker in order to record the number of breathes you inhale during each inhalation session. Your doctor may wish to review these records.
- One Tyvaso ampule suffices for a daily treatment of 4 inhalation sessions. Before the first inhalation of the day, open the ampule by twisting its top, and squeeze its contents into the medicine cup. Throw the remaining solution away at the end of the day. See the instructions for use of the inhalation system.

If you have accidentally used a higher dosage or if a child has accidentally swallowed the medicine, refer immediately to a doctor or a hospital emergency room and bring the medicine package with you. Overdose symptoms may include flushing, headache, nausea, vomiting, diarrhea and low blood pressure.

If you have forgotten to perform an inhalation session with the medicine, take the usual dose as soon as you remember.

Continue with the treatment as recommended by your doctor.

Even if your state of health improves, do not stop the treatment with this medicine without consulting your doctor or your pharmacist.

Do not take or use any medicines in the dark! Check the label and the dose each time you take or use a medicine. Wear glasses if you need them.

If you have any further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of Tyvaso may cause side effects in some users. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

The medicine may cause the following severe side effects:

- **Low blood pressure.** If you suffer from low blood pressure, the medicine may lower your blood pressure even more.
- **Bleeding problems.** The medicine may cause an increase in the risk of bleeding (especially in patients also taking anticoagulants).
- **Acute bronchospasm.**

If you experience these side effects, contact your doctor immediately.

Additional side effects:

Common to very common side effects (appear in more than 4% of the patients): cough, headache, digestive system effects such as nausea, diarrhea; reddening of the face and neck (flushing); throat irritation and pain, dizziness, fainting or loss of consciousness.

Less common side effects (appear in less than 4% of the patients): pains in jaw, bones or muscles; nasal discomfort, bloody mucus.

Additional side effects relating to the administration method of the medicine: various irritations of the respiratory system (cough, throat irritation, throat pain, bloody mucus), nosebleed, wheezing, pneumonia.

Side effects of unknown frequency (effects whose frequency has not yet been determined): angioedema.

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with your doctor.

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads you to an online form for reporting side effects, or by entering the link:

<http://sideeffects.health.gov.il>

5. How to store the medicine?

Avoid poisoning! This medicine, and any other medicine, must be stored in a safe place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: Store below 25°C.
- One new ampule should be used each day.
- Each ampule of the medicine (once opened and transferred to the medicine cup) should remain in the device for no more than one day. Any remaining medicine should be discarded at the end of each day.
- Once a foil pouch is opened, use ampules within 7 days.
- Once a foil pouch is opened, store the ampules in the original pouch, in order to protect from light.
- When the inhalation device is stored in the carrying case be sure to close the dome-type cover (the dome assembly) with the plugs to prevent the medicine from spilling out.

6. Additional information

In addition to the active ingredient, the solution also contains:

Sodium chloride, sodium citrate, hydrochloric acid, sodium hydroxide, water for injection.

What does the medicine look like and what does the package contain?

Tyvaso is a clear, colorless to slightly yellow solution. The solution comes in a plastic ampule containing 2.9 mL. Every 4 ampules are packed in a foil pouch. There are packages containing 4 ampules and packages containing 28 ampules. Use the medicine with the inhalation device intended for it.

Not all the package sizes may be marketed.

Registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301.

Manufacturer: United Therapeutics Corp., USA.

Medicine registration number in the National Medicines Registry of the Ministry of Health:
144 71 33077

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