

Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

TOBI® Podhaler® 28 mg

Inhalation powder hard capsules

Each capsule contains: 28 mg Tobramycin

Inactive ingredients and allergens in the medicine - see section 6 "Additional information"

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

1. What is the medicine intended for?

Tobi Podhaler 28 mg is intended for the treatment of cystic fibrosis patients aged 6 years and older with chronic lung infection due to the *Pseudomonas aeruginosa* bacterium.

Therapeutic group: aminoglycoside antibiotics class.

Tobi Podhaler contains an antibiotic called tobramycin.

Tobi Podhaler capsules contain a powder intended for inhalation. **Tobi Podhaler** capsules intended for oral inhalation should only be used with the inhaler included in the pack. When inhaling the contents of **Tobi Podhaler** capsules, the antibiotic can enter directly into the lungs to act against the bacterium causing the infection and to improve your breathing. *Pseudomonas aeruginosa* is a very common bacterium that infects the lungs of almost anyone with cystic fibrosis at some time during their life. Some people do not get this infection until later on in their lives, while others get it at a very young age. It is one of the most harmful bacteria for people with cystic fibrosis. If the infection is not treated properly, it will continue to damage the lungs and cause further breathing problems.

2. Before using the medicine

Do not use the medicine if:

• You are hypersensitive (allergic) to the active ingredient (tobramycin), to any type of aminoglycoside antibiotic, or to any of the other ingredients this medicine contains (see section 6).
If this applies to you, **tell your doctor without taking Tobi Podhaler**.
If you think you may be allergic, ask your doctor for advice.

Special warnings regarding the use of the medicine

Before the treatment with Tobi Podhaler, tell the doctor if you have or have ever had:

- Hearing problems (including noises in the ears and dizziness)
- Kidney problems
- Unusual difficulty in breathing with wheezing or coughing, chest tightness
- Blood in your sputum (the substance you cough up)
- Muscle weakness that persists or worsens over time, a symptom mostly related to conditions such as myasthenia or Parkinson's disease.

If you are aged 65 or older, your doctor may perform additional tests to determine if **Tobi Podhaler** is right for you.

Inhaling medicines can cause chest tightness and wheezing while breathing; this can happen immediately after inhalation of **Tobi Podhaler**. Your doctor will supervise your first dose of **Tobi Podhaler** and check your lung function before and after taking the medicine. Your doctor may ask you to take other appropriate medicines before taking **Tobi Podhaler**.

Inhaling medicines can also cause cough, this can happen with **Tobi Podhaler**. Consult your doctor if the cough is persistent and a burden for you.

Strains of *Pseudomonas* can become resistant to antibiotic treatment over time. This means that **Tobi Podhaler** may not be as effective as it should be over time. Consult your doctor if you are concerned about this.

If you take tobramycin or another aminoglycoside antibiotic by injection, it can sometimes cause hearing loss, dizziness and kidney damage.

Children

Tobi Podhaler is not intended for children less than 6 years old.

Drug interactions

If you are taking, have recently taken or might take other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

It is recommended that you do not take the following medications while you are taking **Tobi Podhaler**:

- Furosemide or ethacrynic acid, diuretics
- Other medicines with diuretic properties such as urea or intravenous mannitol
- Other medicines which may harm your kidneys or hearing.

The following medicines can increase the chance of harmful effects occurring if they are given to you while you are also receiving **injections** of tobramycin or other aminoglycoside antibiotic:

- Amphotericin B, cefalotin, polymyxins (used to treat bacterial infections), ciclosporin, tacrolimus (used to suppress the activity of the immune system). These medicines may harm the kidneys.
- Platinum compounds such as carboplatin and cisplatin (used to treat some forms of cancer). These medicines may harm your kidneys or hearing.

- Anticholinesterases such as neostigmine and pyridostigmine (used to treat muscle weakness), or botulinum toxin. These medicines may cause muscle weakness to appear or become worse.

If you are taking one or more of the above medicines, discuss with your doctor before you take **Tobi Podhaler**.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or planning to become pregnant, consult a doctor or pharmacist before using this medicine.

It is not known whether inhaling this medicine during pregnancy causes side effects. When tobramycin and other aminoglycoside antibiotics are given by injection, they can cause harm to the fetus, such as deafness.

If you are breastfeeding, talk to your doctor before using this medicine.

Driving and using machines

Tobi Podhaler has no influence (or its influence is negligible) on the ability to drive and use machines.

3. How to use this medicine

Always use this medicine according to the doctor's instructions.

Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

The dosage and manner of treatment will be determined by the doctor only.

Caregivers should provide assistance to children starting treatment with **Tobi Podhaler**, particularly those who are 10 years old and younger, and continue to supervise them until they are able to use **Tobi Podhaler** properly without help.

The usual recommended dosage is:

Contents of 4 capsules should be taken by inhalation twice a day (4 capsules in the morning and 4 capsules in the evening), using the Podhaler inhaler.

The dose is the same for all patients aged 6 and over. **Do not exceed the recommended dose.**

Taking **Tobi Podhaler** at the same time each day will help you remember when to take the medicine.

- Contents of 4 capsules should be taken by inhalation in the morning using the inhaler included in the pack.
- Contents of 4 capsules should be taken by inhalation in the evening using the inhaler included in the pack.

Leave an interval as close as possible to 12 hours between the morning dose (contents of 4 capsules by inhalation) and the evening dose (contents of 4 capsules by inhalation), and not less than 6 hours between doses.

If you are taking several different inhaled treatments and are being treated with other cystic fibrosis therapies, **Tobi Podhaler** should be taken at the end, after all other treatments have been completed. Check the order of medicines with your doctor.

Route of administration

- For inhalation use only.
- Do not swallow the capsules.
- Capsules should be used only with the inhaler provided with this pack. The capsules should remain in the capsule tray until you need to use them.
- When you start a new weekly pack of capsules, use the new inhaler that is supplied in the pack. Each inhaler should be used only for 7 days.
- See the "Instructions for use of **Tobi Podhaler**" section at the end of this leaflet for more information on how to use the inhaler.

Duration of use

After taking **Tobi Podhaler** for 28 days, you should take a 28-day break during which you will not inhale any **Tobi Podhaler**, before starting another cycle. It is important that you keep using the medicine twice every day during the 28 days you are receiving treatment and that you maintain cycles of 28-day with medicine and 28 days without medicine.

Continue taking **Tobi Podhaler** according to the doctor's instructions.

If you have questions about how long to take **Tobi Podhaler**, refer to your doctor or pharmacist. Follow your doctor's instructions carefully.

If you have accidentally taken a higher dosage

If you inhale too much **Tobi Podhaler**, refer to your doctor as soon as possible. If **Tobi Podhaler** capsules are swallowed, do not worry, but refer to your doctor as soon as possible.

If you forgot to take the medicine

If you forget to take **Tobi Podhaler** and there are at least 6 hours to your next dose, take your dose as soon as you can. Otherwise, wait for your next dose. Do not take a double dose to make up for a forgotten dose.

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

If you have further questions on the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Tobi Podhaler** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

People with cystic fibrosis have many symptoms of the disease. These symptoms may still happen while taking **Tobi Podhaler**, but should not be any more frequent or worse than before the treatment. If you feel that your lung disease is getting worse when you take **Tobi Podhaler**, refer to a doctor immediately.

Some side effects can be serious

Stop taking Tobi Podhaler and refer to the doctor immediately if you experience:

- Unusual difficulty in breathing with wheezing or coughing and chest tightness (common).

Refer to a doctor immediately if you experience:

- Coughing up blood (very common).
- Decreased hearing (ringing in the ears is a possible warning sign of hearing loss), noises (such as hissing) in the ears (common).

Additional side effects:

Very common side effects (effects that appear in more than 1 in 10 users):

- Shortness of breath
- Cough, productive cough, voice alteration (hoarseness)
- Sore throat
- Fever

Common side effects (effects that appear in 1-10 out of 100 users):

- Wheezing while breathing, rales (crackles)
- Chest discomfort, chest pain originating from muscles or skeleton
- Blocked nose
- Nosebleed
- Vomiting, nausea
- Diarrhea
- Rash
- Disturbed sense of taste
- Loss of voice

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

- Generally feeling unwell
- Discoloration of the substance you cough up (sputum)

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

Side effects can be reported to the Ministry of Health via the link

"דיווח על תופעות לוואי יקבע טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link:

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

5. How to store the medicine

- Avoid poisoning! This medicine and any other medicine must be stored in a closed 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) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 30°C. Store in the original package in order to protect from moisture. The inhaler should be stored tightly closed in its box when not in use. **When removing a capsule from the tray, use it immediately.**
- Do not throw away any medicines via wastewater. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Hypromellose, sulfuric acid, DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine), purified water, carrageenan (E407), calcium chloride, potassium chloride, carnauba wax, blue ink (shellac, indigo carmine aluminum lake (E132), N-butyl alcohol, titanium dioxide (E171), propylene glycol (E1520), isopropyl alcohol).

What the medicine looks like and what the package contains:

Tobi Podhaler 28 mg hard capsules for inhalation contain white or almost white powder in clear colorless capsules, with "MYL TPH" printed in blue ink on one part of the capsule and the Mylan logo imprinted in blue on the other part of the capsule.

Each monthly pack contains 224 capsules and 5 inhalers (4 weekly cartons containing 56 hard capsules and one inhaler + one reserve inhaler).

Each weekly pack contains 7 blisters (a tray of capsules), with each blister containing 8 capsules, and a Podhaler inhaler in its storage case.

Manufacturer and address: Mylan Pharmaceuticals Inc., Steinhausen, Switzerland

Revised in December 2021 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health: 147-05-33412-00

Tobi Podhaler 28 mg PIL&FU PB1021-08

Registration holder: **Dexcel® Ltd.**

1 Dexcel St., Or Akiva 3060000, Israel

Instructions for use of Tobi® Podhaler®

Read the following instructions carefully in order to learn how to use and look after the Podhaler inhaler.

Monthly pack contents of Tobi Podhaler:

Each monthly pack contains:

- 4 weekly cartons (see contents below).
- 1 reserve inhaler (the Podhaler inhaler) with its storage case.

Weekly pack contents of Tobi Podhaler:

Each weekly carton contains:

- 1 inhaler (the Podhaler inhaler) with its storage case.
- 7 capsule trays (one tray for each day of the week).
- Each capsule tray contains 8 capsules (corresponding to the daily dose: content of 4 capsules to be inhaled in the morning and content of 4 capsules to be inhaled in the evening).



How to inhale the medicine with the Podhaler inhaler

- **Only use the Podhaler inhaler contained in this pack.** Do not use **Tobi Podhaler** capsules with any other device, and do not use the Podhaler inhaler to take any other medicine.
- When you start a new weekly pack of capsules, use the new Podhaler inhaler that is supplied in the pack. Each Podhaler inhaler is only used for 7 days. Ask your pharmacist how to dispose of medicines and inhalers no longer required.
- **Do not swallow the capsules.** The powder in the capsules is for you to inhale.
- Always keep the capsules in the capsule tray until when you need to use them. Do not take the capsules out of the tray in advance.
- Store the Podhaler inhaler in its tightly closed case when not in use.

1. Wash and fully dry your hands.	
2. Just before use, remove the inhaler from its case by holding the base and twisting off the top of the case in an anti-clockwise direction. • Set the top of the case aside. • Look at the inhaler to make sure it is not damaged or dirty. • Stand the inhaler upright in the base of the case.	
3. Hold the body of the inhaler and unscrew the mouthpiece in an anti-clockwise direction. • Set the mouthpiece aside on a clean, dry surface.	
4. Tear along the perforations of the capsule tray lengthwise, then widthwise, as indicated in pictures (1) and (2).	
5. Peel back the aluminum foil from the capsule tray, so that only one capsule is revealed. • Remove the capsule from the tray.	
6. Insert the capsule into the inhaler chamber immediately (1). • Replace the mouthpiece. • Screw the mouthpiece on firmly until it stops. Do not overtighten (2).	
7. Hold the inhaler with the mouthpiece pointing down . • Pierce the capsule by pressing firmly the blue button with your thumb as far as it will go, then release the button. • You are now ready to inhale the capsule in two separate breaths (Steps 8 and 9).	
8. Inhaling the capsule content – first breath: • Before putting the mouthpiece in your mouth, exhale (breathe out) fully, away from the inhaler. • Place your mouth over the mouthpiece – to make a tight seal. • Inhale the powder deeply with a single breath. • Remove the inhaler from your mouth, and hold your breath for about 5 seconds. • Then exhale normally, away from the inhaler.	

9. Inhaling the capsule content – second breath: • Take a few normal breaths away from the inhaler. • When you are ready, take your second breath by repeating Step 8, using the same capsule.	
10. Unscrew the mouthpiece (1) and remove the capsule from the chamber (2).	
11. Look at the used capsule. It should appear pierced and empty. If it is empty, discard the capsule.	
If the capsule is pierced but still contains some powder: • Put the capsule back into the inhaler chamber (Step 6). Put the pierced side of the capsule in first. • Replace the mouthpiece and repeat Steps 8, 9 and 10.	
If the capsule does not look pierced: • Put the capsule back into the inhaler chamber (Step 6). • Replace the mouthpiece and repeat Steps 7, 8 and 9. • After this, if the capsule is still full and appears not to be pierced, replace the inhaler with the reserve inhaler (available in the monthly pack) and repeat Steps 2, 3, 6, 7, 8, 9 and 10.	
12. Take the other 3 capsules in the same way. • So for each remaining capsule, repeat steps 5, 6, 7, 8, 9, 10 and 11. • Discard all the empty capsules.	
13. Replace the mouthpiece and screw it on firmly until it stops. When the full dose (4 capsules) has been inhaled, wipe the mouthpiece with a clean dry cloth. • Do not wash the inhaler with water.	
14. Place the inhaler back in the storage case • Twist the top of the case in a clockwise direction until it is closed tightly.	

Remember:

- For inhalation use only.
- **Do not swallow the Tobi Podhaler capsules.**
- **Only use the inhaler contained in this pack.**
- Always keep the **Tobi Podhaler** capsules in the capsule tray. Only remove a capsule just before you are going to use it. Do not store the capsules in the inhaler.
- Always keep the **Tobi Podhaler** capsules and inhaler in a dry place.
- Never place the **Tobi Podhaler** capsule directly into the mouthpiece of the inhaler.
- Always hold the inhaler with the mouthpiece pointing down when piercing the capsule.
- Do not press the piercing button more than once at a time.
- Never blow into the mouthpiece of the inhaler.
- Never wash the Podhaler inhaler with water. Keep it dry and store it in its case.

Additional information:

- Occasionally, very small pieces of the capsule can get past the screen and get into your mouth.
- If this happens, you may be able to feel these pieces on your tongue.
- It is not harmful if these pieces are swallowed or inhaled.
- The chances of the capsule breaking into pieces will be increased if the capsule is accidentally pierced more than once or if the inhaler is not held with the mouthpiece pointing down during step 7.