TOBI® Podhaler®
Tobramycin Inhalation Powder 28 mg per capsule

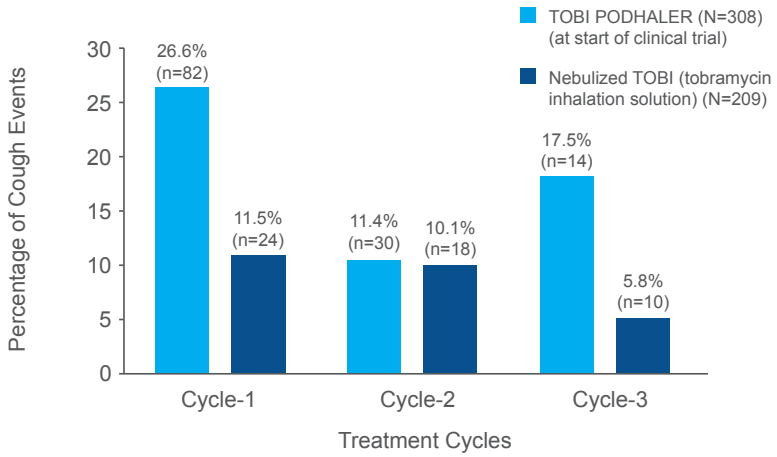
TOBI® PODHALER®

Cough is among the most common side effects of TOBI® PODHALER®. The following information reflects the clinical data regarding cough associated with TOBI® (tobramycin inhalation solution) versus TOBI PODHALER.

Study 1 was a randomized, open-label, active-controlled parallel arm trial. A total of 517 patients were randomized and received TOBI PODHALER (n=308) or TOBI (n=209).[1]

Not actual size

Cough events decreased after Cycle 1 in a 3-cycle study with consistent use of TOBI PODHALER[2]



Cough was the most frequent AE leading to discontinuation in the TOBI PODHALER treatment group (12 patients), with a slightly higher incidence than the TOBI Solution group (2 patients).

In a clinical trial evaluating the safety of TOBI PODHALER vs TOBI nebulizer solution:

- Patients using TOBI PODHALER, the dry-powder inhalation, experienced cough more frequently than patients using TOBI nebulizer solution (48% vs 31%).[1]
- After the first week of treatment, the time to first cough was similar for patients using TOBI PODHALER and TOBI nebulizer solution.[1]
- Five percent of patients using TOBI PODHALER discontinued due to cough compared with 1% of patients using TOBI nebulizer solution.[1]
- Discontinuations due to adverse events across the trial were higher in the TOBI PODHALER arm (14%) than in the TOBI arm (8%).[1]

INDICATION

TOBI® PODHALER® (Tobramycin Inhalation Powder) 28 mg per capsule and TOBI® (Tobramycin Inhalation Solution) 300 mg per 5 mL solution are indicated for the management of cystic fibrosis in adults and pediatric patients with *Pseudomonas aeruginosa*.

Safety and efficacy have not been demonstrated in patients under the age of 6 years, patients with forced expiratory volume in 1 second (FEV_1) <25% or >80% predicted for TOBI PODHALER and <25% or >75% for TOBI, or patients colonized with *Burkholderia cepacia*.

IMPORTANT SAFETY INFORMATION

TOBI PODHALER and TOBI are contraindicated in patients with known hypersensitivity to any aminoglycoside.

Please see accompanying Full Prescribing Information and Patient Information for TOBI PODHALER.
Please see accompanying Full Prescribing Information and Patient Information for TOBI Solution.
See reverse side for additional Important Safety Information.

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How Do I Use TOBI PODHALER?

Your healthcare provider should show you or your caregiver how to use TOBI PODHALER before you use it for the first time.[1]

The recommended dosage of TOBI PODHALER

- **4** 28-mg capsules for inhalation
- **2** times a day (AM and PM) in cycles of
- **28** days on and
- **28** days off

Important Dosing Considerations[1]

- One treatment cycle consists of 28 days on and 28 days off treatment
- Each dose of 4 capsules should be taken as close to 12 hours apart as possible; each dose should not be taken less than 6 hours apart
- The powder from all 4 capsules must be inhaled to receive the full dose of 112 mg
- Inhale 2 times from each capsule in order to empty it
- Capsules are for use with the PODHALER device only
- TOBI PODHALER capsules must not be swallowed and are for oral inhalation only
- Capsules should always be stored in the blister card; each capsule should only be removed IMMEDIATELY BEFORE USE
- The PODHALER device should always be stored in its case and tightly closed when not in use
- When starting a new weekly pack of capsules, use a new PODHALER device and storage case and discard the previous week's device and its case

IMPORTANT SAFETY INFORMATION (Continued)

Bronchospasm can occur with inhalation of TOBI PODHALER or TOBI. Bronchospasm should be treated as medically appropriate

Caution should be exercised when prescribing TOBI PODHALER or TOBI to patients with known or suspected auditory, vestibular, renal, or neuromuscular dysfunction.

Ototoxicity, as measured by complaints of hearing loss or tinnitus, was reported by patients in the TOBI PODHALER and TOBI clinical studies. Tinnitus may be a sentinel symptom of ototoxicity, and therefore the onset of this symptom warrants caution. Ototoxicity, manifested as both auditory and vestibular toxicity, has been reported with parenteral aminoglycosides. Vestibular toxicity may be manifested by vertigo, ataxia, or dizziness.

Cases of ototoxicity with aminoglycosides have been observed in patients with certain variants in the mitochondrially encoded 12S rRNA gene (*MT-RNR1*), particularly the m.1555A>G variant. Ototoxicity occurred in some patients even when their aminoglycoside serum levels were within the recommended range. Mitochondrial DNA variants are present in less than 1% of the general US population, and the proportion of the variant carriers who may develop ototoxicity as well as the severity of ototoxicity is unknown. In case of known maternal history of ototoxicity due to aminoglycoside use or a known mitochondrial DNA variant in the patient, consider alternative treatments other than aminoglycosides unless the increased risk of permanent hearing loss is outweighed by the severity of infection and lack of safe and effective alternative therapies.

Caution should be exercised when prescribing TOBI PODHALER or TOBI to patients with known or suspected renal dysfunction. Nephrotoxicity was not observed during TOBI PODHALER clinical studies but has been associated with aminoglycosides as a class.

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Helpful Tips for Using TOBI PODHALER

1 Preparation

Do not press the blue button on the PODHALER device more than once,
as the capsule may break into pieces if the button is pressed multiple times.[1]

2 Before Use

Tilt head up slightly when inhaling.
This helps straighten your throat out and provides the powder a more direct path to the lungs instead of hitting the back of the throat.[3]

3 During Use

Inhale deeply with an even speed.
This allows for a steady full inhalation of the powder. An inhalation that is too fast may send too much powder to the back of the throat. A slow inhalation may not fully empty the capsule.[3]

4 After Use

Take a sip of water after inhaling each capsule.[3]

IMPORTANCE OF TRAINING

Patients and caregivers should be initially trained by their CF Care Team on the proper use of TOBI PODHALER. In addition to live training, patients should be advised to read and understand the Patient Information and the Full Instructions for Use.

Also be sure to watch the summary video on how to use TOBI PODHALER by visiting www.TOBIPODHALER.com or scanning the QR code.

IMPORTANT SAFETY INFORMATION (Continued)

TOBI PODHALER and TOBI should be used cautiously in patients with neuromuscular disorders, such as myasthenia gravis or Parkinson's disease, since aminoglycosides may aggravate muscle weakness because of a potential curare-like effect on neuromuscular function.

Aminoglycosides can cause fetal harm when administered to a pregnant woman. Patients who use TOBI PODHALER or TOBI during pregnancy, or who become pregnant while taking TOBI PODHALER or TOBI, should be apprised of the potential hazard to the fetus. The amount of tobramycin excreted in human breast milk is unknown. However, systemic absorption of tobramycin following inhaled administration is expected to be minimal. A decision should be made whether to discontinue nursing or TOBI PODHALER. TOBI may cause intestinal flora alteration. Advise a woman to monitor the breastfed infant for loose or bloody stools and candidiasis.

Patients receiving concomitant TOBI PODHALER or TOBI and parenteral aminoglycoside therapy should be monitored as clinically appropriate for toxicities associated with aminoglycosides as a class. Serum tobramycin levels should be monitored.

Concurrent and/or sequential use of TOBI PODHALER or TOBI with other drugs with neurotoxic, nephrotoxic, or ototoxic potential should be avoided. Some diuretics can enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue. TOBI PODHALER or TOBI should not be administered concomitantly with ethacrynic acid, furosemide, urea, or mannitol.

In clinical trials, the most commonly observed adverse events with TOBI PODHALER occurring at a frequency of at least 10% were cough, lung disorder, productive cough, dyspnea, pyrexia, oropharyngeal pain, dysphonia, hemoptysis, and headache. For TOBI, the most common adverse reactions of at least 5% were increased cough, pharyngitis, increased sputum, dyspnea, hemoptysis, decreased lung function, voice alteration, taste perversion, and rash.

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References:
1. TOBI PODHALER (tobramycin) inhalation powder. Prescribing information. Mylan Specialty L.P., Morgantown, WV; 2023. **2.** Data on file [C2302_CSR_Study 1]. **3.** Data on file [Expert consultation with David E. Geller, MD; April 19, 2013].

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