Take back time with TOBI® PODHALER®

(Tobramycin Inhalation Powder) 28 mg per capsule

Not actual size.

Not an actual patient.

INDICATION

TOBI® PODHALER® (Tobramycin Inhalation Powder) 28 mg per capsule is indicated for the management of cystic fibrosis 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, or patients colonized with *Burkholderia cepacia*.

IMPORTANT SAFETY INFORMATION

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

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

Caution should be exercised when prescribing TOBI PODHALER 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 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.

TOBI® Podhaler®
Tobramycin Inhalation Powder
28 mg per capsule

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

VIATRIS™

The only inhaled antipseudomonal treatment using dry powder formulation

Twice-daily treatment with fast administration time of **2 to 7 minutes** as observed in a clinical trial[1*]

No nebulizer, refrigeration or power source needed

No washing, drying, or disinfection required

Simply wipe clean with a dry cloth[1]

TOBI PODHALER is **compact and lightweight**

Each day, **patients can easily carry** what they need while on treatment

*Average time as observed in a randomized, open-label, active controlled study to evaluate safety.

IMPORTANT SAFETY INFORMATION (Continued)

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.

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

PULMOSPHERE® Technology

TOBI PODHALER delivers proprietary PULMOSPHERE powder particles[2]

- Low in density
- Light and porous - Hollow particle
- Particle size: median geometric diameter is 1.7-2.7 µm
- Minimal effort is required to disperse the particles
- Low particle-to-particle cohesion supporting dispersibility
- Lung deposition to both central and peripheral airways

Watch a video on PULMOSPHERE Technology by visiting **TOBIPODHALERHCP.com or scanning the QR code**

IMPORTANT SAFETY INFORMATION (Continued)

Caution should be exercised when prescribing TOBI PODHALER 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.

TOBI PODHALER 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.

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

In a clinical study, patients with moderate to severe CF were able to use the PODHALER device[1]

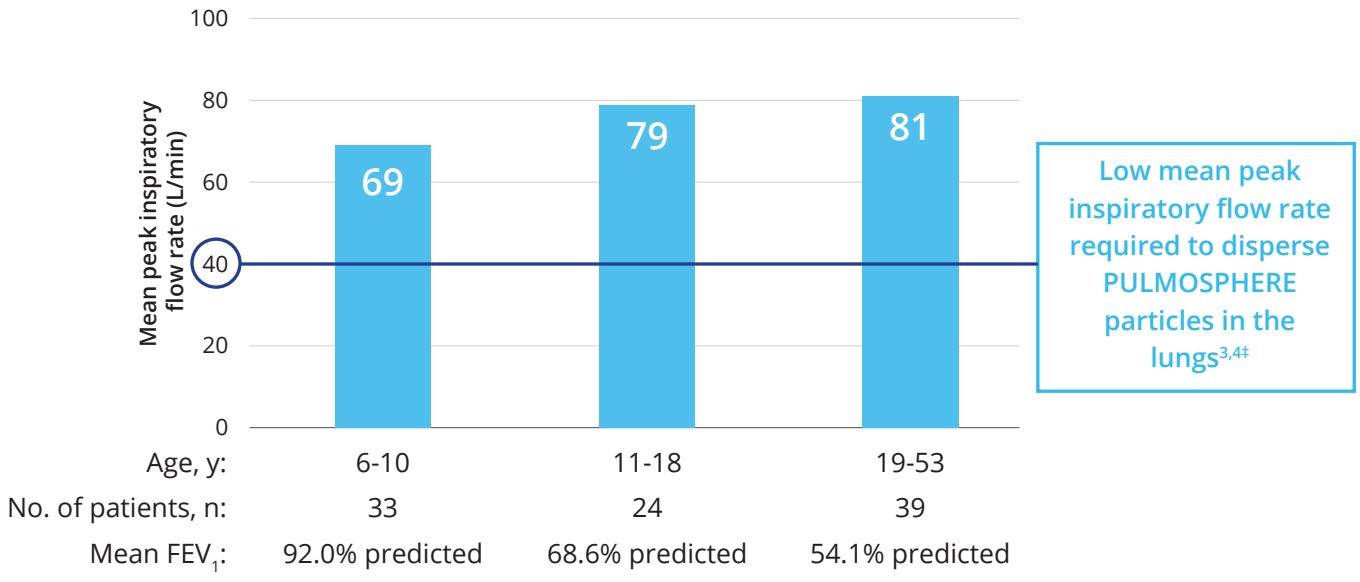
Patient types that were able to generate the inspiratory flow rates and volumes required to receive medication included:[1]

Older patients with significant disease progression and associated decreases in FEV_1

Younger patients (aged >6 years) with inhaled volumes <1 L

Patients followed the Instructions for Use. Pediatric patients aged 6 to 10 years of age with FEV_1 <40% predicted were not evaluated

Mean inspiratory flow rate of 96 CF patients exceeded the minimal requirement for dispersion of PULMOSPHERE particles[3,4‡§]



CF patient profiles with various degrees of lung function[3,4‡]

‡This study explored inspiratory variables of 96 patients with CF aged ≥6 years with varying degrees of lung disease while inhaling through mouthpieces with resistance that simulated dry-powder inhaler devices. Enrolled patients were aged 6 to 53 years, with FEV_1 19% to 126% predicted.[3,4] TOBI PODHALER is indicated for patients with an FEV_1 25% to 80% predicted.[1]

§A flow rate of 40 L/min represents a flow rate more than 2 standard deviations below the mean peak inspiratory flow rates measured for pediatric patients in the study.[2]

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Dosing

- One treatment cycle consists of **28 days on and 28 days off** treatment[1]
- 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[1]
- 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**[1]
- Capsules are for use with the PODHALER device only[1]
- TOBI PODHALER capsules must not be swallowed and are for oral inhalation only[1]
- Capsules should always be stored in the blister card, each capsule should **only be removed IMMEDIATELY BEFORE USE**[1]

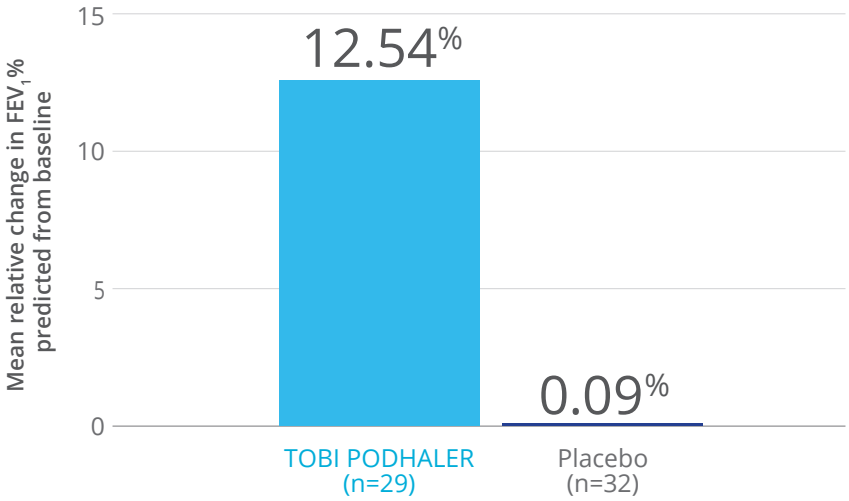
IMPORTANT SAFETY INFORMATION (Continued)

Aminoglycosides can cause fetal harm when administered to a pregnant woman. Patients who use TOBI PODHALER during pregnancy, or who become pregnant while taking TOBI PODHALER, should be apprised of the potential hazard to the fetus. The amount of tobramycin excreted in human breast milk is unknown.

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

In a placebo-controlled study, TOBI PODHALER significantly improved lung function

Mean relative change in FEV_1% predicted from baseline to the end of first 28 days on treatment (*P*=0.002)[1†]



Primary endpoint in EVOLVE (Study 2)

Mean absolute changes in FEV_1% predicted

TOBI PODHALER: +6.38%; placebo: -0.52%; difference of 6.90% (95% CI: 2.40, 11.40)[1]

EVOLVE: EValuate tObramycin inhaLed dry powder efficacy Versus placebo in cystic fibrosis patiEnts.

[†]Each cycle consisted of 28 days on treatment followed by 28 days off treatment.[1]

EVOLVE was a 24-week, randomized, double-blind (during Cycle 1) trial in patients aged 6 to 21 years with CF, *Pa*, and FEV_1 ≥25% and ≤80% predicted at screening. The first cycle was double-blind and placebo-controlled with eligible patients randomized 1:1 to TOBI PODHALER (four 28-mg capsules twice daily) or placebo. For Cycles 2 and 3, patients who were initially randomized to placebo received TOBI PODHALER. Of the 79 patients included in the prespecified interim analysis, 18 were excluded due to a failure to meet spirometry quality review criteria, which resulted in a total of 61 patients included in the primary analysis.[1,5]

IMPORTANT SAFETY INFORMATION (Continued)

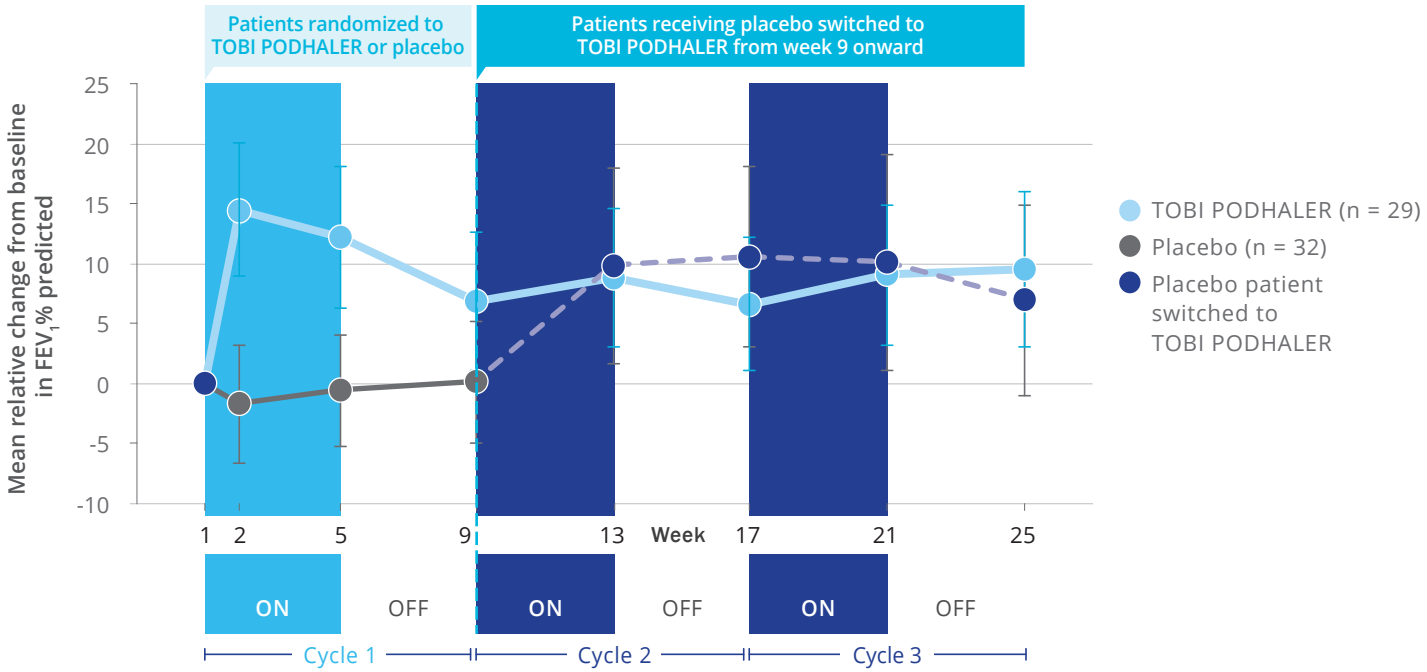
However, systemic absorption of tobramycin following inhaled administration is expected to be minimal. A decision should be made whether to discontinue nursing or TOBI PODHALER. TOBI may cause intestinal flora alteration. Advise a woman to monitor the breastfed infant for loose or bloody stools and candidiasis.

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

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

After cycle 1, patients who switched from placebo to TOBI PODHALER showed improvement in their lung function

Mean relative change in FEV_1% predicted from baseline (Cycles 1 to 3)[1]



Error bars represent mean relative change (95% CI)[1]

Improvements in lung function were achieved during the subsequent cycles of treatment with TOBI PODHALER, although the magnitude of improvement was reduced.[1]

IMPORTANT SAFETY INFORMATION (Continued)

Concurrent and/or sequential use of TOBI PODHALER 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 should not be administered concomitantly with ethacrynic acid, furosemide, urea, or mannitol.

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

In a placebo-controlled study,

Fewer respiratory-related hospitalizations and IV antipseudomonal antibiotics

64%

Reduction in the percentage of patients with respiratory-related hospitalizations in clinical study comparing TOBI PODHALER and placebo[1,5]

Secondary endpoint in EVOLVE (Study 2, Cycle 1)[1]

- 4.4% in the TOBI PODHALER treatment group vs 12.2% in the placebo group

15%

Reduction in the percentage of patients needing IV antipseudomonal antibiotics in clinical study comparing TOBI PODHALER and placebo[1,5]

Secondary endpoint in EVOLVE (Study 2, Cycle 1)[1]

- 8.7% in the TOBI PODHALER treatment group vs 10.2% in the placebo group

EVOLVE was a 24-week, randomized, double-blind (during Cycle 1) trial in patients aged 6 to 21 years with CF, *Pa*, and FEV_1 ≥25% and ≤80% predicted at screening. The first cycle was double-blind and placebo-controlled with eligible patients randomized 1:1 to TOBI PODHALER (four 28-mg capsules twice daily) or placebo. For Cycles 2 and 3, patients who were initially randomized to placebo received TOBI PODHALER. Of the 79 patients included in the prespecified interim analysis, 18 were excluded due to a failure to meet spirometry quality review criteria, which resulted in a total of 61 patients included in the primary analysis.[1,5]

IMPORTANT SAFETY INFORMATION (Continued)

In a clinical trial, 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.

Please see additional Important Safety Information on page 20.

Click here for Full Prescribing Information.

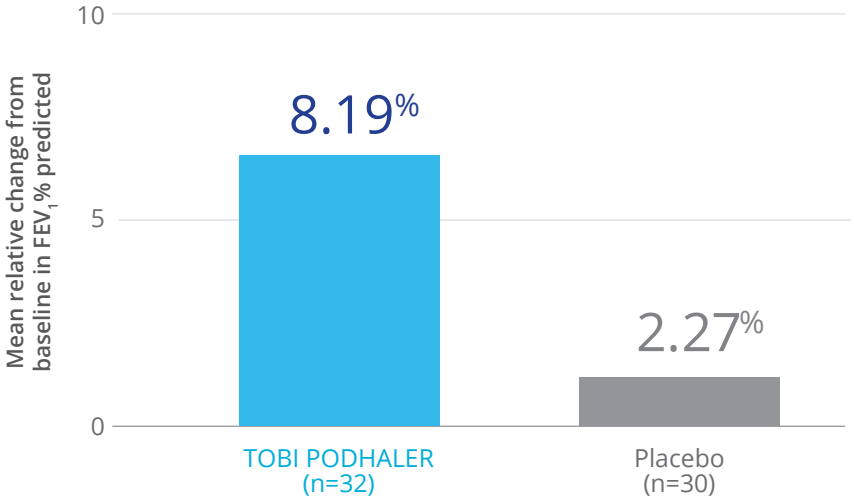
In a separate placebo-controlled study,
Lung function was evaluated in patients treated with TOBI PODHALER *vs.* placebo[1]

EDIT study design[1,6]

- EDIT was an 8-week, randomized, double-blind, placebo-controlled study in patients aged 6 to 21 years with CF, *Pa*, and FEV_1 ≥25% and ≤80% predicted at screening
- Patients with any use of inhaled antipseudomonal antibiotics within 4 months prior to screening were excluded
- Eligible patients were randomized 1:1 to receive TOBI PODHALER (4 times 28-mg capsules twice daily; n=32) or placebo (n=30) for 1 cycle (28 days on treatment and 28 days off treatment)
- The EDIT study was underpowered due to an inability to recruit the prespecified number of TOBI-naïve patients into each arm

EDIT, Establish tobramycin Dry powder effIcacy In cysTic fibrosis.

Mean relative change in FEV_1% predicted from baseline to the end of first 28 days on treatment (*P*=0.167)



Primary endpoint in EDIT (Study 3)[1]

- Results not statistically significant[1]
- Mean absolute change in FEV_1% predicted was 4.86% for TOBI PODHALER and 0.48% for placebo, with a difference of 4.38% (95% CI: -0.17, 8.94)[1]

Decreased susceptibility of *Pa* to tobramycin has been seen with use of TOBI PODHALER. The relationship between in vitro susceptibility test results and clinical outcome with TOBI PODHALER therapy is not clear. Occurrence of decreased susceptibility on treatment should be monitored, and treatment with an alternative therapy should be considered if clinical worsening is observed.[1]

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Safety considerations for patients taking TOBI PODHALER

In a head-to-head study, TOBI PODHALER was evaluated for safety *vs.* TOBI® (Tobramycin Inhalation Solution, USP):[1]

Adverse reactions (≥10%)	TOBI PODHALER (n=308)	TOBI (n=209)
Cough	48.4%	31.1%
Lung disorders[a]	33.8%	30.1%
Productive cough	18.2%	19.6%
Dyspnea	15.6%	12.4%
Pyrexia	15.6%	12.4%
Oropharyngeal pain	14.0%	10.5%
Dysphonia	13.6%	3.8%
Hemoptysis	13.0%	12.4%
Headache	11.4%	12.0%

Discontinuations due to adverse events were higher in the TOBI PODHALER arm (14%) than in the TOBI arm (8%)[1]

EAGER: Establish A new Gold standard Efficacy and safety with tobramycin in cystic fibRosis.

[a]This includes adverse events of pulmonary or CF exacerbations.[1]

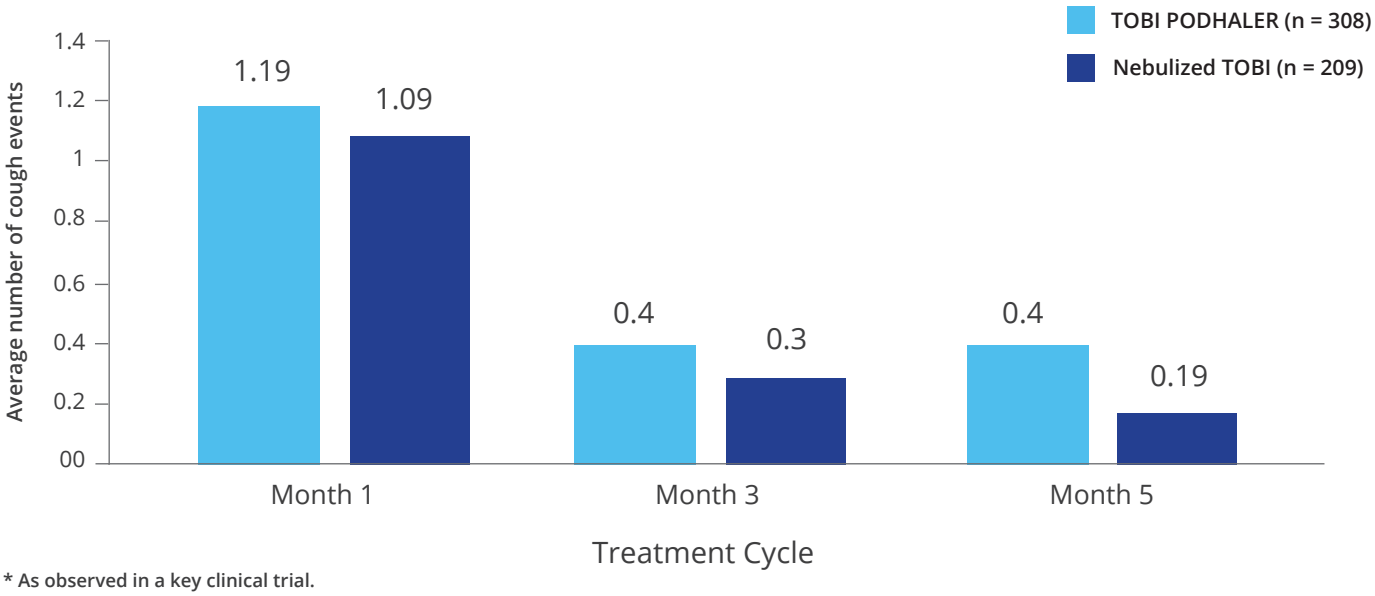
The EAGER study was a randomized, open-label, parallel-group study in 517 patients with CF and *Pa* (within 6 months of screening) aged ≥6 years with FEV_1 ≥25% to ≤75% predicted. The study consisted of 3 cycles; each cycle consisted of 28 days on treatment followed by 28 days off treatment, for a total duration of 24 weeks. Patients were randomized (3:2) to receive TOBI PODHALER 112 mg BID (n=308) or TOBI 300 mg/5 mL BID (n=209).[1,7]

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Managing cough With TOBI PODHALER

Cough is among the most common side effects of TOBI PODHALER but with the following information and tips, it can be managed effectively.

Cough events decrease over time with consistent use of TOBI PODHALER*



* As observed in a key clinical trial.

In a clinical trial evaluating the safety of TOBI PODHALER *vs.* TOBI nebulizer solution:[1]

- Patients using TOBI PODHALER, the dry-powder inhalation, experienced cough more frequently than patients using TOBI nebulizer solution (48% *vs.* 31%)
- After the first week of treatment, the time to first cough was similar for patients using TOBI Podhaler and TOBI nebulizer solution
- Five percent of patients using TOBI PODHALER discontinued due to cough compared with 1% of patients using TOBI nebulizer solution

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

TOBI® Podhaler®
Tobramycin Inhalation Powder 28 mg per capsule

Helpful tips for using TOBI PODHALER

Patients and caregivers should be initially trained by their healthcare provider on the proper use of 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]

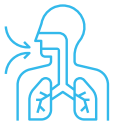
2

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.[8]

3



DURING USE

Inhale deeply with an even medium 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.[1,8]

4

AFTER USE

Take a sip of water after inhaling each capsule.[1,8]

Watch a summary video on how to use TOBI PODHALER

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.

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Counseling TOBI PODHALER patients

Talk to your patients about what to expect

Acknowledge

- Cough is a common symptom of cystic fibrosis[1]
- In a clinical trial, patients taking TOBI PODHALER reported a higher incidence of cough than patients taking TOBI (Tobramycin Inhalation Solution, USP) during the first week of active treatment[1]

Educate

- After the first week of treatment in the same study, the time to first cough was similar in patients taking TOBI PODHALER and patients taking TOBI. Five percent of patients taking TOBI PODHALER discontinued due to cough compared with 1% of patients taking TOBI[1]

Train

- Patients and caregivers should be initially trained by their CF Care Team on the proper use of TOBI PODHALER[1]
- In addition to the training you provide your patients, advise patients to read the Patient Information and the Full Instructions for Use[1]

IMPORTANT SAFETY INFORMATION (Continued)

Aminoglycosides can cause fetal harm when administered to a pregnant woman. Patients who use TOBI PODHALER during pregnancy, or who become pregnant while taking TOBI PODHALER, 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.

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Packaging overview

Each 28 day supply of TOBI PODHALER package contains:[1]

- **4 weekly packs (28-day supply), each containing:**
  - 56 capsules (7 blister cards of 8 capsules). Each blister card contains 8 TOBI PODHALER capsules (4 capsules for inhalation in the morning and 4 capsules for inhalation in the evening)
  - 1 PODHALER device and its storage case
- **1 reserve PODHALER device (to be used if needed) and its storage case**

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Patient profile

TOBI PODHALER (Tobramycin Inhalation Powder)

Case Presentation

Photos do not represent actual patients. For example only.

18 years/Male/50th percentile

First *Pa* diagnosis at age 10

FEV_1: 63%

Average hospitalizations ~1/year

- **looking for ways to help decrease his treatment time**
- High school graduate moving away to college this year
- Believes existing nebulized treatment time will impact his busy class and extracurricular schedule

Photos do not represent actual patients. For example only.

38 years/Female/18.1

First *Pa* diagnosis at age 15

FEV_1: 60%

Average hospitalizations ~1/year

- **Unable to take her treatments with her during her busy day**
- Works as a local wedding coordinator
- Difficulty fitting in all her daily treatments due to travel around town for work and her son's school commitments and sporting events

Please see additional Important Safety Information on page 20.
Click here for Full Prescribing Information.

Access and Adherence Resources

Patient access and coverage

TOBI PODHALER
is COVERED for over

84%

of Commercial and Medicaid Insurance plans combined nationwide*§

A prior authorization to indication for the class may still be required.

TOBI PODHALER is

PREFERRED BRAND on **Express Scripts** National Commercial Formularies.*

COVERED on **Cigna** commercial insurance plans.

COVERED on **OptumRx** National Commercial Formularies.*

COVERED on **United Health Care** National Commercial Formularies.*

*Preferred designation is determined by the plan, i.e. Express Scripts/OptumRx. Preferred does not mean there are no formulary restrictions or utilization management. Commercial plan coverage for 2023 based on 179,707,720 members. Formulary data is provided by Fingertip Formulary® and is current as of May 30, 2023. Formularies vary and are subject to change without notice; please check directly with the plan to determine the most up-to-date information. Not a guarantee of coverage or payment (full or partial); state of residency may impact coverage. Restrictions such as quantity limits, prior authorizations, or step edits may also vary by tier and plan. Formulary designations (e.g., preferred, non-preferred, specialty) are based on individual plan definitions and are not determined by Fingertip Formulary or Viatris Specialty. Individual costs and coverage may vary. Please check with the health plan directly to determine coverage for an individual product.

§Data on file - May 30, 2023.

Patient resources for access

podcare+

PODCARE+ offers support for patients that have been prescribed TOBI PODHALER

Electronic PA Support:

Seamless integration with CoverMyMeds® to efficiently coordinate PA process

covermymeds®

Savings Card:

Eligible, commercially-insured patients may pay as little as $0 for a TOBI PODHALER prescription*
Visit ActivateTheCard.com/TOBI to see eligibility requirements and to view full terms and conditions

Not an actual card

Visit TOBIPODHALERHCP.com or
call 1-877-999-TOBI (8624) for more information

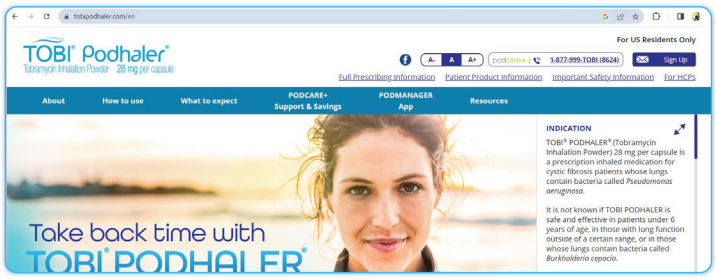
*This Savings Card may be used to reduce the amount of an eligible patient's out-of-pocket costs for TOBI PODHALER up to the full amount of the patient's out-of-pocket cost per 28 day prescription, up to an aggregate maximum of $14,000 per calendar year, while this program remains in effect. No other purchase is necessary. Valid prescription with Prescriber ID# is required. Mylan Specialty L.P., a Viatris Company, reserves the right to amend or end this program at any time without notice. For full terms and conditions, visit www.activatethecard.com/tobi.

Eligibility Requirements: This Savings Card can be redeemed only by patients or patient guardians who are 18 years of age or older and who are residents of the United States and its territories. Patients must have commercial insurance. This program is not valid for uninsured patients (but may be used by commercially insured patients without coverage for TOBI PODHALER) and patients who are covered by any state or federally funded healthcare program, including but not limited to any state pharmaceutical assistance program, Medicare (Part D or otherwise), Medicaid, Medigap, VA or DOD, or TRICARE (regardless of whether TOBI PODHALER is covered by such government program); not valid if the patient is Medicare eligible and enrolled in an employer-sponsored health plan or prescription benefit program for retirees; and not valid if the patient's insurance plan is paying the entire cost of this prescription. This program is void outside the US and its territories or where prohibited by law, taxed, or restricted. Absent a change in Massachusetts law, this program will no longer be valid for Massachusetts residents as of January 1, 2026.

This Savings Card is not health insurance. This Savings Card is not transferable, and the amount of the savings cannot exceed the patient's out-of-pocket costs. This Savings Card cannot be combined with any other rebate/coupon, cash discount card, free trial, or similar offer for the specified prescription. This Savings Card is not redeemable for cash.

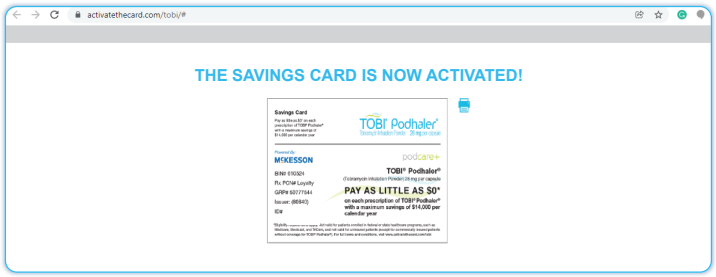
Savings Card Program

- Eligible, commercially insured patients may access the TOBI PODHALER Savings Program by **signing up on TOBIPODHALER.com** under the “PODCARE+ Support & Savings” section tab



- Patients/HCP/caregivers may enroll in the Savings Card Program by **clicking on their specific product**

- Eligible patients will receive their **Savings Card* information on the next screen so that the information can be printed and/or captured.** This information should be shared with the pharmacy that is dispensing the TOBI PODHALER prescription



*This Savings Card may be used to reduce the amount of an eligible patient's out-of-pocket costs for TOBI PODHALER up to the full amount of the patient's out-of-pocket cost per 28 day prescription, up to an aggregate maximum of $14,000 per calendar year, while this program remains in effect. No other purchase is necessary. Valid prescription with Prescriber ID# is required. Mylan Specialty L.P., a Viatris Company, reserves the right to amend or end this program at any time without notice. For full terms and conditions, visit www.activatethecard.com/tobi.
Eligibility Requirements: This Savings Card can be redeemed only by patients or patient guardians who are 18 years of age or older and who are residents of the United States and its territories. Patients must have commercial insurance. This program is not valid for uninsured patients (but may be used by commercially insured patients without coverage for TOBI PODHALER) and patients who are covered by any state or federally funded healthcare program, including but not limited to any state pharmaceutical assistance program, Medicare (Part D or otherwise), Medicaid, Medigap, VA or DOD, or TRICARE (regardless of whether TOBI PODHALER is covered by such government program); not valid if the patient is Medicare eligible and enrolled in an employer-sponsored health plan or prescription benefit program for retirees; and not valid if the patient’s insurance plan is paying the entire cost of this prescription. This program is void outside the US and its territories or where prohibited by law, taxed, or restricted. Absent a change in Massachusetts law, this program will no longer be valid for Massachusetts residents as of January 1, 2026. For full terms and conditions, visit www.activatethecard.com/TOBI.

INDICATION and IMPORTANT SAFETY INFORMATION

INDICATION

TOBI® PODHALER® (Tobramycin Inhalation Powder) 28 mg per capsule is indicated for the management of cystic fibrosis 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, or patients colonized with *Burkholderia cepacia.*

IMPORTANT SAFETY INFORMATION

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

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

Caution should be exercised when prescribing TOBI PODHALER 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 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 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.

TOBI PODHALER 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 during pregnancy, or who become pregnant while taking TOBI PODHALER, 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 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 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 should not be administered concomitantly with ethacrynic acid, furosemide, urea, or mannitol.

In a clinical trial, 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.

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Notes

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TOBI® Podhaler®

Tobramycin Inhalation Powder 28 mg per capsule

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