

TOBI

(tobramycin powder for inhalation)

Effective Date: 4/22/14

Date Developed: 4/9/14 by Dr. Robert Sterling

Last Approval Date: 1/26/16, 1/24/17, 1/22/19, 2/18/20, 2/2/21, 8/3/21, 2/1/22,
1/31/23, 2/13/24

(Archive Date: 1/1/18; 5/13/24)

Unarchived Date: 1/22/19 (Formulary Exclusion – For Exception Review Use Only)

Tobramycin powder is an aminoglycoside antibiotic which interferes with bacterial protein synthesis by binding to 30S and 50S ribosomal subunits, resulting in a defective bacterial cell membrane. This product is for inhalation via a Podhaler device.

Authorization Criteria: Management of cystic fibrosis in adults and pediatric patients ≥6 years of age with *Pseudomonas aeruginosa*.

NOTE: Safety and efficacy have not been demonstrated in patients with FEV₁ <40% or >80% predicted or in patients colonized with *Burkholderia cepacia*.

Off-Label: Non–cystic fibrosis bronchiectasis; Pneumonia, hospital-acquired or ventilator-associated

Dosing:

Pediatric: inhalation of the contents of four 28 mg TOBI capsules twice-daily for 28 days using the Podhaler device followed by 28 days off drug

Adult: 300 mg every 12 hours in repeated cycles of 28 days on drug followed by 28 days off drug.

NOTE: FOR USE WITH THE PODHALER DEVICE ONLY;

How Supplied: 28 mg capsules; nebulization solution 300mg/5 mL

Contraindications/Warnings: contraindicated with a known hypersensitivity to any aminoglycoside; use with caution in patients with renal, auditory, vestibular dysfunction or neuromuscular disorders; may cause bronchospasm

REFERENCES

Sagel SD, Gibson RL, Emerson J, et al. Impact of *Pseudomonas* and *Staphylococcus* infection on inflammation and clinical status in young children with cystic fibrosis. *J Pediatr* 2009; 154:183.

Emerson J, Rosenfeld M, McNamara S, et al. *Pseudomonas aeruginosa* and other predictors of mortality and morbidity in young children with cystic fibrosis. *Pediatr Pulmonol* 2002; 34:91.

Hyatt AC, Chipps BE, Kumor KM, et al. A double-blind controlled trial of anti-*Pseudomonas* chemotherapy of acute respiratory exacerbations in patients with cystic fibrosis. *J Pediatr* 1981; 99:307.

Lindsay CA, Bosso JA. Optimisation of antibiotic therapy in cystic fibrosis patients. Pharmacokinetic considerations. *Clin Pharmacokinet* 1993; 24:496.

Szaff M, Høiby N, Flensburg EW. Frequent antibiotic therapy improves survival of cystic fibrosis patients with chronic *Pseudomonas aeruginosa* infection. *Acta Paediatr Scand* 1983; 72:651.

Ryan G, Mukhopadhyay S, Singh M. Nebulised anti-pseudomonal antibiotics for cystic fibrosis. *Cochrane Database Syst Rev* 2003; :CD001021.

Ramsey BW, Pepe MS, Quan JM, et al. Intermittent administration of inhaled tobramycin in patients with cystic fibrosis. Cystic Fibrosis Inhaled Tobramycin Study Group. *N Engl J Med* 1999; 340:23.

Moss RB. Long-term benefits of inhaled tobramycin in adolescent patients with cystic fibrosis. *Chest* 2002; 121:55.

Burns JL, Van Dalfsen JM, Shawar RM, et al. Effect of chronic intermittent administration of inhaled tobramycin on respiratory microbial flora in patients with cystic fibrosis. *J Infect Dis* 1999; 179:1190.

Bowman CM. The long-term use of inhaled tobramycin in patients with cystic fibrosis. *J Cyst Fibros* 2002; 1:194.

Konstan MW, Flume PA, Kappler M, et al. Safety, efficacy and convenience of tobramycin inhalation powder in cystic fibrosis patients: The EAGER trial. *J Cyst Fibros* 2011; 10:54.

Parkins MD, Elborn JS. Tobramycin Inhalation Powder™: a novel drug delivery system for treating chronic *Pseudomonas aeruginosa* infection in cystic fibrosis. *Expert Rev Respir Med* 2011; 5:609. Bethkis (tobramycin) [prescribing information]. Woodstock, IL: Chiesi USA Inc; May 2021.

Festini F, Ciuti R, Taccetti G, et al, "Breast-Feeding in a Woman With Cystic Fibrosis Undergoing Antibiotic Intravenous Treatment," *J Matern Fetal Neonatal Med*, 2006, 19(6):375-6

Gibson RL, Emerson J, McNamara S, et al; Cystic Fibrosis Therapeutics Development Network Study Group. Significant microbiological effect of inhaled tobramycin in young children with cystic fibrosis. *Am J Respir Crit Care Med*. 2003;167(6):841-849. doi:10.1164/rccm.200208-855OC

Kahler DA, Schowengerdt KO, Fricker FJ, et al, "Toxic Serum Trough Concentrations After Administration of Nebulized Tobramycin," *Pharmacotherapy*, 2003, 23(4):543-5.

Le J, Ashley ED, Neuhauser MM, et al; Society of Infectious Diseases Pharmacists Aerosolized Antimicrobials Task Force. Consensus summary of aerosolized antimicrobial agents: application of guideline criteria. Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy*. 2010;30(6):562-584.

Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Cystic Fibrosis Foundation pulmonary guideline. Pharmacologic approaches to prevention and eradication of initial *Pseudomonas aeruginosa* infection. *Ann Am Thorac Soc*. 2014;11(10):1640-1650.

Ratjen F, Moeller A, McKinney ML, et al. Eradication of early *P. aeruginosa* infection in children <7 years of age with cystic fibrosis: The early study. *J Cyst Fibros*. 2019;18(1):78-85.

Tobi Podhaler (tobramycin) [prescribing information]. San Carlos, CA: Mylan Pharmaceuticals Inc; July 2020.

Treggiari MM, Retsch-Bogart G, Mayer-Hamblett N, et al; Early *Pseudomonas* Infection Control (EPIC) Investigators. Comparative efficacy and safety of 4 randomized regimens to treat early *Pseudomonas aeruginosa* infection in children with cystic fibrosis. *Arch Pediatr Adolesc Med*. 2011;165(9):847-856. doi:10.1001/archpediatrics.2011.136

Guan WJ, Xu JF, Luo H, et al; TORNASOL study group. A double-blind randomized placebo-controlled phase 3 trial of tobramycin inhalation solution in adults with bronchiectasis with *pseudomonas aeruginosa* infection. *Chest*. 2023;163(1):64-76.

Tobi (tobramycin) [prescribing information]. Morgantown, WV: Mylan Specialty LP; February 2023.

Tobi Podhaler (tobramycin) [prescribing information]. Morgantown, WV: Mylan Specialty LP; February 2023.

Ramsey BW, Pepe MS, Quan JM, et al. Intermittent Administration of Inhaled Tobramycin in Patients With Cystic Fibrosis. Cystic Fibrosis Inhaled Tobramycin Study Group. N Engl J Med. 1999;340(1):23-30.

Shaw PK, Braun TL, Liebergen A, et al. Aerosolized Tobramycin Pharmacokinetics in Cystic Fibrosis Patients. J Pediatr Pharm Pract. 1997;2(1):23-26.

Revision History:

Date Approved by P&T Committee: 4/22/14
 Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD
 Date Approved by P&T Committee: 01.27.15
 Date Reviewed/No Updates: 1/26/16 by C. Sanders, MD; R. Sterling, MD
 Date Approved by P&T Committee: 1/26/16
 Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD
 Date Approved by P&T Committee: 1/24/17
 Date Reviewed/Archived: 1/1/18 by C. Sanders, MD; R. Sterling, MD
 Date Approved by P&T Committee: 1/23/18
 Date Reviewed/No Updates/Date Unarchived: 1/22/19 by C. Sanders, MD; R. Sterling, MD
 Date Approved by P&T Committee: 1/22/19
 Date Reviewed/No Updates: 2/18/20 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 2/18/20
 Date Reviewed/No Updates: 2/2/21 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 2/2/21
 Date Reviewed/Updated: 8/3/21 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 8/3/21
 Date Reviewed/No Updates: 2/1/22 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 2/1/22
 Date Reviewed/No Updates: 1/31/23 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 1/31/23
 Date Reviewed/No Updates: 2/13/24 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 2/13/24
 Date Reviewed/Updated: 2/18/25 by H. Taekman, MD; R. Sterling, MD
 Date Approved by P&T Committee: 2/18/25

Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/1/18	No	Catherine Sanders, MD; Robert Sterling, MD	Archived – excluded from the Formulary effective 1/1/18
1/22/19	Yes	Catherine Sanders, MD; Robert Sterling, MD	Unarchived – Formulary Exclusion – For Exception Review

			Use Only Annual Review
2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/2/21	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
8/3/21	Yes	Howard Taekman, MD; Robert Sterling, MD	Added info and references, formatting changes
2/1/22	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
1/31/23	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/13/24	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/18/25	Yes	Howard Taekman, MD; Robert Sterling, MD	Updated authorization criteria, dosing and references. Added Off label use