



Antibiotics, Inhaled Therapeutic Class Review (TCR)

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FDA-APPROVED INDICATIONS

Drug	Manufacturer	FDA-Approved Indications
aztreonam (Cayston®) ¹	Gilead	For the improvement of respiratory symptoms in cystic fibrosis patients with <i>Pseudomonas aeruginosa</i> and a forced expiratory volume in 1 second (FEV ₁) between 25% and 75% predicted
tobramycin (Bethkis®) ²	Chiesi USA	For the management of cystic fibrosis patients with <i>P. aeruginosa</i> and a FEV ₁ between 40% and 80% predicted
tobramycin (Kitabis™ Pak) ³	Pari Respiratory Equipment	For the management of cystic fibrosis in adults and pediatric patients 6 years of age and older with <i>P. aeruginosa</i>
tobramycin (TOBI®) ⁴	Novartis, generic	For the management of cystic fibrosis patients with <i>P. aeruginosa</i> and a FEV ₁ between 25% and 75% predicted
tobramycin (TOBI Podhaler®) ⁵	Novartis	For the management of cystic fibrosis patients with <i>P. aeruginosa</i> and a FEV ₁ between 25% and 80% predicted

OVERVIEW

Cystic Fibrosis (CF) is the most common lethal genetic disease among Caucasians, affecting approximately 30,000 individuals residing in the United States.^{6,7} It has been estimated that 4 to 5% of all Caucasians in North America are carriers of the CF gene. The incidence of CF by ethnic groups has also been reported as follows: Caucasians 1 in 3,200; African-Americans 1 in 15,000; and Asian-Americans 1 in 31,000.⁸ More than 1,000 individuals are diagnosed with CF annually, with 53% of patients being diagnosed by 6 months of age and 74% by 2 years of age.⁹

CF is an autosomal recessive disorder caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene located on chromosome number seven.¹⁰ Loss of functionality of the CFTR protein causes impairment of chloride transport in epithelial cells, which results in different physiologic consequences in different organs.¹¹ The typical manifestation of CF involves progressive obstructive lung disease that has been associated with impaired mucous clearance, difficulty clearing pathogens, and risk of chronic pulmonary infection and inflammation.¹² As a result, respiratory failure is the common cause of death in patients with CF with the median expected survival age of 36 years. CF also manifests as pancreatic insufficiency that has been associated with fat and protein malabsorption and, consequently, malnutrition.¹³

The sweat chloride test is the gold standard of CF diagnosis since it remains to be the most discriminatory test for this disorder.¹⁴ Values of chloride greater than 60 mEq/L in a sweat chloride concentration analysis are considered positive. CF can also be diagnosed by DNA analysis; however, a negative analysis result does not exclude the diagnosis of the disease.

The main objectives of CF treatment are to treat and prevent infection, promote mucus clearance, and improve nutrition.¹⁵ Airway clearance can be achieved through different airway clearance techniques (e.g., manually assisted cough, chest physiotherapy), antibiotics, ibuprofen, inhaled hypertonic saline, inhaled beta₂ adrenergic receptor agonists, and mucolytic enzymes.^{16,17} Since pulmonary infection is the main source of morbidity and mortality, antibiotics play an important role in CF therapy to control the progression of the disease. Chronic use of inhaled tobramycin and inhaled aztreonam are recommended in the 2013 CF Pulmonary Guidelines to reduce exacerbation for patients who are 6 years of age and older with persistent *Pseudomonas aeruginosa* cultures in the airways (strength of recommendation A for moderate to severe disease; strength of recommendation B for mild disease).¹⁸

However, chronic use of oral azithromycin for patients 6 years of age and older with persistent *P. aeruginosa* culture is also recommended, though the strength of recommendation is not as strong. Additionally, in patients with pulmonary exacerbations marked by chronic infection of *P. aeruginosa*, treatment with the combination of aminoglycoside and beta-lactam antibiotic is recommended.¹⁹ Typical duration of treatment is 2 to 3 weeks of intravenous antibiotics, with clinical improvement usually seen after the first week of treatment.

It has been shown that an intermittent regimen of inhaled antibiotic therapy (28 days on drug, followed by 28 days off) provides a sustained clinical efficacy during the off drug period and may reduce the potential for antimicrobial resistance caused by continuous exposure to drug.²⁰

Concomitant use of inhaled and intravenous (IV) antibiotics is frequently employed in the treatment of an exacerbation.²¹ Although use of 2 delivery routes could enhance antibacterial effect due to improved drug exposure, increased risk of toxicity is possible. Few published data examine the safety or efficacy of this dual therapy. Furthermore, serum aminoglycoside levels to guide IV dosing, could be difficult to interpret when inhaled and IV aminoglycoside treatments are both used. The decision to continue an inhaled antibiotic in conjunction with the same IV antibiotic should be determined on a case-by-case basis.

PHARMACOLOGY^{22,23,24,25,26}

Inhaled aztreonam (Cayston) is a beta-lactamase-resistant monobactam antibiotic that only has activity against aerobic gram-negative bacteria, including *P. aeruginosa*.²⁷ Aztreonam exerts its effect by binding penicillin-binding protein of susceptible bacteria, forming elongated filamentous cells that eventually lyse and die.²⁸ Aztreonam is formulated for administration by inhalation through a nebulizer so that the drug is concentrated in the airway.

Inhaled tobramycin (Bethkis, **Kitabis Pak**, TOBI, TOBI Podhaler) is an aminoglycoside antibiotic that binds to a protein of the 30S subunit of the microbial ribosome, interfering with the function of messenger RNA.²⁹ As a result, abnormal, nonfunctional proteins are produced, causing a compromise of cell membrane permeability that eventually leads to cell death. Tobramycin has a bactericidal effect with activity against a wide range of gram-negative bacteria including *P. aeruginosa*. Tobramycin for inhalation is formulated for administration by inhalation through a nebulizer or a dry-powder inhaler so the drug is concentrated in the airway.

PHARMACOKINETICS^{30,31,32,33,34}

Drug	Sputum Concentration After Inhalation	Sputum Concentration During Chronic Use, After 10 Minutes of Inhalation	Serum Concentration After 1 Hour	Elimination Half-life (hour)
aztreonam (Cayston)	726 mcg/g	715 mcg/g	0.59 mcg/mL	2.1
tobramycin (Bethkis)	814 mcg/g	717 mcg/g	0.06 – 1.89 mcg/mL	4.4
tobramycin (Kitabis Pak)	1,237 mcg/g	1,154 mcg/g	0.95 mcg/mL	2
tobramycin (TOBI)	1,237 mcg/g	1,154 mcg/g	0.95 mcg/mL	2
tobramycin (TOBI Podhaler)	1,048 mcg/g	nr	1.02 mcg/mL	3

nr = not reported

Inhalation therapy with either tobramycin or aztreonam does not lead to drug accumulation after chronic use; therefore, no adjustment is necessary for patients requiring long-term use of these antibiotics.^{35,36} Both tobramycin and aztreonam are renally eliminated; however, dose adjustment of aztreonam for patients with renal impairment is not required because the drug has low systemic absorption.³⁷ While tobramycin also has low systemic exposure, no specific guideline for dose adjustment is available for patients with renal impairment.³⁸ Monitoring serum concentration for tobramycin in patients with normal renal function is not required; however, it is at the discretion of the treating physician to monitor serum level in patients with renal dysfunction. Neither of these inhaled antibiotics requires dose adjustment based on weight and age of the patient.^{39,40,41,42} TOBI Podhaler pharmacokinetic values appear generally equivalent to those for TOBI.

CONTRAINDICATIONS/WARNINGS^{43,44,45,46,47}

Aztreonam (Cayston) is contraindicated in patients with a known allergy to aztreonam. Cross-reactivity may occur; therefore, physicians must use caution when prescribing aztreonam in patients with a known history of beta-lactam allergy. Bronchospasm with a reduction of 15% or more in FEV₁ may occur; therefore, healthcare providers should consider measuring a patient's baseline FEV₁ prior to initiating aztreonam for inhalation therapy.

Tobramycin (Bethkis, Kitabis Pak, TOBI, TOBI Podhaler) is contraindicated in patients with a known hypersensitivity to any aminoglycoside. In patients with a known or suspected renal, auditory, vestibular, or neuromuscular dysfunction, physicians must exercise caution when prescribing tobramycin for inhalation. Physicians should also consider performing baseline auditory and renal function screening to determine if a patient is at an increased susceptibility for the adverse effects. Patients who are pregnant or plan to become pregnant should be aware and informed of the possible harm to the fetus.

DRUG INTERACTIONS^{48,49,50,51,52}

No formal drug interactions have been noted with aztreonam for inhalation (Cayston). Concurrent use of inhaled tobramycin (Bethkis, **Kitabis Pak**, TOBI, TOBI Podhaler) with other neurotoxic or ototoxic drugs should be avoided. Diuretics, such as furosemide, ethacrynic acid, mannitol, and urea, can alter tobramycin serum and tissue concentrations; therefore, concurrent use with tobramycin should also be avoided to reduce aminoglycoside toxicity.

ADVERSE EFFECTS^{53,54,55,56,57}

Drug	Bronchospasm	Nasal Congestion	Tinnitus	Voice Alteration	Cough
aztreonam (Cayston)	3 (nr)	16 (12)	nr	nr	54 (51)
tobramycin (Bethkis)	0.5 (0)	nr	0 (0)	6 (2)	nr
tobramycin (Kitabis Pak)	reported	nr	3 (0)	12.8 (6.5)	46.1 (47.3)
tobramycin (TOBI)	reported	nr	3.1 (0)	12.8 (6.5)	46.1 (47.3)
tobramycin (TOBI Podhaler)	1.6 (0.5)	8.1 (7.2)	1.9 (2.4)	13 .6 (3.8)	48.4 (31.1)

Adverse effects are reported as a percentage. Adverse effects data are reported from package inserts and are not meant to be comparative or all-inclusive. Incidences for the placebo group (for tobramycin inhalation in Podhaler data; open-label comparison) are indicated in parentheses. nr = not reported.

Cough was reported with a lower rate in the inhaled aztreonam group compared to the placebo group ($p=0.047$). Three percent of patients using inhaled aztreonam experienced bronchospasm, which can be prevented by the use of a bronchodilator before the administration of aztreonam in at-risk patients. A safety study comparing TOBI Podhaler with TOBI inhalation solution reported bronchospasms in 1.6% of patients who used TOBI Podhaler and 0.5% in those who used the solution; TOBI Podhaler and TOBI labeling advise that bronchospasm should be treated as medically appropriate.

TOBI Podhaler has displayed more throat irritation than Bethkis and TOBI (4.5% for TOBI Podhaler versus 3% for Bethkis and 1.9% for TOBI/**Kitabis Pak**). TOBI Podhaler and Bethkis have displayed similar auditory adverse effects (e.g., hearing loss) but more than with TOBI (1% for TOBI Podhaler and 1.1% for Bethkis versus 0.5% for TOBI/**Kitabis Pak**).⁵⁸

Tinnitus and voice alteration were reported in patients using inhaled tobramycin. Tinnitus was transient and resolved without discontinuation of the drug. Voice alteration was mild in severity and did not cause patient withdrawal from the study. Although tinnitus has not been reported during clinical studies with Bethkis, caution is warranted because it has been observed with other inhaled tobramycin solutions including **Kitabis Pak**, TOBI, and TOBI Podhaler.

Arthralgia and joint swelling have also been reported with inhaled aztreonam.

SPECIAL POPULATIONS^{59,60,61,62,63}

Pediatrics

Safety and efficacy of inhaled aztreonam (Cayston) have not been established in pediatric patients less than 7 years of age. Safety and efficacy of inhaled tobramycin (Bethkis, **Kitabis Pak**, TOBI, TOBI Podhaler) have not been established in pediatric patients less than 6 years of age. No dose adjustment is required in pediatric patients for these drugs. Pyrexia is more commonly reported in pediatric patients than in adult patients during aztreonam treatment.

Pregnancy

Aztreonam: Category B – No well-controlled studies of inhaled aztreonam in pregnant women have been conducted so treatment should be used during pregnancy only if clearly needed.

Tobramycin: Category D – Inhaled tobramycin has not been studied in pregnant women. However, aminoglycosides can cause fetal harm (e.g., congenital deafness) when administered to pregnant women; therefore, patients who are pregnant or plan to become pregnant should be aware of the potential hazard to the fetus.

Renal Impairment

Inhaled aztreonam requires no dose adjustment in patients with renal impairment. Tobramycin inhalation should be prescribed with caution in patients with renal impairment; if a patient experiences nephrotoxicity while on inhaled tobramycin therapy, it should be discontinued until tobramycin serum levels fall below 2µg/mL.

DOSAGES^{64,65,66,67,68}

Drug	Dose	Administration	Duration	Availability
aztreonam (Cayston)*	For adults and pediatric patients > 7 years old: 75 mg 3 times a day	Reconstitute 1 vial of powder with 1 ampule of saline immediately before use and administer dose only with Altera® Nebulizer System	28 days on treatment, followed by 28 days off	75 mg powder for inhalation solution (1 vial)
tobramycin (Bethkis)**	For adults and pediatric patients > 6 years old: 300 mg twice a day	Administer 1 ampule by using a hand-held PARI LC® PLUS Reusable Nebulizer with a PARI Vios® Air compressor	28 days on treatment, followed by 28 days off	300 mg/4 mL (1 ampule) for nebulization
tobramycin (Kitabis Pak)**	For adults and pediatric patients > 6 years old: 300 mg twice a day	Administer drug using PARI LC PLUS™ Reusable Nebulizer with a DeVilbiss® Pulmo-Aid® compressor as close to 12 hours apart as possible (not less than 6 hours between doses)	--	--
tobramycin (TOBI)**	For adults and pediatric patients > 6 years old: 300 mg twice a day	Administer drug using PARI LC PLUS Reusable Nebulizer with a DeVilbiss Pulmo-Aid compressor and as close to 12 hours apart as possible (not less than 6 hours between doses)	28 days on treatment, followed by 28 days off	300 mg/5 mL (1 ampule) for nebulization
tobramycin (TOBI Podhaler)**	For adults and pediatric patients > 6 years old: 112 mg twice daily	Administered only with Podhaler device; capsules are inserted 1 at a time in the device and inhaled sequentially	28 days on treatment, followed by 28 days off	28 mg dry powder capsules for inhalation

* aztreonam: No safety and efficacy information for patients less than 7 years of age, patients with FEV₁ < 25% or > 75% predicted, or patients colonized with *Burkholderia cepacia*.

** tobramycin: No safety and efficacy data for patients less than 6 years of age, patients with FEV₁ < 25% or > 75% predicted, or patients colonized with *Burkholderia cepacia*.

Aztreonam and tobramycin should not be mixed with other medications in the nebulizer cup. Patients prescribed inhaled aztreonam (Cayston) who are taking several inhaled medications should be advised to use the medications in the following order of administration: bronchodilator, mucolytics, and, lastly, aztreonam.

Aztreonam dose is administered over approximately 2 to 3 minutes. Tobramycin nebulized solutions are administered over about 15 minutes.

Altera is a lightweight nebulizer system that operates on batteries or an AC power supply. Four new standard "AA" batteries provide about 2 hours of treatment. The PARI Vios and DeVilbiss Pulmo-Aid compressors are operated using an AC power supply.

The Podhaler is a plastic handheld inhaler device that pierces the tobramycin capsules to allow inhalation of the tobramycin powder. It does not require batteries or electricity. TOBI Podhaler is packaged as 4 weekly packs, each containing 56 capsules (7 blister cards of 8 capsules), 1 Podhaler device, and 1 reserve Podhaler device.

Aztreonam powder for reconstitution and tobramycin solutions (Bethkis, Kitabis Pack, and TOBI) should be refrigerated, but may be stored at room temperature for up to 28 days. TOBI Podhaler blister cards should be kept at room temperature.

CLINICAL TRIALS

Studies were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved use of all drugs in this class. Randomized, comparative, controlled trials comparing agents within this class for the approved indications are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants, and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80% of participants entering the investigation. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship and/or funding must be considered, the studies in this review have also been evaluated for validity and importance.

aztreonam (Cayston) versus placebo

A randomized, double-blind, placebo-controlled international trial was conducted to evaluate the safety and efficacy of inhaled aztreonam 75 mg 3 times daily for 28 days.⁶⁹ A total of 164 CF patients with *P. aeruginosa* were enrolled. Exclusion criteria included recent (within the previous 28 days) administration of antipseudomonal antibiotics, azithromycin, or aerosolized hypertonic saline solution; current oral corticosteroid; positive culture of *Burkholderia cepacia* within the previous 2 years; daily oxygen supplementation; monobactam antibiotic hypersensitivity; intolerance to short-acting beta₂-agonists; lung transplantation; alanine transaminase (ALT) and aspartate aminotransferase (AST) levels more than 5 times the normal values; serum creatinine more than 2 times the normal value; pregnancy; lactation; recent change of antimicrobial, bronchodilator, anti-inflammatory, or corticosteroid medication; or new findings in the chest radiograph within the previous 90 days. The endpoints of the study were respiratory symptoms (determined by CF-Questionnaire-Revised Scale [CFQ-R]), pulmonary function, *P. aeruginosa* density in sputum, and non-respiratory CFQ-R scales. At the end of the 28-day treatment, patients in the treatment arm had a higher mean CFQ-R respiratory score (9.7 points difference; $p < 0.001$), improved pulmonary function (10.3% difference in FEV₁ predicted, $p < 0.001$), and less sputum *P. aeruginosa* density (28-day difference, - 1.453 log₁₀ CFU/g; $p < 0.001$). Inhaled aztreonam was well tolerated with similar adverse effects as the placebo group.

tobramycin (Bethkis) versus placebo

Two randomized, double-blind, placebo-controlled, parallel group studies (Study 1 and Study 2) were performed in 306 patients with CF infected with *P. aeruginosa*.⁷⁰ The osmolality of the to-be-marketed drug differed from the drug used in these studies. To rely on the efficacy and safety established in these studies, an additional study was performed as a bridge to the to-be-marketed drug. The bridging study examined 324 patients with CF and the efficacy and tolerability of aerosolized tobramycin inhaled solution with osmolality comparable to Bethkis over 4 weeks. The compressors used in the placebo-controlled and bridge studies differed from the PARI Vios used with Bethkis; however, *in vitro* cascade impaction studies indicated that the various compressors used in the studies delivered equivalent doses and respirable fractions compared to the PARI Vios used with the PARI LC Plus

Reusable nebulizer. The study concluded that the tobramycin inhalation solution used in the bridge study had similar efficacy as seen in the placebo-controlled studies.

All patients in both studies had a baseline FEV₁ percent predicted greater than or equal to 40% and less than or equal to 80% and infected with *P. aeruginosa*. Study 1 enrolled 59 patients, 30 years old or younger, into a double-blind, single cycle (28 days on treatment followed by 28 days off treatment) study where they were randomized to receive Bethkis (n=29) or placebo (n=30). The study found that Bethkis significantly improved lung function compared to placebo which was indicated by the change in FEV₁ percent predicted from baseline to the end of Cycle 1. The study resulted in absolute increases in FEV₁ percent predicted of 16% and 5% with Bethkis and placebo, respectively (95% CI; p=0.003).

Study 2 randomized (2:1) 247 patients, who were less than or equal to 46 years old, into a double-blind, 3-cycle, placebo controlled trial of Bethkis (n=161) or placebo (n=86). Each cycle consisted of 28 on treatment and 28 days off treatment. The study found that Bethkis significantly improved lung function compared to placebo indicated by the absolute change in FEV₁ percent predicted from baseline to the end of Cycle 3 “on” phase. The study resulted in absolute increases in FEV₁ percent predicted of 7% and 1% for Bethkis and placebo, respectively (95% CI; p<0.001). Study 2 also observed 9.9% of patients treated with Bethkis and 24.7% of patients treated with placebo having an unplanned hospitalization due to the disease. Additionally, the study observed 6.2% and 16.5% of patients treated with Bethkis and placebo, respectively, receiving parenteral tobramycin.

tobramycin (TOBI) versus placebo

Two identical multicenter, double-blind, randomized, placebo-controlled trials were conducted to evaluate the safety and efficacy of inhaled tobramycin 300 mg twice daily for a total of 24 weeks in three on-off cycles.⁷¹ A total of 520 patients with CF and *P. aeruginosa* infection were recruited from 69 CF centers in the United States. Exclusion criteria included receipt of antibiotics within the previous 2 weeks, hypersensitivity to aminoglycosides, impaired renal function (serum creatinine > 2 mg/dL), or recovery of *Burkholderia cepacia* infection within the previous 2 years. The endpoints of the study were pulmonary function, density of *P. aeruginosa* in sputum, and hospitalization. At the end of the study, patients in the treatment groups had an average increase in FEV₁ of 10%, while patients receiving placebo had a 2% decline in FEV₁ (p<0.001). Density of *P. aeruginosa* was decreased by an average of 0.8 log₁₀ colony-forming units (CFU) per gram of sputum in the active treatment groups compared to 0.3 log₁₀ CFU per gram in the placebo groups (p<0.001). Patients in active treatment groups were 26% (95% confidence interval [CI], 2 to 43) less likely to be hospitalized. Inhaled tobramycin was well tolerated with similar adverse effect rates between treatment and placebo groups. However, there were 2 side effects (tinnitus and voice alteration) that only occurred in the active treatment groups. These adverse effects were of mild to moderate severity and did not cause withdrawals from the study.

tobramycin inhalation powder (TOBI Podhaler) versus placebo

Two randomized, double-blind, placebo-controlled trials were conducted to evaluate the efficacy of TOBI Podhaler 4, 28 mg inhalation capsules twice daily versus placebo.⁷² Participants in these studies had a confirmed diagnosis of CF and ranged in ages from 6 to 21 years of age and had not received inhaled antibiotic therapy for at least 4 months directly prior to the trial. In the first study, a total of 95 patients were randomized to TOBI Podhaler or placebo for a 28 day on treatment and 28 day off treatment cycle for a total of 24 weeks. The trial was stopped early due to demonstrated benefit in the

interim analysis. In the study (n=61), TOBI Podhaler significantly improved lung function in comparison to placebo as measured by the relative change in FEV₁ percent predicted from baseline to the end of cycle 1 dosing. After 28 days, treatment with TOBI Podhaler resulted in relative increase of FEV₁ of 12.54% compared to placebo FEV₁ increase of 0.09% (LS mean difference, 12.44%; 95% CI, 4.89 to 20; p=0.002).⁷³ However, a second randomized, double-blind, placebo-controlled trial of similar design which evaluated the efficacy of TOBI Podhaler versus placebo (n=62), failed to show statistically significant improvement in relative lung function FEV₁ for TOBI Podhaler. Treatment in this trial with TOBI Podhaler displayed a relative increase in lung function FEV₁ by 8.19% versus placebo of 2.27% which failed to achieve statistical significance in relative change in FEV₁ predicted (LS mean difference, 5.91%; 95% CI, -2.54 to 14.37; p=0.167).

tobramycin inhalation powder (TOBI Podhaler) versus tobramycin inhalation solution (TOBI)

A randomized, open-label, active-controlled parallel arm trial randomized 517 patients 3:2 to tobramycin inhalation powder (4, 28 mg capsules twice daily) or TOBI (300 mg/5 mL twice daily).⁷⁴ The study included 3 treatment imputation of the missing data, the mean differences (TOBI Podhaler minus TOBI) in the percent relative change from baseline in FEV₁ percent predicted at Weeks 5 and 25 were -0.87% (95% CI, -3.8 to 2.07) and 1.62% (95% CI, -0.9 to 4.14), respectively. Three cycles, each cycle consisting of 28 days on therapy, followed by 28 days off therapy; the total treatment period was 24 weeks. Mean patient age 25.6 years. Patients had no inhaled antipseudomonal antibiotic use within 28 days prior to study drug administration. The open-label design of the study and missing values for the outcome of FEV₁% predicted posed limitations in interpreting the efficacy results. The proportion of patients with missing values for FEV₁ % predicted at Weeks 5 and 25 in the TOBI Podhaler treated group were 13% and 27.9% compared to 7.2% and 19.1% in the TOBI treated group. Using imputation of the missing data, the mean differences (TOBI Podhaler minus TOBI) in the percent relative change from baseline in FEV₁ % predicted at Weeks 5 and 25 were -0.87% (95% CI, -3.8 to 2.07) and 1.62% (95% CI, -0.9 to 4.14), respectively.

SUMMARY

Although there are not many pharmacological treatment options for this disease, antibiotics play a crucial role in cystic fibrosis (CF) therapy. Currently, there are 2 FDA-approved inhaled antibiotics on the market for the management of CF in patients with *Pseudomonas (P.) aeruginosa*. These medications are taken chronically to suppress the growth of *P. aeruginosa* and reduce the risk of CF exacerbation. Inhaled aztreonam (Cayston) and inhaled tobramycin (Bethkis, **Kitabis Pak**, TOBI, TOBI Podhaler) require no dose adjustment based on weight and age and are well tolerated. TOBI Podhaler may provide patients with an additional device option for self-administration of inhaled tobramycin; however, it may also increase risk of cough and throat irritation. Inhaled aztreonam does not require renal dose adjustment. Nephrotoxicity has been associated with aminoglycosides as a class; however, it has not been observed in clinical studies with inhaled tobramycin.

The 2013 CF Pulmonary Guidelines, recommend inhaled tobramycin (Bethkis, **Kitabis Pak**, TOBI, TOBI Podhaler) and inhaled aztreonam (Cayston) at the same rating to reduce exacerbation for patients who are 6 years of age and older with persistent *P. aeruginosa* culture in the airways.

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