



TOBI vs. Inhaled IV Tobramycin

Prior to the introduction of TOBI[®] (tobramycin solution for inhalation), the intravenous (IV) formulation of tobramycin (Nebcin[®]) was administered via a nebulizer, for the management of cystic fibrosis (CF) patients with *Pseudomonas aeruginosa* lung infections¹. TOBI[®] was patented in 1996 and FDA-approved in November 1997 for the treatment of pseudomonal lung infections in people with CF. TOBI[®] is a ready-to-use ampule for nebulization that contains 300 mg of tobramycin in 5 mL with no preservatives. Injectable tobramycin is available as 80mg/2 mL vials and must be diluted with 2 mL of saline solution before administration via a nebulizer (henceforth, “nebulized tobramycin”). Nebulized tobramycin contains phenol and metabisulfites as preservatives. TOBI[®] 300 mg is administered twice daily, whereas nebulized tobramycin has been dosed up to 600mg three times a day. However, nebulized tobramycin is often given at similar doses to TOBI[®]^{2,3}. Both TOBI[®] and nebulized tobramycin improve pulmonary function, decrease the density of *P. aeruginosa* in sputum, and decrease the risk of hospitalization^{4,5}. Two areas of debate surround the use of nebulized tobramycin and TOBI[®]: 1) concern about the adverse effect profile of each product, specifically bronchoconstriction and 2) the cost difference between the products.

The question of whether or not bronchoconstriction occurs with the nebulized tobramycin at a greater frequency than TOBI[®] is often debated. In a study comparing TOBI[®] with nebulized tobramycin that enrolled 19 patients, both preparations of tobramycin had significant rates of bronchoconstriction⁶. TOBI[®] had a rate of 16%, while nebulized tobramycin had a rate of 17% for in high-risk patients⁶. High-risk patients were defined as those having a family history of asthma and previous response to bronchodilators. For low-risk patients (i.e., those not having family history of asthma and previous response to bronchodilators), bronchoconstriction occurred in 12% of patients receiving nebulized tobramycin compared with 4% of those given TOBI[®]⁶. Albuterol has been used to pretreat patients receiving nebulized tobramycin⁷. In a study of 16 patients, the use of albuterol on a daily basis prior to nebulized tobramycin lead to zero incidences of bronchoconstriction⁷. Additionally, the use of phenol-free injectable tobramycin for nebulization has been suggested to decrease the risk of bronchoconstriction; however, all injectable tobramycin solutions available in the US contain phenol^{5,8}.

The cost difference between TOBI[®] and nebulized tobramycin is substantial. The cost of TOBI[®] is \$2,668.00 for a box of 56 vials, while the cost of nebulized tobramycin is \$36.60 for a box of 25 vials⁹. If similar doses of each are used, 9 boxes of nebulized tobramycin at a cost of \$329.40 are needed to equal 1 box of TOBI[®]. The table below compares cost, showing a difference of \$2338.60 which represents a savings of

approximately 87.7% when nebulized tobramycin is used. The addition of nebulized albuterol as pretreatment, has negligible effect on overall cost.

Cost comparison for available tobramycin nebulization products

	Cost / Unit (US dollars)	Cost / Dose (US dollars)
TOBI®	\$2,668.00 ^a	\$47.64
Nebulized Tobramycin	\$329.40 ^b	\$5.86
Cost Difference	\$2338.60	\$41.78
% Savings	87.7%	87.7%

^a Includes 56 unit dose ampules

^b includes total of 225 vials (9 boxes of 25 vials)

In conclusion, the use of injectable tobramycin for administration via a nebulizer, appears to be an effective treatment for lung infection caused by *P. aeruginosa* in patients with CF and carries no apparent increased risk of bronchoconstriction in high-risk patients compared with TOBI®. Furthermore, low-risk patients appear to be at little to no greater risk if pretreated with nebulized albuterol. By using nebulized tobramycin and albuterol in place of TOBI® the correctional facility can save approximately 88%, while providing a safe and effective treatment.

References

1. Ratjen F, Doring G, Nikolaizik W. Effect of inhaled tobramycin on early *Pseudomonas aeruginosa* colonization in patients with cystic fibrosis. *Lancet* 2001; 358:983-984.
2. Pai VB, Nahata MC. Efficacy and safety of aerosolized tobramycin in cystic fibrosis. *Pediatr Pulmonol* 2001; 32(12):314-327.
3. Nikolaizik WH, Trociewicz K, Ratjen F. Bronchial reactions to the inhalation of high-dose tobramycin in cystic fibrosis. *Eur Respir J* 2002; 20:122-126
4. Ramsay BW, Pepe MS, Quan JM, Otto KL, Montgomery AB, Williams-Warren J, et al. Intermittent administration of inhaled tobramycin in patients with cystic fibrosis. *N Eng J Med* 1999; 340:23-40.
5. Antibiotic treatment for cystic fibrosis. (*Report of the UK Cystic Fibrosis Trust Antibiotic Group*). Second Edition, September 2002.
6. Alothman G, Alsaadi M, Ho B, Ho S, Dupuis A, Corey M, et al. Evaluation of bronchial constriction in children with cystic fibrosis after inhaling two different preparations of tobramycin. *Chest* 2002;122:930-934.
7. Ramagopal M, Lands LC. Inhaled tobramycin and bronchial hyperactivity in cystic fibrosis. *Pediatr Pulmonol* 2000;29(5):366-70.
8. “Mary White, Contract Pharmacy Services, oral communications July 2005”
9. Klasco RK (Ed): POISINDEX[®] System. Thomson Micromedex, Greenwood Village, Colorado (Edition expires [date]).