



Background Information

Pulmonary Antibiotics Platform*

Adjunctive Treatment of Pneumonia in Ventilated Patients Diagnosed with Hospital-Acquired or Ventilator-Associated Pneumonia

What is Hospital-Acquired Pneumonia?

Hospital-acquired, gram-negative bacterial pneumonia is a serious problem which afflicts patients even in the world's most advanced clinical settings. Increasing gram-negative antibiotic resistance has been a problem in the setting of hospital-acquired pneumonia. It is commonly acquired by patients in intensive care units who have been put on ventilators for breathing assistance. Current treatment involves the administration of intensive antibiotics, supplemental oxygen, and mechanical ventilatory support. Some 25-50% of those who acquire gram-negative bacterial pneumonia will die.

Included in the category of Hospital-Acquired Pneumonia are:

- **Hospital Acquired Pneumonia (HAP)** – pneumonia that occurs 48 hours or more after admission to a hospital, which was not incubating at the time of admission
- **Ventilator Associated Pneumonia (VAP)** – pneumonia that arises more than 48-72 hours after endotracheal intubation.

(Definitions from the American Thoracic Society, "Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia" *Am J Respir Crit Care Med*, Vol 171. pp. 388-416, 2005.)

How often does it occur?

According to the American Thoracic Society, the incidence of hospital acquired pneumonia is usually between 5 and 10 cases per 1,000 hospital admissions depending on the case definition and study population. The incidence of ventilator-associated pneumonia is 6- to 20-fold greater than in non-ventilated patients. Nektar projects that for peak year sales, there will be 40,000 mechanically ventilated patients with hospital pneumonias (including ventilator-acquired pneumonia) and an additional potential target population of 1 million non-mechanically ventilated patients with hospital pneumonia in US hospitals in 2015.

(Source: American Thoracic Society, "Guidelines for the Management of Adults with Hospital-Acquired, Ventilator-Associated, and Healthcare-Associated Pneumonia," *Am J Respir Crit Care Med* Vol 171. pp. 388-416, 2005)

* This pulmonary antibiotics system is a prototype being tested for NKTR-061 (inhaled amikacin). It is not an approved product.

ICU Units

Pneumonia has accounted for approximately 15% of all hospital-associated infections and 27% and 24% of all infections acquired in the medical intensive-care unit (ICU) and coronary care units, respectively, making it the second most common hospital-associated infection after that of the urinary tract. Being intubated and attached to a mechanical ventilator is the most common risk factor for the infection.

(Source: *Guidelines For Preventing Health-Care-Associated Pneumonia, 2003, Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee*)

Long-term Care Facilities

In long-term care facilities such as nursing homes, pneumonia is the first or second most common infection and accounts for 13-48% of all nursing home-associated infections, according to data culled by the CDC.

(Source: *Guidelines For Preventing Health-Care-Associated Pneumonia, 2003, Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee*)

How serious is the problem?

The fatality rates for hospital-associated pneumonia in general, and ventilator-associated pneumonia in particular, are high. For hospital-associated pneumonia, attributable mortality rates of 20%-33% have been reported; in one study, ventilator-associated pneumonia accounted for 60% of all deaths due to hospital-associated infections.

The case-fatality rate of pneumonia in nursing home residents is reported to be from 6% to 23%.

(Source: *Guidelines For Preventing Health-Care-Associated Pneumonia, 2003, Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee*)

What causes the pneumonia?

Sources of pathogens for hospital acquired pneumonia include the surroundings of the patient (air, water, equipment), and commonly the transfer of microorganisms between the patient and staff or other patients. (Source: American Thoracic Society, "Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia," *Am J Respir Crit Care Med*, Vol 171. pp. 388-416, 2005.)

What is the current treatment?

Current therapy of patients with severe hospital acquired pneumonia or ventilator associated pneumonia requires the use of antibiotics at optimal doses, to ensure maximum efficacy. This can be associated with severe side effects such as kidney and hearing damage.

(Source: American Thoracic Society, "Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia," *Am J Respir Crit Care Med*, Vol 171. pp. 388-416, 2005.)

What is the financial impact?

Analyses of pneumonia-associated morbidity have shown that hospital-associated pneumonia can prolong ICU stay by an average of 4.3-6.1 days and hospitalization by 4-9 days, adding an average of \$40,000 in direct costs per patient.

(Source: *Guidelines For Preventing Health-Care-Associated Pneumonia, 2003, Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee*)

Nektar's Solution

Current therapy for these types of pulmonary infections relies almost exclusively upon high doses of intravenous antibiotics, which can be associated with severe side effects such as kidney and hearing damage.

NKTR-061 (inhaled amikacin) is currently being tested to further evaluate the safety, tolerability, and deep lung concentrations of amikacin formulated for inhalation for the adjunctive treatment of gram-negative pneumonia in ventilated patients diagnosed with hospital or ventilator associated pneumonia. This new inhaled antibiotic product candidate leverages Nektar's proprietary Aerosol Generator that is designed to effectively deliver aerosolized antibiotics to the deep lungs, both within and outside of a ventilator system. The result is a potentially more effective treatment modality which provides key advantages over traditional pneumatic or ultra-sonic nebulizer delivery.

Sources:

http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/CDCpneumo_guidelines.pdf

Arlington Medical Resources (AMR), Hospital Antibiotic Market Guide, 2006-7.

American Thoracic Society, "Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia," *Am J Respir Crit Care Med*, Vol 171. pp. 388-416, 2005

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