

## Ontario Antimicrobial Stewardship Project

### Evidence-Based Summary for Short-Course Antimicrobial Therapy:

#### Community-Acquired Pneumonia

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1. *A minimum treatment duration of 5 days of appropriate antibiotic therapy is recommended for treatment of patients with mild-moderate community acquired pneumonia (CAP), provided patients meet the criteria set out in the IDSA guidelines for clinical stability. For patients admitted to a medical unit (not ICU) with CAP treatment duration of 5-7 days is appropriate provided the patient is afebrile for 48h and meets criteria for clinical stability.*

The 2007 IDSA Consensus Guidelines for the management of CAP in adults recommend that treatment should continue for a minimum of 5 days, with the conditions that the patient be afebrile for 48-72 hours and should have no more than 1 parameter that does not meet the CAP-associated criteria for clinical stability(4). These criteria include a temperature of  $\leq 37.8^{\circ}\text{C}$ , a heart rate of  $\leq 100$  beats per minute, a respiratory rate of  $\leq 24$  breaths per minute, a systolic blood pressure of  $\geq 90$ mmHg, arterial O<sub>2</sub> saturation of  $\geq 90\%$  or pO<sub>2</sub>  $\geq 60$ mmHg on room air, able to maintain oral intake and normal mental status.

A meta-analysis compared the clinical efficacy of a short-course (7 days or less) antibiotic monotherapy regimen versus an extended course (>7 days) regimen (4). Among the 15 randomized controlled trials included which had enrolled patients with radiographically confirmed pneumonia, short-course regimens compared contained primarily azithromycin, and also beta-lactams, fluoroquinolones, and ketolides(4). Overall there was no difference in the risk of clinical failure between the short and extended-course regimens. Additionally there were no differences in the risk of mortality. A key consideration in the application of this data was that the majority of included studies excluded patients with severe disease.

There is evidence supporting shorter treatment duration than 7 days for several individual classes of antibiotics.

##### *Amoxicillin*

A randomized, double blind study in the Netherlands of 121 adults with mild to moderate CAP treated for 3 days with amoxicillin compared continuation with 5 days of active therapy versus placebo in initial responders. Clinical success rate, defined as resolution or improvement of symptoms and clinical signs related to pneumonia without the need for additional or alternative antibiotic therapy, was similar in both groups at days 10 and 28. Radiographic resolution, a secondary endpoint, was also found to be similar between groups. The group excluded from initial randomization due to lack of clinical improvement at 3 days was found to have higher rates of *P. aeruginosa*, *E. coli*, and *S. aureus* positive cultures. If a shorter course is selected, close monitoring is recommended within the first 3 days for response and appropriateness of antibiotic should be evaluated based on culture results. (5)

##### *Levofloxacin*

Due to its concentration-dependent bactericidal activity, using the higher dose of 750mg of levofloxacin maximizes its activity, enabling a shorter treatment duration.(6) A multicenter, randomized, double-blind study compared levofloxacin 750mg per day for 5 days with 500mg per day for 10 days in 528 patients with mild to moderate CAP. (6) Clinical cure was similar between groups, among patients that were clinically evaluable (~92% in both groups), at the 7-14 day post therapy visit. There was no difference in rates of adverse events between groups.

A similar randomized controlled trial was performed using gemifloxacin, comparing 5 and 7 day courses of therapy in 469 outpatients with mild-moderate CAP. Results also demonstrated the shorter course (5 days) to be non-inferior with respect to clinical cure and radiological success. (7)

### *Azithromycin*

The efficacy of azithromycin short-course therapy has also been examined. A randomized, multi-centre study compared azithromycin 500mg once daily for 3 days to clarithromycin 250mg twice daily for 10 days in 203 outpatients with mild-moderate CAP. (8) No difference between groups was found with respect to clinical cure or bacteriological response at the end of therapy (between days 12-16). It should be noted that due to the long half life of azithromycin (~70 hours); a 3 day course of therapy has a similar duration of exposure as a longer course of other alternatives.

Based on a review of available literature, it is recommended that if patients with mild-moderate CAP are clinically stable (as defined by IDSA guidelines (4)), they should be treated for a minimum of 5 days of appropriate antibiotic therapy. This shortened duration of exposure to antibiotics may decrease the risk of CDAD.

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