B.C. Ministry of Health Services Drug Coverage Decision

About PharmaCare	B.C. PharmaCare helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.
PharmaCare Coverage	The Ministry of Health Services (Ministry) makes PharmaCare coverage decisions by considering existing PharmaCare policies, programs and resources and the evidence-based recommendations of an independent advisory body called the Drug Benefit Council (DBC). The DBC's advice to the Ministry is based upon a review of many considerations, including available clinical and pharmacoeconomic evidence, clinical practice and ethical considerations, and the recommendations of the national Common Drug Review, when applicable.
Inside	**Page 1** includes the Ministry's decision and reasons in wording that is easier for readers without a medical background to understand. **Page 2 and 3** summarize the DBC recommendation, the Ministry's decision and the reasons for the Ministry's decision.

Levofloxacin (Levaquin®) for short-course airway infections

Understanding the DBC Recommendation and PharmaCare Coverage Decision

Background

- **Pneumonia** is an infection of the lungs. Infections can be caused by bacteria, viruses or fungi.
- **Bronchitis** is inflamed tissue in the air passages leading to the lungs. This may occur with an infection of the air passages.
- **Sinusitis** is inflamed tissue in the sinus behind the nose. This may occur with an infection of the sinus.
- **Levofloxacin** has the brand name **Levaquin®**.
  - Levofloxacin belongs to the group of drugs that fight infections called **antibiotics**.
  - Levofloxacin belongs to the drug class called **fluoroquinolones**. Moxifloxacin also belongs to this drug class.
  - Antibiotics only work against **bacteria**, not viruses or fungi.
  - Bacteria may become **resistant** to some antibiotics. This means that the antibiotics are no longer helpful.

Why was this drug reviewed?

- Drug company request for treatment of some types of infections (pneumonia, bronchitis, and sinusitis).

What did the review find?

- Sixteen studies compare levofloxacin 500 mg daily to either 750 mg daily or to other antibiotics (amoxicillin/clavulanate, azithromycin, cefdinir, cefuroxime axetil, clarithromycin, gemifloxacin or moxifloxacin) for some types of pneumonia, bronchitis and sinusitis.
  - Levofloxacin 500 mg and 750 mg are no better than any of the other antibiotics for treating some types of pneumonia, bronchitis and sinusitis.
- However, either moxifloxacin or levofloxacin may have a role in treating pneumonia, bronchitis and sinusitis for select patients who are not able to take other antibiotics.
- There is a concern that harmful bacteria may become resistant to this class of antibiotics if it is used too much. As a result, the Ministry consulted a team of outside experts to guide how to select patients who will be helped the most by this class of antibiotics.

What decision was made?

- Levofloxacin will **not be covered** for short-course airway infections (pneumonia, bronchitis, and sinusitis).
- Moxifloxacin will be covered as a regular benefit (see B.C. Ministry of Health Services Drug Coverage Decision for moxifloxacin).

Key Term(s)

- **Regular benefits** are prescription drugs that are covered according to the rules of a patient's PharmaCare plan including any annual deductible requirement. Patients do not need Special Authority from PharmaCare for coverage of these drugs.

Please visit us online to find out more about the Pharmaceutical Services Division and the PharmaCare program at www.health.gov.bc.ca/pharmacare. To find out more about how drugs are considered for PharmaCare coverage, visit www.health.gov.bc.ca/pharmacare/formulary.

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B.C. Ministry of Health Services Drug Coverage Decision

Levofloxacin (Levaquin®) for short-course respiratory tract infections

Drug Class

- Fluoroquinolones

Available Dosage Forms

- 250 mg, 500 mg, 750 mg tablets

Sponsor/Requestor

- Janssen-Ortho Inc.

Submission (Request) to PharmaCare

- Request for coverage for the treatment of short-course community-acquired pneumonia and acute bacterial sinusitis.

Drug Benefit Council (DBC) Recommendations

- That PSD choose to provide coverage for moxifloxacin, levofloxacin or both agents for the indications under review.
- That levofloxacin (Levaquin®) 500 mg oral (po) daily x 7-10 days and 750 mg tablets po daily x 5 days for the treatment of community-acquired pneumonia (CAP), acute bacterial sinusitis (ABS), and acute exacerbation of chronic bronchitis (AECB) be listed as a **limited coverage** benefit with criteria to be developed in consultation with key clinical stakeholders.
- That Pharmaceutical Services Division (PSD) work with key clinical stakeholders to develop specific criteria for use based on the following guidance:
  - Rates of bacterial resistance are on the rise in British Columbia. This is particularly evident with in vitro resistance of *Streptococcus pneumoniae* to macrolide antibiotics, and intermediate and high-level resistance to penicillin. Rates of *Streptococcus pneumoniae* resistance to third generation cephalosporins and fluoroquinolones are less than 2% in British Columbia.
  - Based on current evidence and principles of appropriate antibiotic stewardship, the DBC felt that levofloxacin 500 mg daily for 7-10 days or 750 mg daily for 5 days may have a role in certain clinical circumstances for patients with CAP, ABS and AECB. For example, they may be useful for intravenous-to-oral step-down to complete a course of therapy initiated in hospital; for patients treated with other classes of antibiotics in the previous 3 months; and for patients with bacterial infections where the bacteria have in vitro resistance, clinical failure, or intolerance to other available agents.

Reasons for the Ministry of Health Services Decision

- **Community-Acquired Pneumonia (CAP)**
  - A literature search identified five randomized controlled trials (RCTs) comparing levofloxacin 500 mg daily to either levofloxacin 750 mg daily for five days, moxifloxacin 400 mg daily, a 2000 mg single dose of azithromycin, 1000 mg daily extended-release clarithromycin, or amoxicillin/clavulanic acid 625 mg three times a day.
  - There is insufficient evidence that levofloxacin 500 mg for 7-10 days or 750 mg daily for five days provides a statistically significant or clinically important advantage when compared to other fluoroquinolones or other classes of antibiotics in the treatment of CAP.
  - There is insufficient evidence that levofloxacin 750 mg for 5 days differs significantly from levofloxacin 500 mg for 10 days in the treatment of CAP.
- **Acute Bacterial Sinusitis (ABS)**
  - A literature search identified four RCTs comparing levofloxacin 500 mg daily for 10 days to either levofloxacin 750 mg daily for 5 days, a 2000 mg single dose of azithromycin, cefdinir 600 mg daily, or clarithromycin 1000 mg daily.
  - There is insufficient evidence that levofloxacin 500 mg for 10 days or 750 mg daily for five days provides a statistically significant or clinically important advantage when compared to other classes of antibiotics in the treatment of ABS.
  - There is insufficient evidence that levofloxacin 750 mg for 5 days differs significantly from levofloxacin 500 mg for 10 days in the treatment of ABS.
- **Acute Exacerbation of Chronic Bronchitis (AECB)**
  - A literature search identified seven RCTs comparing levofloxacin 500 mg daily for 7 to 10 days to either moxifloxacin 400 mg daily (2 trials), gemifloxacin 320 mg daily, a 2000 mg single dose of azithromycin, azithromycin 500 mg on day 1 followed by 250 mg daily for 4 days, or 500 mg cefuroxime axetil for 7-10 days (2 trials).

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Levofloxacin (Levaquin®) for short-course respiratory tract infections

Reasons for the Ministry of Health Services Decision *(continued)*

- There is insufficient evidence that levofloxacin 500 mg provides a statistically significant or clinically important advantage when compared to other fluoroquinolones or other classes of antibiotics in the treatment of AECB.

- Based on the available clinical and pharmacoeconomic evidence, there are no clinically important differences between levofloxacin and moxifloxacin for the indications considered here.
- PSD also formed an external multidisciplinary clinical working group (the Working Group) to develop coverage recommendations for fluoroquinolones and advise on an implementation strategy. The Working Group included representatives of infectious diseases specialists, hospital pharmacy - infectious diseases, BC Centre for Disease Control, general practitioners, Guidelines and Protocols Advisory Committee, Do Bugs Need Drugs®, and medical microbiology.

Decision and Status

- Levofloxacin will not be a benefit.
- Moxifloxacin will be a regular benefit (see B.C. Ministry of Health Services Drug Coverage Decision for moxifloxacin).
- Effective January 9, 2009.

Key Term(s)

- **Regular benefits** are prescription drugs that are covered according to the rules of a patient's PharmaCare plan including any annual deductible requirement. Patients do not need Special Authority from PharmaCare for coverage of these drugs.
- **Limited Coverage** drugs are not normally considered the first choice in treatment, or other drugs may offer better value. To receive coverage, the patient's physician must submit a Special Authority request to PharmaCare. If the request is approved, the drug is covered up to the usual PharmaCare coverage limits. Actual reimbursement depends on the rules of a patient's PharmaCare plan including any annual deductible requirement.