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. **Page 4 and 5** contain an Appendix of the Ministry's recommendations for prescribing.

Moxifloxacin (Avelox®) for 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.
- **Moxifloxacin** has the brand name **Avelox®**.
  - Moxifloxacin belongs to the group of drugs that fight infections called **antibiotics**.
  - Moxifloxacin belongs to the drug class called **fluoroquinolones**. Levofloxacin also belongs to this drug class.
  - Antibiotics only work against **bacteria**, not viruses or fungi.
  - Bacteria may become **resistant** to some antibiotics. This means 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?

- Eleven studies compare moxifloxacin 400 mg daily to other antibiotics (amoxicillin, azithromycin, clarithromycin, levofloxacin or telithromycin) for some types of pneumonia, bronchitis and sinusitis.
  - Moxifloxacin 400 mg is no better than any of the other antibiotics.
- However, either moxifloxacin or levofloxacin may have a role in treating pneumonia, bronchitis and sinusitis for select patients who cannot 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?

- Moxifloxacin 400 mg tablet will be covered as a **regular benefit** for select patients who will be helped the most. The person who prescribes moxifloxacin will decide if the patient belongs in the group who will be helped the most (see Appendix on page 4 and 5).

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.

BRITISH COLUMBIA
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B.C. Ministry of Health Services Drug Coverage Decision

Moxifloxacin (Avelox®) for respiratory tract infections

Drug Class

Fluoroquinolones

Available Dosage Forms

400 mg tablets

Sponsor/Requestor

- Bayer Healthcare Pharmaceuticals

Submission (Request) to PharmaCare

- Request for coverage for the treatment of community-acquired pneumonia (CAP), acute bacterial sinusitis (ABS) and acute exacerbation of chronic bronchitis (AECB).

Drug Benefit Council (DBC) Recommendations

- That PSD choose to provide coverage for moxifloxacin, levofloxacin or both agents for the indications under review.
- That moxifloxacin (Avelox®) for the treatment of CAP, ABS and 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 moxifloxacin may have a role in certain clinical circumstances for patients with CAP, ABS and AECB. For example, it 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 two randomized controlled trials (RCTs) comparing moxifloxacin 400 mg daily to levofloxacin 250 mg to 500 mg daily. A literature search also identified four RCTs comparing moxifloxacin 400 mg daily to either amoxicillin 500 mg three times a day, amoxicillin 1000 mg three times a day, or clarithromycin 500 mg twice a day.
  - There is insufficient evidence that moxifloxacin 400 mg provides a statistically significant or clinically important advantage when compared to other fluoroquinolones or other classes of antibiotics in the treatment of CAP.
- **Acute Bacterial Sinusitis (ABS)**
  - A literature search identified one RCT comparing moxifloxacin 400 mg daily to telithromycin 800 mg daily.
  - There is insufficient evidence that moxifloxacin 400 mg provides a statistically significant or clinically important advantage when compared to other classes of antibiotics in the treatment of ABS.
- **Acute Exacerbation of Chronic Bronchitis (AECB)**
  - A literature search identified two RCTs comparing moxifloxacin 400 mg daily to levofloxacin 500 mg daily.
  - A literature search also identified two RCTs comparing moxifloxacin 400 mg daily to either 500 mg azithromycin for three days or azithromycin 500 mg on day 1 followed by 250 mg daily for 4 days.
  - There is insufficient evidence that moxifloxacin 400 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 moxifloxacin and levofloxacin for the indications considered here.
- PSD also formed an external multidisciplinary 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.

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Moxifloxacin (Avelox®) for respiratory tract infections

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

- Based on the available clinical and pharmacoeconomic evidence, there are no clinically important differences between moxifloxacin and levofloxacin for the indications considered here.
- PSD also formed an external multidisciplinary working group (the Working Group) to develop coverage recommendations for fluoroquinolones and advise on an implementation strategy. The Working Group included representatives of infectious disease specialists, hospital pharmacy - infectious diseases, BC Centre for Disease Control, general practitioners, Guidelines and Protocols Advisory Committee, Do Bugs Need Drugs®, and medical microbiology.
- Although covered as a regular benefit, it is expected that moxifloxacin will only be prescribed within the Ministry's Recommendations (see Appendix, page 4 and 5).

Decision and Status

- **Regular benefit** with the expectation to prescribe within recommended criteria.
  - In order to give better access to this drug, it was determined not to designate this drug as limited coverage. Prescribers will determine if the criteria for coverage is met. Submission of a special authority request is not necessary.
- In collaboration with stakeholders, the Ministry will assist with antimicrobial stewardship by monitoring general aggregate utilization trends to check recommendations for use and to check antimicrobial resistance patterns.
- The manufacturer also agreed to market the product in BC according to the Ministry Recommended Guidelines (see Appendix page 4 and 5).
- Effective January 15, 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.

Moxifloxacin (Avelox®) for respiratory tract infections

Appendix

Ministry's Recommendations for Prescribing Moxifloxacin (Avelox®).

Excerpted from Medical Services Plan (MSP) Physician's Newsletter Summer 2009 (July).
Full guidelines including references: http://www.health.gov.bc.ca/msp/infoprac/physnews/july_2009.pdf
pages 8-9.
Effective **January 15, 2009**, moxifloxacin 400 mg tablets became a regular benefit under PharmaCare.

I. Clinical Pearls: Limiting Fluoroquinolone Resistance

1. Do not use antibiotics when a viral etiology is suspected.[3]
2. Do not use moxifloxacin to treat a urinary tract infection.[3-5]
3. Do not prescribe two quinolones at the same time.[3]
4. Do not use fluoroquinolones if used in the last three months.[3]
5. Use fluoroquinolones appropriately.[3]
6. Use according to prescribing criteria.[1]

II. Acute Bacterial Sinusitis

Moxifloxacin is recommended only when the following criteria are met:

1. Patient has not received a quinolone in the past three months **AND any of the following:**
   - **a)** failure of at least two complete courses of recommended therapy (amoxicillin, doxycycline, trimethoprim/sulfamethoxazole [TMP/SMX, cotrimoxazole], amoxicillin-clavulanate, cefuroxime axetil, or clarithromycin), **OR**
   - **b)** prescription by an ENT specialist following culture and sensitivity reports of an appropriately collected sample showing bacterial resistance to recommended therapies and sensitivity to fluoroquinolones, **OR**
   - **c)** documented allergy to recommended therapies which precludes their use, **OR**
   - **d)** for completion of therapy initiated in the hospital setting for an indication where alternative antibiotics are not appropriate.

Appendix (continued)

Ministry's Recommendations for Prescribing Moxifloxacin (Avelox®).

III. Acute Exacerbation of Chronic Bronchitis

Nearly 50 per cent of acute exacerbations of chronic bronchitis are caused by viruses.[3,7]

Moxifloxacin is recommended only when the following criteria are met:

1. Patient has not received a quinolone in the past three months, **AND**
2. Patient has a complicated exacerbation: i.e. COPD with increased sputum, increased purulence, increased shortness of breath and at least one **risk factor***[7], **AND any of the following:**
   - **a)** for this exacerbation**,** failure of two complete courses of recommended therapy (amoxicillin, doxycyline, TMP/SMX, cefuroxime axetil, amoxicillin-clavulanate, or clarithromycin), **OR**
   - **b)** documented allergy to recommended therapies which precludes their use, **OR**
   - **c)** for completion of therapy initiated in the hospital setting for an indication where alternative antibiotics are not appropriate.

* **Risk factors include:** ≥ four exacerbations per year **OR** FEV1 < 50% predicted **OR** ischemic heart disease **OR** use of home oxygen **OR** chronic oral corticosteroid use.[7]

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IV. Community Acquired Pneumonia

Moxifloxacin is recommended when the following criteria are met:

1. Patient has not received a quinolone in the past three months, **AND any of the following:**
   - **a)** community care patient with **clinical failure†** of recommended therapy[8]
     - **recommended therapy with no comorbid factors‡:** doxycycline, clarithromycin, or erythromycin
     - **recommended therapy if comorbid factors‡:** beta lactam + macrolide; or beta lactam + doxycycline (beta lactam = high dose amoxicillin or amoxicillin-clavulanate or cefuroxime axetil), **OR**
   - **b)** residential care patient with **clinical failure†** of recommended therapy[8] (amoxicillin +/- [macrolide or doxycycline]; cefuroxime +/- [macrolide or doxycycline]; or if aspiration pneumonia suspected: amoxicillin-clavulanate +/- [macrolide +/- doxycycline]), **OR**
   - **c)** documented allergy to recommended therapies which precludes their use, **OR**
   - **d)** for completion of therapy initiated in the hospital setting for an indication where alternative antibiotics are not appropriate.

† **Clinical Failure of therapy:** hemodynamic compromise, no improvement in symptoms after completion of recommended therapy, clinical deterioration after 72 hours of antibiotic therapy [3]

‡ **Comorbid risk factors defined as:** Chronic lung disease (asthma, smoking, COPD), diabetes, alcoholism, chronic renal or liver disease, congestive heart failure (CHF), malnutrition or acute weight loss (>5 per cent), hospitalization in past three months, lung cancer or other malignancies; immunosuppressing conditions like HIV/AIDS and asplenia or use of immunosuppressing drugs.)[3,8]