B.C. Ministry of Health Services Drug Coverage Decisions

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. **Pages 2 and 3** summarize the DBC recommendation, the Ministry's decision, and the reasons for the Ministry's decision.

Clopidogrel (Plavix®) for unstable angina or heart attack

Understanding the DBC Recommendation and PharmaCare Coverage Decision

Background

- When fat builds up inside blood vessels, the vessels become narrow, and less blood and oxygen flow to the heart. This may cause symptoms such as chest pain (**unstable angina**). Chest pain can also result from a blood clot in a blood vessel of the heart (**heart attack**).
- Patients who have had one event of unstable angina or heart attack may be at risk for having a second event. Some patients may be at a higher risk for having a second event (**high-risk patients**).
- **Clopidogrel** has the brand name **Plavix®**.
  - This drug stops blood cells called platelets from clumping together to form a clot. It belongs to the class of drugs called **platelet aggregation inhibitors**.
  - ASA (acetylsalicylic acid or Aspirin®) is another drug that prevents platelets from clumping together.
  - Clopidogrel plus ASA, or ASA alone, is used to stop blood clots from forming in patients who have had unstable angina or a heart attack.

Why was this drug reviewed?

- Before this review, clopidogrel was covered for 30 days for patients who had unstable angina or a heart attack. A request was made to increase this to 12 months.

What did the review find?

- One study shows that clopidogrel plus ASA is better than ASA alone for preventing death, heart attack or stroke during the first year after having unstable angina or a heart attack.
- In the same study, patients who receive clopidogrel plus ASA are more likely to have bleeding as a side effect compared to the patients who receive only ASA.
- When considering both benefits and side effects of clopidogrel plus ASA, this therapy is expected to be cost-saving when used in high-risk patients with unstable angina or heart attack.

What decision was made?

- Clopidogrel tablets will have limited coverage for up to 12 months, given together with ASA, for high-risk patients with *unstable* angina or heart attack.

Key Term(s)

- **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.

This document is intended for information only. It does not take the place of advice from a physician or other qualified health care provider.

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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Clopidogrel (Plavix®) for Acute Coronary Syndrome (ACS)

Drug Class

- Platelet aggregation inhibitor

Available Dosage Forms

- 75 mg tablets

Sponsor/Requestor

- Pharmaceutical Services Division

Submission (Request) to PharmaCare

- Request to extend the Special Authority coverage for clopidogrel bisulphate (Plavix®) in combination with ASA for medically-treated patients with Acute Coronary Syndrome (ACS) from 30 days to 12 months.

Drug Benefit Council (DBC) Recommendations

- Clopidogrel **limited coverage** criteria be modified to:
  - Up to 12 months of coverage, in combination with ASA, in high-risk medically-treated acute coronary syndrome patients (diffuse three-vessel disease not amenable to revascularization, previous history of TIA, stroke or symptomatic peripheral artery disease, or patients who develop secondary ACS within the initial 30 days of clopidogrel therapy).

Reasons for the Ministry of Health Services Decision

- A literature search identified one randomized controlled trial (RCT) in medically-treated patients with ACS, hospitalized within 24 hours after onset of symptoms of ACS, without ST-segment elevation and not considered at high risk of bleeding (CURE trial). This trial compared clopidogrel plus ASA to ASA alone (n=12,562) and patients were followed for up to 12 months with the mean treatment duration of 9 months.
  - There was a statistically significant reduction in the first primary end point, which was a composite of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke at one month of therapy (4.3% vs. 5.4%, absolute risk reduction [ARR] of 1.1% and a number needed to treat [NNT] of 91) and at the end of the study period (9.3% vs. 11.4%, ARR =2.1%, and NNT = 48).
  - There was a statistically significant reduction in the second primary end point, which was a composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or refractory ischemia at one month of therapy (ARR = 1.5%) and at the end of the study period (ARR = 2.3%).
  - There was a statistically significant reduction in myocardial infarction (ARR = 1.5%) and severe ischemia (ARR = 1.0%) at the end of the study period.
  - Compared to the ASA group, the clopidogrel plus ASA group had a statistically significant increase in major bleeding (absolute risk increase [ARI] = 0.5%, and number needed to harm [NNH] = 200) at one month and at the end of the study period (ARI = 1.0%, NNH = 100), minor bleeding at the end of the study period (ARI = 2.7%, NNH = 37), and total bleeding complications at the end of the study period (ARI = 3.5%, NNH = 29).
- Due to both the incremental clinical benefits and bleeding risks associated with clopidogrel plus ASA, there is still uncertainty as to the overall net clinical benefits and cost-effectiveness in this patient population. As a result, the DBC is more comfortable recommending coverage in a defined high-risk sub-population rather than all medically-treated ACS patients.
- While there is limited pharmacoeconomic evidence to guide the recommendation, treatment with clopidogrel plus ASA for up to 12 months is expected to be more cost-effective when used in the high-risk sub-population than if used in all medically-treated ACS patients.

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

- The limited coverage criteria definition of high-risk patients was based on the recommendation of the DBC and consultations with external clinicians.

Decision and Status

Limited coverage criteria:

- For high-risk, medically-treated patients following hospital-diagnosed Acute Coronary Syndrome **in combination with ASA.** High-risk patients are those who have:
  - a history of arterial disease; **OR**
  - a recurrent vascular event while on ASA alone or within the initial 30 days of combination clopidogrel plus ASA; **OR**
  - a contraindication to or a pattern of coronary artery disease not amenable to mechanical revascularization.
- Notes**:**
  1. Acute Coronary Syndrome (ACS) is defined as unstable angina or non-ST elevation myocardial infarction.
  2. A history of arterial disease is defined as previous transient ischemic attack (TIA), stroke, or symptomatic peripheral artery disease.
  3. Clinical judgement is warranted to assess the increased bleeding risk of combining clopidogrel with ASA and/or oral anticoagulants.

Approval Period/Duration:

- Up to twelve months
- No coverage for ASA
- Effective March 16, 2010

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