Update on the Reimbursement Coding for Clopidogrel in Quebec — RAMQ Formulary

by André Roussin MD, FRCP and Richard Harvey, MD, FRCP, FACC

Introduction

The *Régie de l'assurance maladie du Québec* (RAMQ) has updated its formulary coding related to the reimbursement of clopidogrel. This update, which came into effect on June 2, 2008, follows last year's first phase of changes to clopidogrel's formulary coding, and simplifies for physicians the use of formulary-covered clopidogrel in secondary prevention.

The new coding (see side column for detailed descriptions of formulary coverage) uses the same code numbers as last year's update (CV18 and CV19), with revised descriptions of the reimbursement coverage. Since last year, clopidogrel has been eligible for reimbursement under CV18 when used for the prevention of ischemic events in combination with aspirin in post-angiography patients (with or without stenting). CV18 now also includes an indication for the reimbursement of clopidogrel in patients with an acute coronary syndrome who have not previously received aspirin. As well, CV19 now covers the reimbursement of clopidogrel as secondary prevention for ischemic events in patients for whom an antiplatelet agent is indicated but for whom aspirin is ineffective (*e.g.*, aspirin failure), contraindicated or poorly tolerated.

This piece is aimed at helping physicians incorporate the RAMQ's new formulary coverage into their practices. Two short case studies are presented and describe situations where clopidogrel is indicated and eligible for reimbursement. A brief description of how the new RAMQ coding is applied follows each case.

Case Study 1: Mrs. D

By André Roussin MD, FRCP

Mrs. D is a 70-year-old woman. Two years ago, she consulted for pain in her calves when walking,

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Clopidogrel Reimbursement Update – RAMQ Formulary

CV18

- For the prevention of ischemic vascular events, in combination with acetylsalicylic acid, in persons who have undergone angioplasty with or without the insertion of a coronary stent.
- In persons presenting with acute coronary syndrome who were not already receiving acetylsalicylic acid.

Note: The maximum length of authorization in both these situations is 12 months.

All requests for authorization to continue treatment for more than 12 months must be forwarded using the patient exception form or the Internet.

CV19

- For the secondary prevention of ischemic vascular events in persons for whom an antiplatelet agent is indicated but in whom acetylsalicylic acid is found to be ineffective, contraindicated or poorly tolerated.

Note: The use of clopidogrel as primary prevention (*i.e.,* in persons who have never presented ischemic vascular events) does not qualify for this payment indication.

Codification à jour du clopidogrel sur le formulaire de la RAMQ

CV18

- Pour la prévention des manifestations vasculaires ischémiques, en association avec l'acide acétylsalicylique, chez les personnes pour lesquelles une angioplastie avec ou sans la pose d'une endoprothèse coronarienne a été effectuée.
- Chez les personnes présentant un syndrome coronarien aigu qui ne recevaient pas d'acide acétylsalicylique au préalable.

Note : Pour ces deux situations, la durée maximale de l'autorisation est de 12 mois.

Toute demande d'autorisation pour poursuivre le traitement au-delà de 12 mois doit être transmise en utilisant le formulaire du patient d'exception ou Internet.

CV19

- Pour la prévention secondaire des manifestations vasculaires ischémiques chez les personnes pour lesquelles un antiplaquettaire est indiqué mais chez qui l'acide acétylsalicylique est inefficace, contre-indiqué ou mal toléré;

Note : Ne répond pas à cette indication de paiement, l'utilisation du Clopidorel en prévention primaire. i.e. chez les personnes qui n'ont jamais présenté de manifestations vasculaires ischémiques.

which disappeared rapidly when she stopped. She had smoked one pack of cigrettes per day since the age of 20 years. At her visit two years ago, her medical history included hypertension for which she had been treated for the previous five years. She also indicated that her father had died of a heart attack at 72 years of age and her mother from stroke at 75 years. Mrs. D was sedentary and her only medication was hydrochlorothiazide 25 mg/day. Physical examination revealed a blood pressure (BP) of 148/88 mmHg; her body mass index (BMI) was 30 kg/m² and her waistline circumference was 99 cm. She presented an abdominal murmur and a diminished pulse at the ankles. Her blood sugar was measured at 6.1 mmol/L, with an HDL-C level of 1.01 mmol/L, an LDL-C level of 4.2 mmol/L and a TG level of 2.6 mmol/L. Mrs. D's claudication was deemed to be indicative of symptomatic peripheral arterial disease (PAD).

In addition to advice on improving her lifestyle—the most important aspect being to stop smoking—Mrs. D was given prescriptions for aspirin 81 mg/day, atorvastatin 80 mg/day and ramipril 10 mg/day. These three treatments are among the level 1A recommendations of the Canadian Cardiovascular Society. Antiplatelet therapy should reduce the risk of myocardial infarction and stroke; the introduction of a statin was intended to achieve an LDL-C level of < 2 mmol/L, and the addition of a second antihypertensive agent (in this case an ACE inhibitor) targeted a BP of < 140/90 mmHg. It should be noted that ACE inhibitors are indicated even in normotensive patients with PAD symptoms. Still in accordance with 1A recommendations, if Mrs. D had been allergic to or intolerant of aspirin, clopidogrel could have been introduced.

Mrs. D consulted again after experiencing a stroke with brachiofacial paresis lasting one week. An ECG revealed signs of an inferior infarction which had not been present at the first consultation. Carotid Doppler examination showed bilateral carotid stenosis of approximately 50%. This indicated diffuse vascular disease involving at least two vascular beds (if not three, counting the patient's silent infarction). The risk of vascular events in such patients is almost doubled compared to those with single-bed disease, from about 5% to more than 10% per year. More aggressive management is therefore indicated.

Substituting Mrs. D's aspirin with clopidogrel is amply justified given the involvement of multiple vascular beds that manifested while she was already taking aspirin and complicates her PAD and atherosclerotic coronary disease. Combining two antiplatelet agents (aspirin and clopidogrel) can also be considered, given the patient's recent vascular events, but should always be done with caution in consideration of an individual patient's risk of bleeding.

This case illustrates the way in which many patients progress towards having signs and symptoms of multi-bed disease. Atherothrombosis is a diffuse vascular disease in which the rate of annual complications doubles when a second area becomes symptomatic. Clopidogrel represents a better option than aspirin in such patients, because of its well demonstrated superior efficacy. Administration of an aspirin + clopidogrel combination can be considered for these very high risk vascular patients, but each patient's risk of bleeding must be taken into account.

Application of RAMQ Formulary Code

This patient would be eligible for reimbursement of clopidogrel under RAMQ formulary code CV19, as she suffered an ischemic stroke while being treated with aspirin (*i.e.*, an aspirin failure). If the physician chooses to initiate clopidogrel therapy, code CV19 should be indicated on the prescription.

Case Study 2: Mr. J.

By Richard Harvey, MD, FRCP, FACC

Mr. J is 65 years of age. He was brought to the emergency room by ambulance because of persistent retrosternal pain that occurred while he was mowing his lawn. Upon his arrival in the ER, he was rapidly treated by the care team who confirmed an acute coronary syndrome (ACS).

Examination showed that the patient was well-perfused despite his intense retrosternal pain. His blood pressure (BP) was 105/75 mmHg and his heart rate was 90 bpm. In addition, heart auscultation revealed the presence of a B4, but no heart murmur.

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A 12-lead ECG was performed and confirmed elevation of ST segments in leads V1 to V6; marker results were positive. The diagnosis of myocardial infarction was therefore rapidly confirmed, since two of the three WHO criteria were met: 1) ischemic type retrosternal pain > 20 minutes; 2) ECG showing a lesion or transmural myocardial ischemia (STEMI); 3) positive markers (troponin).

The patient was given four 80-mg aspirin tablets, 5000 IU heparin IV bolus, and three doses of 5-mg metoprolol IV q 5 minutes. After contacting the hemodynamics specialist on duty, eight 75-mg clopidogrel tablets (600 mg) were given.

The patient was quickly transferred to the hemodynamics room (our team is available 24 hours a day) for a percutaneous coronary intervention (primary PCI) and optimal myocardial reperfusion.

Coronary angiography showed occlusion of the proximal anterior descending artery, with TIMI flow of 0. Following thrombo-aspiration, a bare-metal stent was implanted, completely correcting the occlusion. A dramatic normalization of ST segments was noted, with disappearance of the retrosternal pain and re-establishment of TIMI flow 3, confirmed by injecting a contrast agent. Myocardial reperfusion was successfully realized in an emergency-stent time of 45 minutes. This is well within the < 90-minute recommendation published in various guidelines.

Mr. J's hospital stay was short (72 hours), and aortic ultrasound confirmed a normal ejection fraction (EF) with the presence of discrete anteroseptal hypokinesia. The original ECG showed non-significant repolarization abnormalities and the absence of a Q wave (aborted transmural infarction).

His drug regimen when discharged from the hospital was: aspirin 80 mg/day, an ACE inhibitor, a beta-blocker, a xanthine, and sublingual NG prn (CCS 1A recommendations).

A separate prescription for clopidogrel (code CV18) is routinely entered on patients' charts following a primary PCI, with or without implantation of a bare-metal stent.

Unfortunately, serious complications have occurred in the past due to the fact that the pharmacy did not supply the dual antiplatelet therapy (aspirin + clopidogrel) under the pretext that the famous fax or permission from the RAMQ was not available. Premature termination of clopidogrel therapy, whether initiated by the patient or by health professionals other than the cardiologist, has also created serious complications, such as subacute stent thrombosis, transmural infarction and even death.

Application of the ***new RAMQ formulary codes: CV18 and CV19*** will allow patients needing dual antiplatelet therapy to receive these medications from their pharmacy without undue confusion.

In addition, the CV18 code will apply not only to ACS patients (with STEMI/NSTEMI or unstable angina) who have undergone emergency primary PCI with or without stenting, but also to ACS patients who do not require PCI.

These new CV18 and CV19 codes will simplify the task of medical specialists and general practitioners managing patients with cardiac and/or vascular conditions, allowing them to prescribe clopidogrel when indicated in accordance with the reimbursement requirements of the RAMQ.

These codes will mean we no longer have to routinely send thousands of faxes to the RAMQ on weekdays and, above all, on weekends.

In conclusion, we can remember that ***CV18 applies to*** patients presenting with an ACS who have not received aspirin therapy; and to patients who have undergone an angioplasty with or without implantation of a coronary stent for the prevention of ischemic vascular conditions, in combination with aspirin.

It should be noted that, in both situations, the maximum length of authorization is 12 months. Any request for authorization to continue treatment for longer than 12 months (for patients with drug-eluting stents) must be forwarded to the RAMQ using the exception form or the Internet.

However, under CV19, all patients suffering a second event while taking aspirin are eligible for lifelong reimbursement of clopidogrel.

CV19 is applicable in persons for whom an antiplatelet agent is indicated but for whom aspirin is ineffective, contraindicated or poorly tolerated in the secondary prevention of ischemic vascular events.

It should be noted that the use of clopidogrel as primary prevention in patients who have never presented ischemic vascular events does not qualify for this type of reimbursement.