pCODR EXPERT REVIEW COMMITTEE (pERC)
INITIAL RECOMMENDATION

The pan-Canadian Oncology Drug Review (pCODR) was established by Canada's provincial and territorial Ministries of Health (with the exception of Quebec) to assess cancer drug therapies and make recommendations to guide drug-funding decisions. The pCODR process brings consistency and clarity to the cancer drug assessment process by looking at clinical evidence, cost-effectiveness and patient perspectives.

Providing Feedback on this Initial Recommendation
Taking into consideration feedback from eligible stakeholders, the pERC will make a Final Recommendation. Feedback must be provided in accordance with *pCODR Procedures*, which are available on the pCODR website. The Final Recommendation will be posted on the pCODR website once available, and will supersede this Initial Recommendation.

Drug:
Ipilimumab (Yervoy)

Funding Request:
For the treatment of advanced melanoma (unresectable Stage III and Stage IV melanoma) in patients who have received prior systemic therapy

Submitted By:
Bristol-Myers Squibb Canada

Manufactured By:
Bristol-Myers Squibb Canada

NOC Date:
February 1, 2012

Submission Date:
December 1, 2011

Initial Recommendation Issued:
March 29, 2012

RECOMMENDATION	The pCODR Expert Review Committee (pERC) **considers recommending funding ipilimumab (Yervoy) if the cost-effectiveness of ipilimumab is improved to an acceptable level.** To be eligible for treatment, patients should have received at least one prior systemic treatment for unresectable stage III or IV melanoma and have good performance status (ECOG ≤ 1). Ipilimumab should be given at a dosage of 3 mg/kg every three weeks for four doses. At the time of disease progression, reinduction may be considered if patients have had stable disease for at least three months duration or have previously experienced a complete or partial response to ipilimumab. The Committee made this recommendation because it was satisfied that there is a net clinical benefit with ipilimumab treatment in this group of patients based on an overall survival advantage compared with no ipilimumab therapy. However, the Committee noted that, at the submitted price and best estimates of the incremental cost-effectiveness ratio, ipilimumab could not be considered cost-effective compared with dacarbazine or other therapies commonly used to treat metastatic melanoma.
POTENTIAL NEXT STEPS FOR STAKEHOLDERS	**Pricing Arrangements to Improve Cost-Effectiveness** Given pERC was satisfied that there is a net clinical benefit with ipilimumab, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of ipilimumab to an acceptable level. **Access to Expertise in Managing Side Effects** pERC noted that the potential immune-related side effects of ipilimumab are serious and that administration will require access to a treatment centre that has the professional expertise required to monitor and manage these side effects.

SUMMARY OF pERC DELIBERATIONS

pERC noted that there is currently no standard treatment for metastatic melanoma in previously treated patients and that there is a need for effective therapies. Although there are several systemic therapies commonly used in this clinical setting, including dacarbazine, temozolomide, and interleukin-2, pERC discussed that there is limited evidence that these treatments improve overall survival. The one double-blind randomized controlled trial included in the pCODR systematic review was a three-arm trial that compared ipilimumab plus gp100, placebo plus gp100 and ipilimumab plus placebo (Hodi 2010). pERC noted that gp100 is an experimental vaccine and not a standard therapy for melanoma. However, pERC also considered that a meta-analysis summarized as contextual information in the pCODR review indicated that gp100 is likely to be no worse than placebo (Korn 2008).

pERC's *Deliberative Framework* for drug funding recommendations focuses on four main criteria:

CLINICAL BENEFIT	PATIENT-BASED VALUES
ECONOMIC EVALUATION	ADOPTION FEASIBILITY

pERC discussed the design and results of the Hodi 2010 study and determined that there are net clinical benefits associated with ipilimumab. Overall, the results reported in Hodi 2010 demonstrated a clinically meaningful benefit across multiple relative and absolute measures including hazard ratios for overall survival, median survival time and the proportion of patients surviving at one year and two years. The Hodi 2010 study only included patients with HLA-A*0201 positive melanoma since the gp100 vaccine is specifically designed to target this patient population due to its biologic mechanism. However, pERC agreed that ipilimumab therapy should not be restricted to HLA-A*0201 positive patients after reviewing evidence in previously untreated patients demonstrating that, ipilimumab is effective in both HLA-A*0201 positive and HLA-A*0201 negative patients (Robert 2011).

pERC also discussed the toxicity profile of ipilimumab as reported in the Hodi 2010 trial. The Committee noted there are serious immune-related side effects associated with ipilimumab but these adverse events are manageable by specialists with the support of other therapies directed at these symptoms and close patient monitoring of adverse events. pERC considered that patients receiving ipilimumab should be managed in specialized cancer treatment centres with the medical expertise required to manage these side effects. However, it was noted that this could impact the feasibility of implementing ipilimumab treatment, and therefore a funding recommendation, as there would likely be additional costs associated with patient management and for adverse event monitoring.

pERC also reviewed patient advocacy group input indicating that patients have a high tolerance for side effects from new treatments if they can be managed effectively and if the treatment has the possibility of extending life. Given this input, pERC considered that ipilimumab aligns with patient values. However, pERC noted that quality of life is a patient-expressed value and that quality of life was poorly captured in the Hodi 2010 trial. pERC recognized that quality of life is an important outcome and trial sponsors, including manufacturers, should collect good quality data in clinical trials on this patient-important outcome. pERC noted that the patient advocacy group input was based upon responses from a small number of patients. While recognizing the difficulty patient advocacy groups may have in accessing a large number of patients, pERC considered that it would be helpful to get input from a larger number of patients who may have had both positive and negative experiences with ipilimumab.

pERC discussed the burden of illness of metastatic melanoma. It was noted that although this affects a small patient population, it is not a rare disease and the incidence is increasing. pERC also considered patient advocacy group input and noted that, melanoma patients are often young and the ability to work and financially support their family can be negatively impacted.

pERC discussed the cost-effectiveness of ipilimumab at 3 mg/kg in previously treated patients. It was concluded that ipilimumab is not cost-effective using either the Economic Guidance Panel's best estimates or the manufacturer's estimates. pERC considered that the price of ipilimumab would need to be reduced substantially in order for it to be considered cost-effective. pERC also discussed the

Economic Guidance Panel's best estimates of ipilimumab's cost-effectiveness, which were higher than the manufacturer's estimates, primarily due to differences in the time horizon assumed in the economic model. pERC expressed concern that the manufacturer would not publicly disclose the time horizon that was used in the manufacturer's economic model and this information was redacted from the economic guidance report provided to pERC. As a result, pERC considered it challenging to interpret the cost-effectiveness evidence provided by the manufacturer. pERC noted that the time horizon used in the Economic Guidance Panel's best estimates was five years and that the Economic Guidance Panel indicated this was shorter than the time horizon used by the manufacturer. pERC reviewed the overall survival data from Hodi 2010 and some considered that a time horizon somewhere between five and ten years could be appropriate.

EVIDENCE IN BRIEF

pERC deliberated upon a pCODR systematic review, other literature in the Clinical Guidance Report providing clinical context, an evaluation of the manufacturer's economic model and budget impact analysis, guidance from pCODR clinical and economic review panels, input from two patient advocacy groups (Melanoma Network of Canada and Save your Skin Foundation) and input from pCODR's Provincial Advisory Group.

OVERALL CLINICAL BENEFIT

pCODR review scope

The pCODR review evaluated the effect of ipilimumab, either alone or in combination, on patient outcomes compared to commonly used therapies, placebo, or best supportive care in the treatment of patients with unresectable advanced melanoma (stage III or stage IV disease) who have previously received systemic therapy.

Studies included

The pCODR systematic review included one double-blind, randomized controlled trial (Study MDX010-20, Hodi 2010) comparing ipilimumab plus placebo, ipilimumab plus gp100 vaccine and placebo plus gp100 vaccine in patients with unresectable Stage III or IV melanoma whose disease had progressed while receiving therapy for metastatic disease.

The pCODR review also provided contextual information on a meta-analysis summarizing overall survival results from phase II trials evaluating treatments for metastatic melanoma (Korn 2008) and on a randomized controlled trial (Study CA 184-024, Robert 2011) that evaluated ipilimumab in the first-line metastatic melanoma setting. The Robert 2011 study was not included in the systematic review because it was conducted in untreated patients, however, it was thought to provide indirect evidence that could address some of the limitations in the Hodi 2010 trial, which was conducted in previously treated patients.

Patient population: Previously treated, HLA positive patients with good performance status

pERC noted that the baseline characteristics of patients in the Hodi 2010 study were generally balanced between the three treatment groups. pERC also noted that the Hodi 2010 study only included patients with an ECOG score of 0 or 1, representing patients with good performance status.

pERC discussed that the Hodi 2010 study was limited to HLA-A*0201–positive patients because the gp100 vaccine is designed to target only these patients based upon its biologic mechanism. pERC also discussed the results of the Roberts 2011 study, which included both HLA-A*0201–positive and negative patients. Patients were not selected based on HLA-A*0201 status in this trial because ipilimumab was compared with dacarbazine, and the gp100 vaccine was not part of the comparator or intervention groups. pERC considered that ipilimumab appeared to be effective in patients regardless of HLA-A*0201 status and that therefore, ipilimumab use in previously treated patients should not be limited to only HLA-A*0201–positive patients, even though these were the only patients included in the Hodi 2010 study. As a result, pERC noted that HLA testing would not be required nor impact the implementation of a funding recommendation for ipilimumab.

Key efficacy results: Overall survival benefit for ipilimumab

The key efficacy outcome deliberated upon by pERC was overall survival. The primary endpoint of the Hodi 2010 study was overall survival for the ipilimumab plus gp100 group compared to the placebo plus gp100 group. pERC noted that a statistically significant difference in overall survival was observed for ipilimumab plus gp100 compared to placebo plus gp100 (hazard ratio = 0.68, 95% confidence interval 0.55 to 0.85, P < 0.001). The median overall survival was 10.0 months in the ipilimumab plus gp100 group compared with 6.4 months in the placebo plus gp100 group, which pERC considered to be a clinically meaningful difference. pERC also noted that the overall survival in the ipilimumab plus placebo arm was 10.1 months, which was similar to that in the ipilimumab plus gp100 arm.

pERC also discussed that the proportion of patients alive after one year was similar for the ipilimumab plus gp100 group and for the ipilimumab plus placebo group (43.5% and 45.6%, respectively) and higher than the proportion of patients in the placebo plus gp100 group (25.3%). A similar trend was observed in the proportion of patients surviving at two years (21.6% and 23.5% versus 13.7%, respectively).

pERC also reviewed the Kaplan-Meier survival curves and noted that both the ipilimumab plus gp100 curve and the ipilimumab plus placebo curve separated from the curve for the control group, placebo plus gp100, after approximately four months and that a separation in curves was sustained over time. It was noted that the median follow-up was 21.0 months in the ipilimumab plus gp100 group, 27.8 months in the ipilimumab plus placebo group, and 17.2 months in the placebo plus gp100 group.

Quality of life: Limited reporting of quality of life data

pERC reviewed the quality of life data provided on ipilimumab from the Hodi 2010 study; however, pERC noted that very few details were reported and it was not possible to determine with confidence the impact of ipilimumab on quality of life. pERC further noted that quality of life is important to patients and that trial investigators and manufacturers should collect and report good quality data for this outcome in clinical trials.

Ipilimumab Dosing: Variability in number of doses received

pERC discussed that while the standard course of ipilimumab therapy in previously treated patients is to administer 3 mg/kg every three weeks for four doses, in the trial, only 60% of patients in the ipilimumab plus gp100 group, 64.2% of patients in the ipilimumab plus placebo group, and 57.4% patients in the placebo plus gp100 group received all four doses of ipilimumab or placebo. The most frequent reason for discontinuation of therapy was disease progression.

Furthermore, pERC noted that there were only a small number of patients in the trial who received more than four ipilimumab doses. Forty patients (i.e. approximately 6%) were offered an additional course of therapy (i.e. reinduction) after they had experienced disease progression. In order to receive reinduction therapy patients had to have stable disease for three months duration after week 12 or a confirmed partial or complete response to ipilimumab. pERC noted that this was a small number of patients and that no firm conclusions could be drawn regarding the effectiveness of reinduction with ipilimumab. However, reinduction was part of the Hodi 2010 study protocol, therefore, pERC concluded that reinduction could be considered at time of disease progression.

Safety: Immune-related serious adverse events require management and monitoring

In the Hodi 2010 study, grade three and grade four immune-related adverse events occurred in a higher proportion of patients in both the ipilimumab plus gp100 group and the ipilimumab plus placebo group as compared to the placebo plus gp100 group (10.3% and14.5% versus 3.0%, respectively). These included immune-related gastrointestinal, dermatologic, and endocrine adverse events. pERC noted that these are clinically significant adverse events that should be looked for during therapy; however they are manageable by specialists through close monitoring, early therapeutic intervention and the use of other therapies and supportive care measures. pERC further noted that administration of ipilimumab would require adverse event monitoring and intervention in centres with specialized expertise, which would affect the organizational feasibility of implementing a funding recommendation for ipilimumab.

Limitations: gp100 vaccine and HLA-A*0201 status

The key limitation discussed by pERC was that the Hodi 2010 study was limited to HLA-A*0201–positive patients because the gp100 vaccine is designed to target only these patients based upon its biologic mechanism. pERC discussed the challenges associated with the manufacturer's decision to include gp100 vaccine as a comparator and interpreting the resulting data in HLA-A*0201–positive patients. pERC also considered the possibility that gp100 may be worse than placebo. However, when considering results from the three arms of the Hodi 2010 study and the pCODR Melanoma Clinical Guidance Panel's interpretation that gp100 is likely no worse than placebo based on a meta-analysis summarizing overall survival results from phase II trials evaluating metastatic melanoma therapies (Korn 2008), pERC also considered that gp100 is likely no worse than placebo.

pERC noted that the primary endpoint of the Hodi 2010 study was changed from best overall response rate to overall survival during the trial, however, pERC considered that because survival results remained blinded, the integrity of the trial was not compromised by this change.

Need: New treatment options available that improve overall survival

pERC noted that there is currently no effective standard treatment for metastatic melanoma in previously treated patients and that there is a need for such therapies. It was discussed that commonly used systemic therapies include dacarbazine, temozolomide and interleukin-2 but there is limited evidence that these treatments improve overall survival. pERC also noted that patients with metastatic melanoma are often younger than those affected by other types of cancer and while this cancer may affect a small patient population, incidence is increasing and it cannot be considered a rare disease.

PATIENT-BASED VALUES

Values of patients with advanced melanoma: Extending life and improving quality of life

Patient advocacy group input indicated that there are limited therapies available for patients with advanced melanoma and new therapies that could extend their life expectancy are very important. pERC considered that patients receiving ipilimumab plus gp100 in the Hodi 2010 study had approximately a 3.6 month improvement in overall survival compared to patients receiving placebo plus gp100. pERC also noted that none of the current agents used to treat advanced melanoma appear to have demonstrated an improvement in overall survival.

Input from patient advocacy groups also indicated that patients are looking for a therapy that will help to improve quality of life for themselves and their families. Patients would prefer more manageable treatment regimens that have milder side effects that will enable them to continue to work and provide financially for their families. pERC discussed quality of life data but noted that interpretation was challenging as there was limited information reported from the Hodi 2010 study. pERC emphasized that manufacturers should collect and report good quality data on this outcome, which is so important to patients. pERC noted that both survival and quality of life estimates were incorporated into the economic evaluation of ipilimumab.

Patient values on treatment: Willing to tolerate side effects

Although therapy with ipilimumab may be associated with side effects, input from patient advocacy groups indicated that patients would be willing to tolerate certain side effects if it extended their life expectancy. pERC noted that there are serious immune-related adverse events associated with ipilimumab that require monitoring and management but pERC acknowledged that patients have a high tolerance for side effects from new treatments, if those side effects can be effectively managed and the treatment has the potential to extend their life.

In reviewing the patient advocacy group input, pERC noted that it was based upon responses from a small number of patients. While recognizing the difficulty patient advocacy groups may have in accessing a large number of patients, pERC considered that it would be helpful to get input from a larger number of patients who may have had both positive and negative experiences with ipilimumab.

ECONOMIC EVALUATION

Economic model submitted: Cost-effectiveness and cost-utility analysis

pCODR assessed an economic model looking at the cost-effectiveness and cost-utility of ipilimumab compared to [redacted] for previously treated patients with unresectable (stage IIIC) or metastatic (stage IV) melanoma (*Non-disclosable information was provided to pERC in the pCODR guidance reports for deliberation on a recommendation and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed)*. pERC considered dacarbazine as an appropriate comparator as it is currently considered a standard of care in patients with advanced melanoma. However, pERC noted that in previously treated patients, there are other therapies that could be used and the submitted economic model allowed for comparisons with other chemotherapies. pERC also noted that none of these comparators were evaluated in the Hodi 2010 trial, which creates uncertainty in the economic analysis.

Basis of the economic model: Clinical and economic inputs

Costs included direct drug costs and healthcare costs associated with medical follow-up. Costs associated with monitoring serious adverse events were also included. The key driver in the economic model was the price of ipilimumab.

Key clinical effects included overall survival and progression-free survival estimates from the Hodi 2010 study and utility values from the general population. pERC considered it a limitation that good quality of life data were not available from the Hodi 2010 to inform the economic evaluation and so general population data had to be used to inform the utility values.

Drug costs: Affected by drug wastage and variability in dosing

At the list price and at a strength of 5 mg per mL, one 10 mL vial of ipilimumab costs $5800.00. The recommended dose of ipilimumab in previously treated patients is 3 mg/kg intravenously every three weeks for four doses. At the submitted price, one dose of ipilimumab costs $24,360 and four doses would cost $97,440, assuming a body mass of 70 kg. pERC noted that this is substantially more than any of the systemic therapies currently used in previously treated patients with advanced melanoma. For example, dacarbazine costs approximately $200.20 per 600 mg/vial. At the recommended dose of 200 to 250 mg/m² administered intravenously on days one to five, every 21 to 28 days, and assuming a body surface area of 1.7 m^2 and no wastage, the average cost of dacarbazine per day is between $20.26 and $33.76 in a 28-day course.

pERC also discussed that the submitted economic evaluation assumed [redacted] for ipilimumab or comparators and that the Economic Guidance Panel estimated that incorporating drug wastage into the evaluation would increase the incremental cost-utility ratio by 6.4% (*Non-disclosable information was provided to pERC in the pCODR guidance reports for deliberation on a recommendation and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed)*.

pERC noted that the recommended course of ipilimumab is four doses; however, not all patients in the Hodi 2010 study received four doses. A large proportion of patients received less than four doses and a small number of patients received additional doses of ipilimumab at the time of reinduction. pERC discussed that while Economic Guidance Panel reanalyses considered the effects of additional ipilimumab doses, the possibility of receiving fewer doses of ipilimumab could also be considered.

Sensitivity Analyses: Submitted economic model sensitive to drug price

pERC noted that based on the submitted economic evaluation, the Economic Guidance Panel estimated that a 10% decrease in the ipilimumab drug price would result in a 12.9% decrease in the incremental cost-utility ratio.

Cost-effectiveness estimates: Shorter time horizon increases incremental cost-utility ratio

pERC considered that the Economic Guidance Panel's best estimate of the incremental cost-utility ratio in previously treated patients is approximately $269,299 per QALY when ipilimumab 3 mg/kg is compared with [redacted], assuming a time horizon of five years and incorporating drug wastage into the economic evaluation. (*Non-disclosable information was provided to pERC in the pCODR guidance reports for deliberation on a recommendation and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed)*.

pERC noted that the Economic Guidance Panel's best estimates were considerably higher than the manufacturer's estimates; however, pERC concluded that ipilimumab is not cost-effective using either the Economic Guidance Panel's best estimates nor the manufacturer's estimates. pERC considered that the price of ipilimumab would need to be reduced substantially in order for it to be cost-effective.

pERC also discussed that the Economic Guidance Panel's best estimates of ipilimumab's incremental cost-effectiveness ratios were higher (i.e. less favourable) than the manufacturer's estimates, primarily because the Economic Guidance Panel assumed a shorter time horizon in the economic model. pERC expressed concern that the manufacturer would not publicly disclose the time horizon that was used in their economic model and this information was redacted from the Economic Guidance Report provided to pERC. As a result, pERC considered it very challenging to interpret the cost-effectiveness evidence without knowing the time horizon used in the manufacturer's economic model. pERC noted that the time horizon used in the Economic Guidance Panel's best estimate was five years based on input from the pCODR Melanoma Clinical Guidance Panel. pERC reviewed the overall survival data from Hodi 2010 and some considered that a time horizon somewhere between five and ten years could also be appropriate.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: Ipilimumab dosing, patient management and adverse event monitoring

pCODR's Provincial Advisory Group indicated that dosing issues with ipilimumab would be important to consider. pERC discussed that in previously treated patients, ipilimumab should be considered at the Health Canada approved dosage of 3 mg/kg every three weeks for four doses. pERC noted that reinduction may be considered as was done in the Hodi 2010 study; however, the effectiveness of reinduction is uncertain given the small proportion of patients who received additional doses.

pCODR's Provincial Advisory Group indicated that the additional resources required to administer ipilimumab and monitor for potential serious side effects could impact on the feasibility of adoption. pERC discussed serious immune-related adverse events associated with ipilimumab and noted that patients will require access to a treatment centre that has the professional expertise required to manage patients and monitor these side effects. pERC noted adverse event monitoring and the management of adverse events may result in additional costs. Costs associated with monitoring adverse events were incorporated into the submitted economic evaluation; however, they were not a key driver in the model.

DRUG AND CONDITION INFORMATION

Drug Information	• Monoclonal antibody that blocks cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) • 5 mg/mL concentration reviewed by pCODR • Recommended dosage of 3 mg/kg every 3 weeks for four doses
Cancer Treated	• Advanced or metastatic melanoma, previously treated
Burden of Illness	• Small proportion of patients but incidence increasing. Affects a young patient population.
Current Standard Treatment	• Dacarbazine, temozolomide, interleukin-2 and other systemic therapies.
Limitations of Current Therapy	• Complete responses rare and survival improvement has not been demonstrated. Side effects of therapies not always tolerated.

ABOUT THIS RECOMMENDATION

The pCODR Expert Review Committee (pERC)

Recommendations are made by the pCODR Expert Review Committee following the pERC Deliberative Framework. pERC members and their roles are as follows:

Dr. Anthony Fields, Oncologist (Chair)
Dr. Maureen Trudeau, Oncologist (Vice-Chair)
Dr. Chaim Bell, Economist
Dr. Scott Berry, Oncologist
Bryson Brown, Patient Member
Mario de Lemos, Pharmacist
Mike Doyle, Economist;
Dr. Tallal Younis, Oncologist
Dr. Bill Evans, Oncologist
Dr. Allan Grill, Family Physician
Dr. Paul Hoskins, Oncologist
Danica Lister, Pharmacist
Carole McMahon, Patient Member Alternate
Jo Nanson, Patient Member
Dr. Peter Venner, Oncologist
Dr. Sunil Desai, Oncologist

All members participated in deliberations and voting on the initial recommendation except:

- Dr. Maureen Trudeau, Dr. Scott Berry and Dr. Sunil Desai who were not present
- Carole McMahon who did not vote due to her role as a patient member alternate

Avoidance of conflicts of interest

All members of the pCODR Expert Review Committee must comply with the *pCODR Conflict of Interest Guidelines*; individual conflict of interest statements for each member are posted on the pCODR website and pERC members have an obligation to disclose conflicts on an ongoing basis. For the review of ipilimumab for advanced melanoma, through their declarations, five members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, however, no members were excluded from voting.

Information sources used

The pCODR Expert Review Committee is provided with a *pCODR Clinical Guidance Report* and a *pCODR Economic Guidance Report*, which include a summary of patient advocacy group and Provincial Advisory Group input, as well as original patient advocacy group input submissions to inform their deliberations.

pCODR guidance reports are developed following the pCODR review process and are posted on the pCODR website. Please refer to the pCODR guidance reports for more detail on their content.

Consulting publicly disclosed information

pCODR considers it essential that pERC recommendations be based on information that may be publicly disclosed. All information provided to the pCODR Expert Review Committee for its deliberations was handled in accordance with the *pCODR Disclosure of Information Guidelines*. Bristol-Myers Squibb Canada, as the primary data owner, did not agree to the disclosure of some economic information, therefore, this information was redacted from guidance reports provided to pERC and has been redacted in this recommendation and publicly available guidance reports, as needed.

Use of this recommendation

This recommendation from the pCODR Expert Review Committee (pERC) is not intended as a substitute for professional advice, but rather to help Canadian health systems leaders and policymakers make well-informed decisions and improve the quality of health care services. While patients and others may use this Recommendation, it is for informational and educational purposes only, and should not be used as a substitute for the application of clinical judgment respecting the care of a particular patient, for professional judgment in any decision-making process, or for professional medical advice.

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