pCODR EXPERT REVIEW COMMITTEE (pERC)
FINAL RECOMMENDATION

The CADTH 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 assessment of cancer drugs by looking at clinical evidence, cost-effectiveness, and patient perspectives.

pERC Final Recommendation
Upon consideration of feedback from eligible stakeholders, pERC members considered that criteria for early conversion of an Initial Recommendation to a Final Recommendation were met and reconsideration by pERC was not required.

Drug: Ibrutinib (Imbruvica) **Submitted Funding Request:** For the treatment of patients with relapsed/refractory mantle cell lymphoma (MCL)	
Submitted By: Janssen Inc.	**Manufactured By:** Janssen Inc.
NOC Date: June 24, 2016	**Submission Date:** January 29, 2016
Initial Recommendation: June 30, 2016	**Final Recommendation:** July 19, 2016

pERC RECOMMENDATION

pERC recommends reimbursement of ibrutinib (Imbruvica) for the treatment of patients with relapsed or refractory mantle cell lymphoma conditional on the cost-effectiveness being improved to an acceptable level. Treatment should be for patients with a good performance status and until disease progression or unacceptable toxicity.

pERC made this recommendation because it was satisfied that compared with temsirolimus, ibrutinib demonstrated an overall net clinical benefit based on a clinically meaningful and statistically significant improvement in progression-free survival, a moderate but manageable toxicity profile, and an improvement in quality of life. However, pERC acknowledged that there was uncertainty regarding the magnitude of the clinical benefit compared with standard of care options in Canada, as there is no direct evidence available that compares ibrutinib with Canadian standard of care options.

Ibrutinib also aligned with patient values, as there is a need for more effective treatment options for patients with relapsed or refractory mantle cell lymphoma.

However, pERC considered ibrutinib to be not cost-effective compared with standard of care options in Canada, due to its high cost. pERC also highlighted that the submitted potential budget impact of ibrutinib is likely underestimated and could be substantial.

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POTENTIAL NEXT STEPS FOR STAKEHOLDERS

Pricing Arrangements to Improve Cost-Effectiveness
Given that pERC was satisfied that there is a net clinical benefit with ibrutinib compared with Canadian standard of care options, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of ibrutinib to an acceptable level.

Factors Affecting Budget Impact and Adoption Feasibility
pERC noted the unknown duration of treatment with ibrutinib, as it continues until confirmed disease progression or unacceptable toxicity, whichever comes first. In considering the high cost of ibrutinib, the large prevalent eligible population, and the unknown but potentially long duration of treatment, pERC concluded that a substantial reduction in drug price would be required to improve affordability.

Optimal Sequencing of Ibrutinib and Other Therapies Unknown
pERC concluded that the optimal sequencing of ibrutinib and other treatments (e.g., intravenous chemotherapy) for the treatment of relapsed or refractory mantle cell lymphoma is currently unknown. pERC was, therefore, unable to make an evidence-informed recommendation on sequencing. However, pERC recognized that provinces will need to address this issue upon implementation of ibrutinib funding and noted that collaboration among provinces to develop a common approach would be of value, as would the development and implementation of an evidence-based clinical practice guideline.

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SUMMARY OF pERC DELIBERATIONS

Mantle cell lymphoma (MCL) is the fourth most common non-Hodgkin lymphoma in North America. MCL is diagnosed in approximately 500 to 600 new cases per year in Canada, with the majority of patients developing relapsed or refractory disease. MCL is an incurable disease. Current treatment options for relapsed or refractory MCL include monotherapy or combination therapies with fludarabine, rituximab, bortezomib, bendamustine, gemcitabine, and alkylating agents. These treatment options have limited effectiveness and are associated with toxicities. There is no clearly established standard of care option in this setting. pERC, therefore, agreed that there is an unmet need for more effective and tolerable treatment options for patients with relapsed or refractory MCL.

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

CLINICAL BENEFIT	PATIENT-BASED VALUES
ECONOMIC EVALUATION	ADOPTION FEASIBILITY

The pCODR systematic review included one open-label, randomized controlled trial, MCL-3001, that evaluated ibrutinib compared with temsirolimus in patients with relapsed or refractory MCL who had received at least one prior rituximab-containing chemotherapy regimen. Although temsirolimus is not a treatment option used in Canada, pERC considered it to be a reasonable comparator, given that there is no standard of care for relapsed or refractory MCL in Canada and that efficacy of temsirolimus has been demonstrated in phase II trials and is favourable when compared to other historical treatments for relapsed or refractory MCL. pERC noted that there was a clinically and statistically significant improvement in progression-free survival (PFS) in favour of patients in the ibrutinib group compared with those in the temsirolimus group. pERC noted that the absolute magnitude of benefit in median PFS (8.4-month difference) was impressive and meaningful in this patient population. Improvements in overall response rate were also seen in favour of ibrutinib compared with temsirolimus (72% versus 40%). While pERC noted that median overall survival (OS) was in favour of ibrutinib, there was no statistically significant difference in OS for ibrutinib compared with temsirolimus. The Committee noted that the median OS had not been reached for the ibrutinib group at the time of the published analysis and that the trial was not powered to detect differences in OS. Furthermore, 23% of patients in the temsirolimus group crossed over to ibrutinib, which may have confounded the OS results and limited the conclusions that could be drawn regarding the OS data.

pERC noted that several patient-reported outcome measures were collected in MCL-3001, which provided robust information on assessing the impact of ibrutinib on symptoms and health-related quality of life (QoL) of patients with relapsed or refractory MCL. Compared with the patients in the temsirolimus group, a greater proportion of patients in the ibrutinib group experienced clinically meaningful improvements in lymphoma symptoms (62% versus 35%, respectively); data were collected up to 100 weeks. The median time to clinically meaningful improvement was 6.3 weeks versus 57.3 weeks in the ibrutinib and temsirolimus groups, respectively. Health-state preferences (utilities) values based on EQ-5D-5L (using UK time trade-off values) in the ibrutinib group were improved from baseline up to week 40, while values for patients in the temsirolimus group were consistently lower. pERC discussed the toxicity profile of ibrutinib and noted that it was moderate and manageable. pERC acknowledged that grade 3/4 adverse events occurred in patients in both the ibrutinib and temsirolimus groups, such as fatigue (4% versus 7%), atrial fibrillation (4% versus 1%), and major bleeding (8% versus 5%). pERC noted that ibrutinib was well tolerated, as the majority of patients received the full dose of ibrutinib. Additionally, compared with temsirolimus, there were fewer dose interruptions and delays. Overall, pERC concluded that there is a net clinical benefit with ibrutinib based upon clinically meaningful and statistically significant improvements in PFS and QoL, as well as a manageable toxicity profile.

pERC deliberated upon patient advocacy group input. pERC noted that patients valued having access to effective treatment options that provide disease control, delay the progression of disease, and relieve cancer-related symptoms. Respondents' experience with current therapies varied widely, as there is a lack of well-defined standard treatments in relapsed or refractory MCL. Respondents reported that ibrutinib improved QoL compared with previous therapies. pERC noted that as an oral treatment option, ibrutinib improved ease of administration for patients with relapsed or refractory MCL. pERC noted that although ibrutinib was associated with significant improvements in PFS and QoL, adverse events such as

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fatigue and bleeding were still observed in patients who received ibrutinib. pERC concluded that overall, ibrutinib aligned with patient values.

pERC deliberated upon the cost-effectiveness of ibrutinib compared with a treatment mix reflecting different standard of care options and noted that there is currently no single standard of care in Canada in this clinical setting. pERC noted that efficacy inputs for the treatment mix were based on an indirect treatment comparison provided by the submitter. pERC acknowledged and agreed with the pCODR Clinical Guidance Panel that the results of the indirect comparison suggest that compared with investigator's choice of therapy, ibrutinib showed improvements in PFS but no improvement in OS, which was similar to the results from the MCL-3001 study comparing ibrutinib to temsirolimus. pERC noted that treatment options used in Canada include, but are not limited to, regimens containing bendamustine, bortezomib, and/or rituximab. These treatments were not included in the treatment mix, which increases the uncertainty in the results of the indirect comparison. pERC considered estimates provided by the submitter and reanalysis estimates provided by the pCODR Economic Guidance Panel (EGP) and noted uncertainty regarding the survival estimates. As OS results for ibrutinib directly compared with temsirolimus and indirectly compared with investigator's choice were not statistically significant, pERC agreed with the EGP's modifications to the hazard ratio for OS to explore uncertainty in these data. pERC accepted the EGP's use of the upper and lower bounds of the estimate of effect to account for the uncertainty in the magnitude of clinical benefit. The Committee, therefore, agreed that the uncertainty in the magnitude of clinical benefit introduced a large amount of uncertainty into the cost-effectiveness estimates and concluded that the true estimate of the incremental cost-effectiveness ratio is higher than the EGP's point estimate and likely at the higher end of the range provided by the EGP. pERC, therefore, concluded that ibrutinib is not cost-effective in this setting.

pERC considered the feasibility of implementing a reimbursement recommendation for ibrutinib. pERC noted that although the incidence of MCL is low, uptake would be high, as ibrutinib is an oral drug and there is a large prevalent population of patients with relapsed or refractory MCL. pERC acknowledged that there is no standard of care for relapsed or refractory MCL in Canada and that ibrutinib would provide a new treatment option for this group of patients. pERC also discussed that the cost of ibrutinib is very high and that treatment is continued until disease progression or unacceptable toxicities, which together increases the uncertainty regarding the potential budget impact. pERC noted that the median treatment duration of ibrutinib was 14.4 months in the MCL-3001 study; however, the treatment duration of ibrutinib is unknown as 47% of patients in the ibrutinib arm were still on treatment at the time of the data cut-off date. The Committee also noted that the budget impact of ibrutinib was likely substantially underestimated in the budget impact analysis, as the market share of ibrutinib will be high, given the large prevalent population eligible for reimbursement. As there is no standard of care in relapsed or refractory MCL, ibrutinib will likely be used in earlier lines of therapy and would not replace current treatment options. Overall, pERC noted that the budget impact of ibrutinib could be substantial and that provinces will need to consider pricing arrangements and/or cost structures to improve both the cost-effectiveness and the affordability of ibrutinib.

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EVIDENCE IN BRIEF

The CADTH pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (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 three patient advocacy groups (Canadian Cancer Survivor Network [CCSN], the Leukemia & Lymphoma Society of Canada [LLSC], and Lymphoma Canada [LC])
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- pCODR's Provincial Advisory Group
- three patient advocacy groups (Canadian Cancer Survivor Network [CCSN], the Leukemia & Lymphoma Society of Canada [LLSC], and Lymphoma Canada [LC])
- the Submitter (Janssen Inc.)

The pERC Initial Recommendation was reimbursement of ibrutinib (Imbruvica) for the treatment of patients with relapsed or refractory mantle cell lymphoma conditional on the cost-effectiveness being improved to an acceptable level.

Feedback on the pERC Initial Recommendation indicated that the submitter agreed in part with the pERC Initial Recommendation. Patient advocacy groups and pCODR's Provincial Advisory Group agreed with the pERC Initial Recommendation. The pERC Chair and pERC members reviewed the feedback and it was determined that the pERC Initial recommendation was eligible for early conversion to a pERC Final Recommendation without reconsideration by pERC because there was unanimous consensus from stakeholders on the recommended clinical population outlined in the pERC Initial Recommendation.

OVERALL CLINICAL BENEFIT

pCODR review scope

The purpose of this review is to evaluate the safety and efficacy of ibrutinib (Imbruvica) as compared with an appropriate comparator in patients with relapsed or refractory mantle cell lymphoma (MCL).

Studies included: One open-label randomized controlled trial, crossover permitted

The pCODR systematic review included one open-label, randomized controlled trial, MCL-3001, comparing ibrutinib (n = 139) with temsirolimus (n = 139) in patients with relapsed or refractory MCL who received at least one prior rituximab-containing chemotherapy regimen. Patients received ibrutinib at a dose of 560 mg orally once daily. Temsirolimus was given at a dose of 175 mg intravenously on days 1, 8, and 15 of the first cycle, followed by 75 mg on days 1, 8, and 15 of each subsequent 21-day cycle. Both ibrutinib and temsirolimus were given until disease progression or unacceptable toxic effects. MCL-3001 included only patients with an Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) of 0 to 1. Crossover of patients who had progressed on temsirolimus to ibrutinib was permitted following confirmation of disease progression by an independent review committee.

Patient populations: Pre-treated population with one to five prior lines of therapy, ECOG PS 0 to 1

Patient characteristics appeared to be balanced between the two groups in the MCL-3001 trial. The majority of patients were male (74%), white (87%), and had stage IV MCL (83%). Seventy per cent of patients had relapsed disease and 30% had refractory disease. ECOG PS was balanced between 0 (48%) and 1 (51%). Three patients (1%) had an ECOG PS of 2; however, according to the study authors, these patients were inadvertently enrolled in the study. The median number of prior lines of therapy was two; 67% of patients had one to two prior lines of therapy and 31% of patients had three to five prior lines of therapy. Prior therapies included rituximab (< 100%), bortezomib (18%), and lenalidomide (5%). Patients who had central nervous system lymphoma were not eligible for inclusion.

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Key efficacy results: Improved progression-free survival

Ibrutinib demonstrated a statistically significant improvement in the primary outcome of progression-free survival (PFS) compared with temsirolimus (hazard ratio [HR] 0.43; 95% confidence interval [CI], 0.32 to 0.58; $P < 0.0001$). The median PFS was 14.6 months for the patients in the ibrutinib group, compared with 6.2 months for those in the temsirolimus group. pERC noted that the absolute magnitude of benefit in median PFS (8.4-month difference) was impressive and meaningful in this patient population.

Overall response rate (ORR) and overall survival (OS) were secondary end points in the MCL-3001 study. The ORR was 72% and 40% for ibrutinib and temsirolimus, respectively. There was no statistically significant difference in median OS between ibrutinib and temsirolimus. After a median follow-up of 20 months, the median OS was not reached for the ibrutinib group, while the median OS for the temsirolimus group was 21.3 months. pERC noted that the trial was not powered to detect differences in OS. pERC also noted that 23% of patients in the temsirolimus group crossed over to ibrutinib, which confounded the OS results and limited the conclusions that could be drawn regarding OS. pERC considered that the improvements in ORR, as well as the trend in OS, were clinically meaningful in this patient setting.

Quality of life: Clinically meaningful improvement in QoL

Quality of life (QoL) end points collected in the MCL-3001 study included the time to worsening in the Lymphoma (Lym) subscale of the FACT-Lym and the mean change from baseline in EuroQol 5-Dimensions Health-Related Quality of Life Questionnaire, 5 Levels (EQ-5D-5L) scores. The median time to clinically meaningful worsening was not reached in the ibrutinib group and was 9.7 weeks in the temsirolimus group (HR = 0.27; 95% CI, 0.18 to 0.41; $P < 0.0001$). The change from baseline for EQ-5D-5L utility values were positive and statistically different for the ibrutinib group compared with the temsirolimus group. Similar results were seen for a post-hoc analysis of time to clinically meaningful improvement in the Lym subscale; the median time to clinically meaningful improvement was 6.3 weeks in the ibrutinib group compared with 57.3 weeks in the temsirolimus group (HR = 2.19; 95% CI, 1.52 to 3.14; $P < 0.0001$). pERC was impressed by the robust reporting of QoL outcomes in the MCI-3001 study and concluded there were clinically meaningful improvements in QoL with ibrutinib.

Safety: Moderate but manageable toxicities with ibrutinib

Treatment-emergent adverse events (TEAEs) leading to deaths were reported in 6% versus 8% of patients in the ibrutinib and temsirolimus groups, respectively. Grade ≥ 3 TEAEs were less frequent among patients in the ibrutinib group compared with those in the temsirolimus group (68% versus 87%). TEAEs leading to discontinuation were also less frequent among patients in the ibrutinib group compared with those in the temsirolimus group (6% versus 26%). pERC acknowledged that grade 3/4 adverse events occurred in both the ibrutinib and temsirolimus groups, such as fatigue (4% versus 7%), atrial fibrillation (4% versus 1%), and major bleeding (8% and 5%). pERC reviewed the toxicity profile of ibrutinib and concluded that the toxicities were generally manageable.

Comparator information: Multiple treatment options; temsirolimus not used in Canada

MCL-3001 compared ibrutinib with temsirolimus in patients with relapsed or refractory MCL who received at least one prior rituximab-containing chemotherapy regimen. pERC noted that the submitter conducted an indirect treatment comparison comparing ibrutinib with investigator's choice of therapy to inform the cost-effectiveness analyses. Investigator's choice of therapy included gemcitabine, fludarabine, chlorambucil, cladribine, etoposide, cyclophosphamide, thalidomide, vinblastine, alemtuzumab, and lenalidomide. pERC acknowledged and agreed with the pCODR Clinical Guidance Panel that the results of the indirect comparison suggest that compared with investigator's choice of therapy, ibrutinib showed improvements in PFS but no improvement in OS, which was similar to the results from the MCL-3001 study. pERC noted that treatment options used in Canada include, but are not limited to, regimens containing bendamustine, bortezomib, and/or rituximab; this affects the degree of certainty in the conclusions that can be drawn. These treatments were not included in the treatment mix, which increases the uncertainty in the results of the indirect comparison.

Need and burden of illness: Incurable lymphoma and no standard of care in this setting

MCL is diagnosed in approximately 500 to 600 new cases per year in Canada, with the majority of patients developing relapsed or refractory disease. MCL is currently an incurable lymphoma with current standard therapies. Treatment for relapsed or refractory MCL varies across provinces and there is no standard of care. Treatment options include monotherapy or combination therapies with fludarabine, rituximab, bortezomib, bendamustine, gemcitabine, and alkylating agents. Overall, pERC considered there to be a

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need for new and effective therapies for patients with relapsed or refractory MCL that provide improvements in patient survival, have more favourable toxicity profiles, and improve QoL.

PATIENT-BASED VALUES

Values of patients with mantle cell lymphoma: Improved management of disease symptoms
pERC deliberated upon patient advocacy group input for ibrutinib for MCL and discussed the values of patients with relapsed or refractory MCL. Patients noted that the symptoms that have the most impact on day-to-day living were fatigue, loss of appetite, and weight loss. The symptoms that were most important for ibrutinib to manage were pain, bruising and/or bleeding, nausea, and vomiting. pERC acknowledged that patients indicated it is important to have access to therapies that provide disease control, delay the progression of disease, and relieve cancer-related symptoms.

Patient values on treatment: Disease control with acceptable toxicities
pERC noted that patients' expectations for ibrutinib were to manage cancer symptoms including pain, bruising and/or bleeding, nausea, and vomiting. pERC acknowledged that adverse events such as fatigue and bleeding were still observed in patients who received ibrutinib in the MCL-3001 study. pERC noted that six patients who provided input had direct experience with ibrutinib. These patients reported that ibrutinib managed, or managed better than previous therapies, symptoms of loss of appetite, weight loss, and fatigue. Overall, ibrutinib was reported to improve QoL of patients compared with previous therapies. pERC, therefore, agreed that overall ibrutinib aligns with patient values as it is an effective oral treatment option that provides ease of administration, demonstrates PFS and QoL benefit, and has a manageable toxicity profile.

ECONOMIC EVALUATION

Economic model submitted: Cost-utility analysis
The pCODR Economic Guidance Panel (EGP) assessed a cost-utility analysis in the relapsed or refractory MCL setting. Ibrutinib was compared with a standard of care treatment mix. The efficacy data for the treatment mix were based on an indirect treatment comparison to compare ibrutinib with investigator's choice of therapy from the phase 3 OPTIMAL study. The comparators and proportion of comparators in the treatment mix were based on clinical expert opinion in the Canadian context. The OPTIMAL study compared investigator's choice of therapy with two doses of temsirolimus (75 mg and 25 mg) in the relapsed or refractory MCL setting. Therapies included gemcitabine, fludarabine, chlorambucil, cladribine, etoposide, cyclophosphamide, thalidomide, and vinblastine, alemtuzumab, and lenalidomide. pERC noted that although overall these treatments are similar to treatment options in Canada, combination therapies, as well as bortezomib and bendamustine, were not included in the OPTIMAL study. Therefore, pERC noted there was increased uncertainty in the results of the indirect comparison.

Basis of the economic model: Clinical and economic inputs
Costs considered in the model provided by the submitter included drug costs, drug administration costs, adverse event costs, and end-of-life costs. The key clinical outcomes considered in the model provided by the submitter were PFS, OS, and utilities. The submitter also provided another approach using the efficacy of temsirolimus from the MCL-3001 study as a proxy for efficacy for standard of care.

Drug costs: High drug cost, treatment until disease progression
Ibrutinib costs $90.65 per 140 mg capsule. At the recommended dose of 560 mg once daily, ibrutinib costs $362.60 per day and $9,776.00 per 28-day course. Having discussed that the median treatment duration is not yet known and that ibrutinib is administered until disease progression or unacceptable toxicity, pERC noted that the cost of treating patients with ibrutinib may be substantial. pERC noted that the once-daily oral route of administration should enhance patient compliance and provide ease of administration to patients. pERC also noted that dose adjustments are not expected to lead to wastage, as only one strength is available.

Cost-effectiveness estimates: Not cost-effective at submitted price
pERC deliberated upon the cost-effectiveness of ibrutinib compared with the standard of care treatment mix used in the comparator group, reflecting different local standards of care. pERC noted that the EGP

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provided a wide range of cost-effectiveness estimates which reflects a large amount of uncertainty in the incremental benefit for ibrutinib compared with standard of care treatment mix. This range is based on the most optimistic and pessimistic scenarios of the analysis provided by the submitter, as well as reanalyses by the EGP. pERC noted that the main factors that influence the change in effect for the best estimate are the HR for OS and a shortened time horizon (from 10 years to five years). As OS results for ibrutinib directly compared with temsirolimus and indirectly compared with investigator's choice of therapy were not statistically significant, pERC agreed with the EGP's modifications to the HR for OS to explore uncertainty in these data. pERC accepted the EGP's use of the upper and lower bounds of the estimate of effect to account for the uncertainty in the magnitude of clinical benefit. pERC acknowledged that this had a substantial impact on the cost-effectiveness estimate and agreed that it reflected the uncertainty in the magnitude of benefit. pERC also noted that shortening of the time horizon to five years was appropriate, as it further accounts for the immaturity of the clinical trial data as well as the lack of inclusion of subsequent therapies in the cost-effectiveness estimates.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: Large budget impact

pERC discussed the feasibility of implementing a funding recommendation for ibrutinib. pERC noted that while the incidence of MCL is low, there is a potentially large prevalent population of patients with relapsed or refractory disease. pERC acknowledged that there is no standard of care for relapsed or refractory MCL and ibrutinib would provide a new treatment option for these patients. pERC also discussed the very high cost of ibrutinib and the fact that treatment is continued until disease progression. pERC noted that, although the median treatment duration of ibrutinib was 14.4 months in the MCL-3001 study, the budget impact estimate for ibrutinib is uncertain and may increase due to the large population eligible for treatment and the indefinite length of treatment duration as 47% of patients in the ibrutinib arm were still on treatment at the time of the data cut-off date. The Committee also noted that the budget impact of ibrutinib was likely substantially underestimated in the budget impact analysis, as the market share of ibrutinib will be high given the large prevalent population potentially eligible for reimbursement. As there is no standard of care in relapsed or refractory MCL, ibrutinib will likely be used in earlier lines of therapy and would not replace current treatment options. Subsequent therapies following progression on ibrutinib may include rituximab-based regimens, pERC noted that this may be a barrier to implementation for jurisdictions. Consequently, pERC agreed that the budget impact of ibrutinib could be substantial and that the provinces will need to consider pricing arrangements and/or cost structures to improve the affordability of ibrutinib.

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DRUG AND CONDITION INFORMATION

Drug Information	• Selective Bruton's tyrosine kinase (BTK) inhibitor • 140 mg capsule size • Recommended dosage of 560 mg administered orally, once daily
Cancer Treated	• Relapsed or refractory MCL
Burden of Illness	• MCL is the fourth most common non-Hodgkin lymphoma in North America • It is estimated that in Canada, approximately 400 to 500 patients per year would be candidates for ibrutinib therapy for relapsed or refractory MCL.
Current Standard Treatment	• No clearly established standard of care in relapsed or refractory MCL setting
Limitations of Current Therapy	• MCL is at present incurable with current therapies

ABOUT THIS RECOMMENDATION

The pCODR Expert Review Committee (pERC)

Recommendations are made by the CADTH pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC) 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. Scott Berry, Oncologist
Dr. Kelvin Chan, Oncologist
Dr. Matthew Cheung, Oncologist
Dr. Craig Earle, Oncologist
Dr. Allan Grill, Family Physician
Dr. Paul Hoskins, Oncologist
Don Husereau, Health Economist
Dr. Anil Abraham Joy, Oncologist
Carole McMahon, Patient Member
Dr. Catherine Moltzan, Oncologist
Valerie McDonald, Patient Member Alternate
Jo Nanson, Patient Member
Karen MacCurdy-Thompson, Pharmacist
Danica Wasney, Pharmacist

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

- Paul Hoskins, who was not present for this meeting
- Valerie McDonald, who was the patient member alternate for this meeting.

Because the pERC Initial Recommendation met the criteria for early conversion to a pERC Final Recommendation, reconsideration by pERC was not required and deliberations and voting on the pERC Final Recommendation did not occur.

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Avoidance of conflicts of interest

All members of pERC 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 ibrutinib (Imbruvica) for mantle cell lymphoma, through their declarations, six members had a real, potential, or perceived conflict, and based on application of the *pCODR Conflict of Interest Guidelines*, none of these members was excluded from voting.

Information sources used

pERC 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 its 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 pERC for its deliberations was handled in accordance with the *pCODR Disclosure of Information Guidelines*.

Use of this Recommendation

This Recommendation from pERC is not intended as a substitute for professional advice, but rather to help Canadian health systems leaders and policy-makers 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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