pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pCODR EXPERT REVIEW COMMITTEE (pERC)
FINAL 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.

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: Idelalisib (Zydelig) **Submitted Funding Request:** For the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) in combination with rituximab	
Submitted By: Gilead Sciences Canada Inc.	**Manufactured By:** Gilead Sciences Canada Inc.
NOC Date: March 27, 2015	**Submission Date:** April 7, 2015
Initial Recommendation Issued: July 30, 2015	**Final Recommendation:** August 18, 2015

pERC RECOMMENDATION

The pCODR Expert Review Committee (pERC) recommends funding idelalisib (Zydelig), conditional on cost-effectiveness being improved to an acceptable level, when used in combination with rituximab for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL). Treatment should continue until unacceptable toxicity or disease progression.

pERC made this recommendation because compared to rituximab alone, the Committee considered there may be a net clinical benefit of idelalisib plus rituximab. The combination demonstrated a clinically meaningful improvement in progression-free and overall survival, improved quality of life compared to rituximab alone, and had manageable early phase toxicity. The Committee expressed some concern about the lack of longer term data to inform late developing toxicities.

pERC agreed that idelalisib plus rituximab aligns with patient values.

The Committee noted that idelalisib plus rituximab could not be considered cost-effective based on the submitted estimates and Economic Guidance Panel's estimates of the range of incremental cost-effectiveness ratios when compared with chlorambucil in this population.

POTENTIAL NEXT STEPS FOR STAKEHOLDERS

Pricing Arrangements to Improve Cost-effectiveness
Given that pERC was satisfied that there may be a net clinical benefit of idelalisib plus rituximab in patients with relapsed chronic lymphocytic leukemia (CLL), jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of idelalisib plus rituximab to an acceptable level.

Optimal Sequencing of Idelalisib and Other Therapies Unknown
pERC concluded that the optimal sequencing of idelalisib plus rituximab and other therapies, such as Bruton's tyrosine kinase inhibitors, in relapsed CLL is currently unknown. In the absence of direct evidence, pERC was unable to make an informed recommendation. However, pERC recognized that the provinces will need to address this issue upon implementation of funding idelalisib plus rituximab and noted that collaboration among provinces to develop a common approach would be of value.

Longer term data required
pERC suggested that longer term clinical data on idelalisib plus rituximab be collected to assess both long term efficacy and potential long term harms associated with idelalisib plus rituximab. Jurisdictions may wish to request the on-going collection of these data from the manufacturer, if they proceed with implementation, so that they can anticipate and manage, in particular, any long term harms that were not reported at the time of the publication of the study.

SUMMARY OF pERC DELIBERATIONS

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

CLINICAL BENEFIT	PATIENT-BASED VALUES
ECONOMIC EVALUATION	ADOPTION FEASIBILITY

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia with a long natural history. While there are an increasing number of options for frontline treatment of CLL, there is no standard of care for patients who have relapsed disease. The choice of therapy in patients with CLL, who are often older and usually have other comorbidities, is a significant challenge. In particular, patients with multiple comorbidities who have relapsed or progressed on frontline therapy have few tolerable treatment options. Additionally, the presence of mutations in TP53 tumour suppressor gene or deletions of 17p are associated with resistance to standard chemoimmunotherapy, and agents with activity in this biologically aggressive subgroup are needed. When the pivotal trial for idelalisib was designed, there was a clear need for more effective therapies to treat these patients. However, since that time, ibrutinib has been approved by Health Canada and recommended by pERC for patients with relapsed CLL after treatment with chemotherapy. There will be a subset of patients who will not be suitable for treatment with ibrutinib, such as those who are on anti-coagulants or those who have recently experienced a stroke or a serious bleeding episode. These patients may be candidates for treatment with idelalisib plus rituximab.

pERC deliberated upon one randomized controlled trial by Furman et al that compared idelalisib plus rituximab to rituximab plus placebo in patients who had experienced progression of their CLL disease and who were not sufficiently fit to receive cytotoxic therapy because of chemotherapy-induced bone marrow damage or comorbidities. pERC considered the results of the well-conducted study by Furman et al which reported a statistically significant and clinically meaningful improvement in progression-free survival (PFS) in favour of idelalisib plus rituximab. One year overall survival (OS) rates were also improved in favour of the patients in the idelalisib plus rituximab arm. pERC had several concerns with the application of the Furman et al study to the Canadian context, including 1) that rituximab plus placebo was not a relevant comparator arm in Canada; 2) that the population included in the study was likely more fit than patients who would be considered candidates for idelalisib plus rituximab in a real-world setting given their baseline CIRS score and mixture of previous therapies; and 3) that the short duration of follow-up in the study did not allow for sufficient time to assess long term efficacy or potential long term toxicity, where treatment may be several years in duration. Although there is no clearly defined standard of care for patients with relapsed CLL, pERC agreed with the Clinical Guidance Panel (CGP) that rituximab alone would not be considered a common treatment in Canada.

pERC noted that the toxicities of grade 3 or higher were generally uncommon, and manageable. pERC also considered the quality of life data reported in the Furman et al study that found that the Functional Assessment of Cancer Therapy Leukemia (FACT- Leu) scale exceeded the minimally clinically important difference in the idelalisib plus rituximab arm. However, as noted previously, pERC was concerned about the potential for long term harms associated with idelalisib plus rituximab. Given that neither the median PFS nor OS were reached in the Furman et al study for patients in the idelalisib plus rituximab arm, these patients have potential for longer term survival and long term harms associated with idelalisib plus rituximab, such as colitis, pneumonitis and hepatotoxicity. Therefore, pERC concluded that there may be a net clinical benefit of idelalisib plus rituximab because even though there was evidence of a clinically meaningful improvement in PFS and OS, manageable early phase toxicity, and improvement in quality of life, there is uncertainty regarding the appropriateness of rituximab as a comparator, the lack of data to inform long term efficacy and toxicity, and the generalizability of the study population to the real-world Canadian setting.

pERC considered input from three patient advocacy groups who had experience with relapsed CLL and idelalisib. pERC noted that commonly reported symptoms of CLL include fatigue, increased white blood count, and enlarged lymph nodes. Patients also expressed difficulties with concentration, insomnia, and mood swings. They also acknowledged that respondents indicated they wanted longer remissions with less

toxicity and more treatment choices. pERC discussed that most respondents reported that their CLL symptoms improved with the use of idelalisib; however, a few respondents noted that idelalisib failed to manage their symptoms. The Committee concluded idelalisib plus rituximab aligns with patient values because, overall, it provides an improvement in PFS and OS, and it offers patients another choice in treatment with a different toxicity profile than current treatments such as ibrutinib.

pERC deliberated upon the cost effectiveness of idelalisib plus rituximab compared with chlorambucil. pERC queried why chlorambucil was used by the submitter as the comparator treatment in the economic model when it was not used as the comparator in the Furman et al study. pERC noted that chlorambucil may be a relevant comparator in some, but not all provinces in Canada. pERC considered that the submitted model assumed that the efficacy of chlorambucil was equivalent to the efficacy of rituximab plus placebo in the Furman et al study. pERC noted that using chlorambucil as the comparator was the most conservative estimate of cost that could have been used as opposed to rituximab plus chlorambucil or ibrutinib (or a relevant case-mix of therapies), which are considerably more expensive than chlorambucil. The submitter likely provided the highest incremental cost effectiveness ratio (ICER) for idelalisib plus rituximab compared to other potentially relevant therapies (e.g. rituximab plus chlorambucil or ibrutinib). Nonetheless, pERC noted that the range of estimates provided by the submitter and the Economic Guidance Panel's reanalysis were outside of what would be considered cost-effective, and therefore, concluded that at the submitted price, idelalisib plus rituximab could not be considered cost-effective using either the submitted estimates or EGP's re-analysis of the estimates.

pERC discussed the feasibility of implementing a funding recommendation for idelalisib plus rituximab. pERC reiterated that there currently is no standard of care for patients with relapsed CLL in Canada. Therefore, jurisdictions will have to consider the relative cost-effectiveness of idelalisib plus rituximab compared to the standard of care in their individual jurisdictions. In addition, the Committee noted that since idelalisib is an oral drug, it is more convenient for patients to access and take. However, since it is used in combination with rituximab, which is administered intravenously, patients will still need to travel to chemotherapy centres for treatment. In some jurisdictions, oral drugs may also pose a limitation to access where an application to the respective pharmacare program is required to obtain funding. This is usually associated with co-payments and deductibles which were not incorporated in the submitted analysis. In addition, pERC noted that a potential problem with drug wastage may arise if dose reductions need to be made before the previously dispensed tablet strength is exhausted.

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 (Chronic Lymphocytic Leukemia Patient Advocacy Group (CLL PAG), Leukemia and Lymphoma Society of Canada (LLSC) and Lymphoma Foundation Canada (LC))
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- input from pCODR's Provincial Advisory Group.
- Two patient advocacy group (Chronic Lymphocytic Leukemia Patient Advocacy Group (CLL PAG), Leukemia and Lymphoma Society of Canada (LLSC) and Lymphoma Foundation Canada (LC)
- the Submitter (Gilead Sciences Canada Inc.)

The pERC initial recommendation was to fund idelalisib (Zydelig), conditional on cost-effectiveness being improved to an acceptable level, when used in combination with rituximab for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL). Treatment should continue until unacceptable toxicity or disease progression.

Feedback on the pERC Initial Recommendation indicated that the manufacturer, patient advocacy groups and pCODR's Provincial Advisory Group agreed with the 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 the review is to evaluate the safety and effectiveness of idelalisib (Zydelig) in combination with rituximab, compared to an appropriate comparator, for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL).

Studies included: One well-conducted RCT, but not clinically relevant comparator for Canada

The pCODR systematic review included one double-blind, phase III study (Furman et al) which randomized patients with relapsed CLL to receive idelalisib plus rituximab (n=110) or rituximab plus placebo (n=110). pERC considered that rituximab monotherapy is not a commonly used treatment in Canada for relapsed CLL. Patients in this stage of disease are likely to receive a variety of therapies including retreatment with initial therapies, novel therapies through clinical trials, conventional chemotherapies (if there are no contraindications), alemtuzumab, or ibrutinib.

Idelalisib was administered as a 150 mg tablet taken orally twice daily while rituximab was administered intravenously with the first cycle at 375 mg/m^2 and subsequent cycles (2-8) at 500 mg/m^2. pERC noted that the Provincial Advisory Group (PAG) indicated the dose of rituximab was higher in the study than would typically be prescribed in a Canadian setting.

Patients were stratified by 17p deletion or p53 mutation in CLL cells (either or neither), immunoglobulin heavy chain variable region (IgHV) mutation (unmutated or IgHV3-21) and prior therapy with anti-CD20 therapeutic antibody (yes or no). pERC commented that patients with these biomarkers have a poorer prognosis than those without.

Patient populations: Concern regarding generalizability of the study population

Patients in the Furman et al study had relapsed CLL and were not sufficiently fit to receive cytotoxic therapy due to chemotherapy-induced bone marrow damage or comorbidities. They had also experienced CLL progression less than 24 months since completion of their last therapy.

Baseline patient characteristics were balanced between arms. Patients in both the idelalisib plus rituximab and rituximab plus placebo arms had a median age of 71 years, a median Cumulative Illness Rating Scale (CIRS) score of 8 and a median number of previous CLL drugs of 3. pERC noted that the patients enrolled in the Furman et al study may not be reflective of the general relapsed CLL population as not all patients had been treated with fludarabine, rituximab, or chlorambucil, although the median number of lines of therapies was three. Furthermore, patients had moderate renal dysfunction and the median CIRS score was 8 on a range from 0 to 56, with higher scores indicating a greater number or severity of coexisting illnesses.

Key efficacy results: Clinically meaningful improvements in PFS and OS

pERC was impressed by the progression-free survival (PFS) and overall survival (OS) reported in the Furman et al study. The primary outcome in the study was progression-free survival (PFS). At 24 weeks, PFS in the idelalisib plus rituximab arm was 93% compared with 46% in the rituximab plus placebo arm. The median PFS was not met in the idelalisib group but was 5.5 months in the placebo group (HR 0.18; CI: 0.10-0.32; p<0.0001). Pre-specified sub-group analysis showed that PFS favoured the idelalisib arm for all subgroups, including those stratified by the 17p deletion or TP53 mutation and IgHV mutational status.

Median OS was not reached in either group by the time of data cut-off but interim analysis at 12 months showed the rate of OS to be 92% in the idelalisib group compared to 80% in the placebo group. pERC considered the short duration of follow-up and the immature study results. The Committee noted that longer follow-up data would provide more certainty in the efficacy results.

Quality of life: Clinically meaningful improvement measured

Quality of life was assessed using the 44-item Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) scale. A higher score indicates a higher quality of life. The FACT-Leu Total score was significantly higher in the idelalisib plus rituximab arm than the rituximab plus placebo arm. Moreover, a mixed-effects model evaluating change from baseline and between arms showed that leukemia-related symptoms significantly improved in the idelalisib plus rituximab arm compared to the rituximab plus placebo arm in week 8 and became clinically significant by week 12. pERC noted the meaningful improvement in quality of life in the patients receiving idelalisib plus rituximab compared to rituximab plus placebo.

Safety: Toxicity manageable in the short term, long term toxicity unknown

pERC discussed the toxicity profile of idelalisib and noted that toxicities were slightly more common in the idelalisib plus rituximab arm compared to the rituximab plus placebo arm. Overall, grade ≥3 toxicities or treatment discontinuation due to adverse events were uncommon. The most common side effects reported by patients receiving idelalisib were fever, fatigue, nausea, chills and diarrhea. These appeared to be manageable with dose reduction after treatment interruption.

pERC reported that idelalisib has an acceptable toxicity profile. However, the Committee also noted that there are no long term follow-up data on patients in the Furman et al study, and that idelalisib does have the potential to cause significant long term and late occurring toxicities such as hepatotoxicity, pneumonitis and colitis.

Limitations: Not clinically relevant comparator, no long term data, concerns of generalizability

pERC commented that the applicability of the study in the Canadian context is limited due to the comparator, rituximab monotherapy, not being commonly used. Also, there is no long term data from the Furman et al study to inform the long term efficacy or long term harms potentially associated with idelalisib. Finally, the Committee was concerned that the study population may be more fit than the general population who would be considered candidates for idelalisib, which creates uncertainty regarding the effectiveness and safety of idelalisib in the general population.

Need: Provides another possible treatment option

There is no standard of care for patients who have refractory or relapsed CLL. The choice of therapy in patients with CLL, who are most frequently older and who usually have other comorbidities, is a significant challenge. In particular, patients with multiple comorbidities who have relapsed or progressed on first line therapy have few non-toxic effective treatment options. When the Furman et al study for idelalisib was designed, there was a need for more effective therapies to treat these patients. However, since that time, ibrutinib has been approved by Health Canada and recommended by pERC for patients with relapsed CLL after treatment with chemotherapy. There will be a subset of patients who will not be suitable for treatment with ibrutinib, including patients prescribed anti-coagulants or those experiencing a recent stroke or a serious bleeding episode, who may be candidates for treatment with idelalisib plus rituximab.

PATIENT-BASED VALUES

Values of patients with CLL: Quality of life and symptom management

pERC deliberated upon input from three patient advocacy groups with experience with CLL. The patient advocacy group input indicated fatigue, increased white blood count and enlarged lymph nodes as the most commonly reported symptoms experienced by patients. All of these interfere with a patient's ability to work, travel and conduct other daily activities. It was also noted that while "watch and wait" is a common strategy at the time of CLL diagnosis, it often confuses and worries patients. Moreover, the diagnosis itself comes with a heavy emotional burden resulting in stress, anxiety and depression as reported by patients.

Patient values on treatment: Mostly positive experience with idelalisib

pERC noted that a total of 35 patients reported direct experience with idelalisib, the majority (94%) of whom noted an improvement in their CLL since taking idelalisib. Patients reported that the drug brought their disease under control, often quite quickly, and made them feel much as they had before their diagnosis of CLL. However, patients noted that it does come with side effects such as elevated liver function tests, diarrhea, cough and mouth sores, amongst other side effects. pERC noted that a few respondents noted that idelalisib failed to manage their symptoms and made them feel less well. The Committee concluded idelalisib plus rituximab aligns with patient values because, overall, it provides an improvement in PFS and OS and offers another choice in treatment with a different side effect profile.

ECONOMIC EVALUATION

Economic model submitted: Cost-effectiveness and cost-utility

The pCODR Economic Guidance Panel (EGP) assessed a cost-effectiveness and cost-utility analysis of idelalisib plus rituximab compared to chlorambucil for patients with relapsed CLL. pERC commented that the submitted model assumed the same efficacy estimates for chlorambucil as the rituximab plus placebo arm from the Furman et al study. They noted that there is no direct evidence to indicate that chlorambucil is equivalent to rituximab.

Basis of the economic model: Clinical and economic inputs

There is no uniform or clearly established standard of care for patients with relapsed CLL across Canada. The CGP deemed chlorambucil a reasonable comparator in the context of Ontario where it is the standard of care for many patients. However, this may not be as applicable to other provinces where another therapy (or case-mix of therapies) may be more common practice. There is no other alternate assumption that would be more appropriate in the context of Canada as a whole, although chlorambucil in combination with rituximab or ibrutinib may also be appropriate comparators.

The model included drug treatment acquisition costs, as well as costs associated with pre-medication, adverse event management, pre- and post-progression follow-up and palliative care.

The key clinical outcomes considered in the model provided by the submitter were overall survival, progression-free survival and health state utilities.

Drug costs: High drug cost

At the list price, idelalisib costs $85.35 per 150 mg tablet. At the recommended dose of 150 mg twice daily, the cost of idelalisib for a 28-day cycle is $4,779.60.

Rituximab costs $453.10 for a 100 mg vial and $2,265.50 for a 500 mg vial. At the recommended dose of 375 mg/m^2 on the first cycle and 500 mg/m^2 thereafter (cycles 2-8), the average cost of rituximab per 28-day cycle is $4974.66.

The average total cost of idelalisib plus rituximab per 28-day cycle is $9,754.26.

The average total cost of chlorambucil per 28-day cycle is $85.37.

Clinical effect estimates: Assumed chlorambucil had same efficacy as rituximab

The Committee discussed that the submitted model assumed the same efficacy estimates for chlorambucil as the rituximab plus placebo arm from the Furman et al study. They noted that there is no direct evidence to indicate that chlorambucil is clinically equivalent to rituximab. This assumption was made by the submitter, since chlorambucil would be the standard of care in some Canadian provinces. pERC noted that using chlorambucil as the comparison was the most conservative estimate of cost that could have been used as opposed to rituximab plus chlorambucil or ibrutinib, which are considerably more expensive than chlorambucil. It is unclear how chlorambucil would compare relative to rituximab from an efficacy or safety perspective.

Cost-effectiveness estimates: Estimates greatly impacted by shorter time horizon

pERC deliberated upon the cost-effectiveness of idelalisib plus rituximab compared with chlorambucil, and noted that the Economic Guidance Panel's re-analysis of the estimates were higher than the submitted estimates. Shortening the time horizon to a more clinically plausible period of 5 years had the greatest impact on the difference between the estimates. Other factors that contributed to the difference in the estimates, although to a lesser extent, were: 1) the EGP included wastage but the submitted model did not; wastage is likely to occur with the multiple tablet strengths being used in early dose adjustments; 2) EGP adjusted the utilities for chlorambucil because they were based on the effects of rituximab in the trial and likely would be lower with chlorambucil; and 3) mean body surface area was lower in the submitted model than in the EGP's re-analysis. pERC noted that the main cost driver was the cost of idelalisib.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: High cost

pERC discussed factors that could impact the feasibility of implementing a funding recommendation for idelalisib plus rituximab. pERC noted PAG's concern over the large prevalent number of previously treated CLL patients who could be eligible for idelalisib treatment. Moreover, ibrutinib will become available for this same patient population. As such, pERC acknowledged the uncertainty in the budget impact estimate of idelalisib plus rituximab due to the unknown number of patients who might be candidates for either ibrutinib or idelalisib and the undefined length of treatment duration with idelalisib. . Also, pERC was unable to comment on the comparative efficacy of idelalisib plus rituximab compared to other relevant comparators as such data were not available. It was also noted that rituximab monotherapy is not funded for the re-treatment of CLL, and that the 28-day cycle cost of rituximab is substantially higher than the 28-day cycle cost of chlorambucil.

pERC noted that idelalisib is the first in a new class of drug that could fill the gap in therapy for CLL in the relapse/refractory setting, particularly those with poor prognostic features due to p17 deletion, TP 53 mutations or unmutated IGHV. However, additional health resources will be required to monitor, manage and treat the toxicities associated with idelalisib as health care professionals gain familiarity with this novel treatment.

pERC noted that the oral administration of idelalisib, with one dose reduction, is an enabler to implementation. However, this may also pose a limitation to access in jurisdictions where an application

to the respective pharmacare program is first required to obtain an oral medication. This is usually associated with co-payments and deductibles which were not incorporated in the submitted economic analysis. In addition, pERC noted that a potential problem with drug wastage may arise if dose reductions need to be made before the previously dispensed tablet strength is exhausted.

DRUG AND CONDITION INFORMATION

Drug Information	• Oral, targeted inhibitor of phosphatidylinositol 3-kinase p110δ (PI3Kδ) isoform • Available as 100 mg and 150 mg tablets • The recommended dose is 150 mg administered orally twice daily in combination with rituximab administered intravenously (8 cycles with the first cycle at 375 mg/m^2 and subsequent cycles at 500 mg/m^2)
Cancer Treated	• Relapsed Chronic Lymphocytic Leukemia (CLL)
Burden of Illness	• CLL is one of the most common hematological malignancies with an incidence of 4.8 cases/100,000 persons. • In 2010, 2,195 Canadians were diagnosed with CLL and 600 were expected to die from this disease in 2011.
Current Standard Treatment	• There is no uniform standard of care across Canada for relapsed CLL
Limitations of Current Therapy	• Limited available treatment options in the relapsed setting, especially in the older and less fit population

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. Scott Berry, Oncologist
Bryson Brown, Patient Member
Dr. Matthew Cheung, Oncologist
Mario de Lemos, Pharmacist
Dr. Sunil Desai, Oncologist
Mike Doyle, Economist
Dr. Bill Evans, Oncologist
Dr. Allan Grill, Family Physician
Dr. Paul Hoskins, Oncologist
Danica Wasney, Pharmacist
Carole McMahon, Patient Member Alternate
Jo Nanson, Patient Member
Dr. Tallal Younis, Oncologist
Dr. Kelvin Chan, Oncologist

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

- Drs. Scott Berry, Sunil Desai, Kelvin Chan who were not present for the meeting
- Danica Wasney who was not present for the voting
- Dr. Matthew Cheung who was excluded from voting due to a conflict of interest
- Jo Nanson who was the designated non-voting Patient Alternative 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.

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 idelalisib (Zydelig) for chronic lymphocytic leukemia, through their declarations, five members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, and one of these members was 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*. There was no non-disclosable information in this recommendation document.

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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