Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

venetoclax (Venclexta) Reassessment

(AbbVie Corporation)

Indication: Venclexta (venetoclax), in combination with obinutuzumab, is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL).

November 15, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0362-000
Brand name (generic)	Venclexta (venetoclax)
Indication(s)	Chronic lymphocytic leukemia (CLL)
Organization	The Leukemia & Lymphoma Society of Canada
Contact information[a]	Name: Colleen McMillan

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
We agree that this treatment may offer an improvement in progression-free survival (PFS) compared to chemotherapy. In addition, this treatment offers an additional treatment option for patients with CLL.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
Our organization did not submit input into the initial review of this treatment. However, we support the input provided on behalf of patients by Lymphoma Canada and CLL Canada		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Colleen McMillan*
Position	*Advocacy Lead*
Date	*15-11-2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☒
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AbbVie	☐	☐	☐	☒
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	**PC0362-000**
Brand name (generic)	**Venclexta (venetoclax)**
Indication(s)	Venclexta (venetoclax), in combination with obinutuzumab, is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL).
Organization	Lymphoma Canada
Contact information[a]	Name: Gurjot Basra [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

Lymphoma Canada agrees with the recommendation that venetoclax, in combination with obinutuzumab, be reimbursed for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL). Ven + O is in alignment with CLL patients preferences of wanting to transition from an era of chemotherapy to an era of targeted therapy with proven efficacy in treating a range of patients, with fewer and more tolerable side effects.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

If not, what aspects are missing from the draft recommendation?

Yes, as it relates to the patient feedback we have provided, the committee has demonstrated that it has recognized the importance of the preferences of the surveyed patient population, namely that patients have emphasised the importance of having a choice in their treatment plan and having increased treatment options available to choose from.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

While the reimbursement conditions are clearly outlined, we believe that in regard to condition number 5, which focuses on pricing, the feasibility of adoption should not be tied solely to budgetary impacts. Instead, the emphasis should be on the manageable toxicity profile, the improvement in health-related quality of life (QoL), and the prolonged response duration, all of which should take precedence.

Additionally, the pricing is currently being compared only to FCR. By excluding BTK inhibitors from this analysis, the CDA overlooks the actual treatment landscape and fails to capture the true cost-effectiveness of Venetoclax + Obinutuzumab (Ven+O) within the context of modern therapeutic options. This oversight could further delay patient access to this important therapy.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Gurjot Basra*
Position	*Manager of Patient Programs, Research, and Advocacy*
Date	*Please add the date form was completed (15-11-2024)*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PG0362
Brand name (generic)	Venclexta (venetoclax)
Indication(s)	Venetoclax, in combination with obinutuzumab for the subgroup of previously untreated CLL patients considered potentially fludarabine-eligible, who were not included in the reimbursement request or recommendation criteria in the previous CADTH review (PC0212-000). Note that based on this request, the reimbursement criteria for venetoclax in combination with obinutuzumab would be expanded for the previously untreated CLL patients, irrespective of age or eligibility for fludarabine treatment (i.e., aligned with the Health Canada indication
Organization	OH (CCO) Hematology Cancers Drug Advisory Committee
Contact information[a]	Name: Dr. Tom Kouroukis

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. Clarify duration of therapy. From the protocol, 48 weeks total from start of Obin day 1.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. The economic comparison using FCR is considered obsolete. FCR is not commonly used anymore as first-line therapy. A better comparison would be BTK-containing first-line therapy or venetoclax-containing first-line therapy.		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
If yes, please detail the help and who provided it. Ontario Health (Cancer Care Ontario) provided secretariat support to the group.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Tom Kouroukis • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Dr. Christopher Cipkar

Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*07-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	Dr. Joanna Graczyk
Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*07-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3

Name	Dr. Lee Mozessohn
Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*07-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Abbvie	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	Dr. Selay Lam
Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*07-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Abbvie	☐	☒	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	Rami El-Sharkaway
Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*07-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Abbvie	☒	☐	☐	☐

Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	Dr. Guillaume Richard-Carpentier
Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*07-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 7	
Name	*Please state full name*
Position	Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0362
Name of the drug and Indication(s)	Venetoclax (Venclexta) in combination with obinutuzumab for the treatment of patients with previously untreated chronic lymphocytic leukemia.
Organization Providing Feedback	PAG

1. Recommendation revisions

Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.

Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions

Complete this section if major or minor revisions are requested

Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation

Complete this section if editorial revisions are requested for the following elements

a) Recommendation rationale

Please provide details regarding the information that requires clarification.

b) Reimbursement conditions and related reasons

Please provide details regarding the information that requires clarification.

c) Implementation guidance

Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

In table 2, under Considerations for initiation of therapy, PAG suggested clarifying the treatment duration: "In patients who had to stop or delay therapy for reasons other than disease progression, it may be clinically reasonable to re-start treatment, based on clinical judgement, provided that the entire/cumulative treatment duration is for a total of 48 weeks."

In table 2, under Generalizability, PAG suggested removing "fit" from the following statement: "The clinical experts advised that eligibility for venetoclax plus obinutuzumab should be extended to **fit** patients...", to align with the statement 2 rows below: "The clinical experts advised that all patients should be eligible for venetoclax, in combination with obinutuzumab, regardless of fitness...".

In table 2, under Funding algorithms, PAG requested mentioning patients with Richter's syndrome should be excluded (similarly to the 2020 recommendation).

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. An update to the rapid algorithm is needed. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0362-000
Brand name (generic)	VENCLEXTA® (venetoclax)
Indication(s)	VENCLEXTA (venetoclax), in combination with obinutuzumab, is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL).
Organization	AbbVie Corporation
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Yes, AbbVie agrees with the positive draft recommendation.

Rationale: In the draft recommendation, pERC recommended that venetoclax, in combination with obinutuzumab (VenO), be reimbursed with conditions for the treatment of patients with previously untreated CLL. The clinical conditions support patient access to VenO in alignment with the Health Canada indication (i.e., irrespective of age or eligibility for fludarabine treatment). pERC recognized that the CLL13 trial demonstrated that VenO results in an improvement in progression-free survival (PFS) compared to chemoimmunotherapy for patients with previously untreated CLL. In addition, pERC recognized that VenO was favoured over chemoimmunotherapy, based on undetectable minimal residual disease (MRD) at month 15.

Moreover, pERC concluded that VenO met some of the needs identified by patients because it prolongs disease remission and offers an additional treatment option for patients with CLL. The draft recommendation also highlighted clinician input which indicated that alternative treatment options, that are targeted, chemoimmunotherapy-free and/or Bruton's tyrosine kinase (BTK) inhibitor-free, and time-limited, are needed for fit patients with previously untreated CLL. Based on clinician input, the requested change in funding for VenO may reduce confusion and ensure fairness and equitable access across Canada for patients with CLL.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
Yes, the draft recommendation generally demonstrates that the committee has considered the input AbbVie has provided to CDA-AMC.		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Yes, the reasons for the recommendation are clearly stated.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
Yes, the implementation issues have been clearly articulated and adequately addressed in the recommendation.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

Yes, the reimbursement conditions are clearly stated in general and the rationale for the conditions are provided in the recommendation. However, AbbVie has feedback regarding the economic comparison with fludarabine in combination with cyclophosphamide and rituximab (FCR):

Page 3, Rationale for the Recommendation (paragraph 5): *"Using the sponsor submitted price for venetoclax and publicly listed prices for all other drug costs, the incremental cost-effectiveness ratio (ICER) for venetoclax plus obinutuzumab was $167,257 per quality-adjusted life-year (QALY) gained compared with FCR. At this ICER, venetoclax is not cost-effective compared with FCR at a willingness to pay (WTP) threshold of $50,000 per QALY gained for the treatment of patients with previously untreated CLL. A price reduction for venetoclax is required for venetoclax plus obinutuzumab to be considered cost-effective at a $50,000 per QALY gained threshold compared with FCR."*

Page 4, Reimbursement Conditions and Reasons, Pricing Section in Table 1: CDA-AMC has stated the following as a reimbursement condition: *"5. A reduction in price. The ICER for venetoclax plus obinutuzumab is $167,257 per QALY gained when compared with FCR. A price reduction of 75% for venetoclax would be required for venetoclax plus obinutuzumab to achieve an ICER of $50,000 per QALY gained compared to FCR."*

Page 19, Economic Evidence, CDA-AMC reanalysis results in Table 3: *"In the CDA-AMC base case, the cost-effectiveness frontier was comprised of BR, FCR, VEN+O, and VEN+I, representing the optimal treatment strategies. In sequential analysis, VEN+O was associated with an ICER of $167,257 per QALY gained compared to FCR (incr. costs = $82,007; incr. QALYs = 0.49). A price reduction of 75% for venetoclax would be required for VEN+O to be cost-effective compared with FCR at a WTP threshold of $50,000 per QALY gained."*

The focus on FCR as a comparator to determine cost-effectiveness does not reflect the current Canadian clinical practice for treating CLL patients considered fit and potentially fludarabine-eligible. The economic evidence sections within the recommendation should acknowledge the potential for cost savings relative to the currently used BTK inhibitor therapies. As such, please also report the

findings from the CDA re-analysis on the comparative cost-effectiveness of VEN+O versus BTK inhibitor therapies in the final recommendation.

As stated on **page 15, paragraph 8,** of the draft recommendation:

> *"According to the guidelines, FCR and BR are appropriate comparators in fit patients without TP53 aberrations (del[17p] and TP53 mutation) and with mutated IGHV in the frontline setting; albeit* ***FCR is infrequently used****, and BR is not used in practice as per clinician group and clinical expert input. As mentioned above, fit patients without TP53 aberrations and with unmutated IGHV do not typically receive chemoimmunotherapy in the frontline setting; instead, a BTK inhibitor would have been a more appropriate comparator in this subset of patients, as per the guideline."*

These statements align with clinician input and the latest Canadian evidence-based guideline for frontline treatment of CLL and should be taken into consideration when presenting the economic results. The economic comparison of VenO against FCR alone applies to a very limited patient subset but is not reasonable when considering all fit patients with CLL. To provide a balanced analysis, other comparators must be included to prevent any bias in interpreting the results.

Moreover, minimal and decreasing market shares are expected for FCR, as supported by CDA's re-analysis of the budget impact analysis with 7.6% in year 1, 3.4% in year 2 and 1.5% in year 3 in the new drug scenario. Compared with the presentation of the pharmacoeconomic analysis findings (Table 3, page 19), the budget impact analysis (page 19) more accurately represents the current treatment patterns, in which all relevant comparators are incorporated (i.e., FCR, acalabrutinib, ibrutinib, zanubrutinib, and venetoclax plus ibrutinib) and most patients are treated with BTK inhibitor therapies. The CDA-AMC base case suggests that the 3-year budget impact of reimbursing VenO for previously untreated adult patients with CLL considered fit and potentially fludarabine-eligible is expected to result in **cost savings** of $8,371,343.

AbbVie requests that economic evaluation results, ICERs and price reduction recommendations be presented for VenO against each comparator, as the current wording in the draft recommendation focuses only on FCR, a chemoimmunotherapy option not commonly used in current clinical practice. A more comprehensive presentation will ensure an unbiased draft recommendation while enhancing the relevance and completeness of the economic evaluation.

[a] CADTH may contact this person if comments require clarification.