1 Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Venetoclax as mono-therapy for treatment of chronic lymphocytic leukemia (CLL) who have received at least one prior therapy and who have failed a B-cell receptor inhibitor (BCRi)	
Name of registered patient group:	CLL Patient Advocacy Group and Lymphoma Canada	
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**pCODR may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by pCODR.*

1.1 Comments on the Initial Recommendation

a) Please indicate if the patient group agrees or disagrees with the initial recommendation:

____ agrees ____ agrees in part **X** disagree

Please explain why the patient group agrees, agrees in part or disagrees with the initial recommendation.

Venclexta should have been recommended for funding, subject to an acceptable price negotiation, given that there is a positive clinical guidance report, supportive registered clinician and patient advocacy input and that pERC itself concludes that results are promising and there is a need for effective treatment options for this subset of patients.

Waiting for more mature OS data, when a clear OS benefit has already been demonstrated, means an unacceptable delay for patients who have no reasonable treatment options remaining.

The provided data was sufficient to obtain approval for use and reimbursement in Finland, France, Norway, Denmark, Germany, Israel, Italy, Scotland, Belgium, Austria, Netherlands, Slovakia, Luxembourg and the UK. Why does pERC disagree not only with local experts (the clinical guidance panel and clinicians) but also their counterparts in other countries?

It is unacceptable to risk patients' lives by suggesting an RCT when the clinicians who treat this population believe it would be unethical, as up to 50% of patients would receive an ineffective treatment. For patients, enrolling in such an RCT would be tantamount to flipping a coin to determine whether they die or receive a treatment that can lead to meaningful survival and, for some, the possibility of proceeding to an allo-transplant (a potentially curative therapy). Why is pERC willing to expose patients to ineffective, toxic therapies?

There is a disconnect between pERC's assessment of the evidence and their recommendation. pERC

agrees that 1) there is a need for effective treatment options in this patient population; 2) there is a net clinical benefit of venetoclax compared with comparators (i.e. rituximab and rituximab plus HDMP); and 3) the comparators are ineffective treatment options (with all of which we agree). pERC then states venetoclax could not be considered cost effective compared with available therapies, yet pERC already stated there are no other effective therapy options for this population. Is pERC suggesting patients be treated with an ineffective treatment because it is cheaper?

b) Notwithstanding the feedback provided in part a) above, please indicate if the patient group would support this initial recommendation proceeding to final pERC recommendation ("early conversion"), which would occur two (2) Business Days after the end of the feedback deadline date.

____ Support conversion to final recommendation.

Recommendation does not require reconsideration by pERC.

X Do not support conversion to final recommendation.

Recommendation should be reconsidered by pERC.

c) Please provide feedback on the initial recommendation. Is the initial recommendation or are the components of the recommendation (e.g., clinical and economic evidence) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	**Section Title**	**Paragraph, Line Number**	**Comments and Suggested Changes to Improve Clarity**
2	Summary of pERC Deliberations	2, 6	pERC was not satisfied that there was a net overall benefit to patients, yet peer-reviewed, interim results of the M14-032 study (at a median follow-up of 14 months) estimated 12-month PFS for all patients was 80%, and neither median PFS or OS had yet been achieved. This is a significantly better outcome than the < 6 months survival for this heavily pre-treated patient population that pERC acknowledges in paragraph 1 of the same section.
2	Summary of pERC Deliberations	3, 6	Regarding QoL data, the report notes that there is no data comparing venetoclax with available options. Given that the report concludes that treatment options for this sub-group of patients are especially poor and most people die within months, in addition to the clearly established well tolerated nature of venetoclax, we question what value further QoL data would bring to the discussion.
2	Summary of pERC Deliberations	3, 10	After TLS was seen in early trials, the dosing schedule was changed to reduce the likelihood of TLS, and patients are pre-tested for tumour burden to determine who is at high risk of developing TLS, so they can be better managed. With the adoption of the ramp-up schedule, the risk of TLS is managed well before clinical symptoms develop. Why is TLS a concern for pERC when clinicians state they can effectively manage the risk of its development?

2	Summary of pERC Deliberations	4, 5	Why is pERC willing to risk patients' lives by suggesting an RCT is feasible when the clinicians who treat this population believe it would be unethical, as up to 50% of patients would receive an ineffective treatment. Why is pERC willing to expose patients to ineffective, toxic therapies?
3	Overall Clinical Benefit	1, 7	Regarding low rates of CR, CR is not often seen in this patient population with available therapies and the results achieved with venetoclax are in fact better than other therapies. Why the focus on CR rather than the prolonged PFS, OS, and favourable side effect profile compared to historical outcomes with chemotherapy in these poor risk patients?
9	Adoption Feasibility	1, 4	Management of TLS has been cited to cause an increase in costs of treatment yet, with the concomitant prophylaxis prior to and during the venetoclax ramp-up period, clinical TLS does not typically occur. Registered clinical input indicates the cost will not be greater than management of side effects of other treatments.

1.2 Comments Related to Patient Group Input

Page Number	Section Title	Paragraph, Line Number	Comments related to initial patient group input
3	Overall Clinical Benefit	3, 6	80% of patients on the venetoclax trials were alive at 12 months and median PFS and OS had not been reached. pERC acknowledges that this patient population usually has a PFS of less than 6 months with currently available therapies and the clinicians estimate this patient group has a 3-month life expectancy. We would argue a longer remission and being alive (i.e. not dead) completely aligns with patient values.
8	Patient-Based Values	3, 5	80% of patients on the venetoclax trials were alive at 12 months and median PFS and OS had not been reached. pERC acknowledges that this patient population usually has a median PFS of less than 6 months with currently available therapy and the clinicians estimate this patient group has a 3-month life expectancy. We would argue a longer remission and being alive completely aligns with patient values, especially when considered alongside the data in the patient input submission—provided by patients with venetoclax experience—who reported manageable side effects while taking the medication.