CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Patient Advocacy Group)

Midostaurin (Rydapt) for Systemic Mastocytosis

April 2, 2020

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Rydapt (midostaurin)
Eligible Stakeholder Role	Patient Groups
Organization Providing Feedback	Mastocytosis Society Canada (MSC) with the support of the Canadian Organization for Rare Disorders (CORD)

** CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the initial recommendation:

☐ Agrees ☐ Agrees in part ☒ Disagrees

b) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☐ Agrees ☐ Agrees in part ☒ Disagrees

The negative recommendation for Rydapt (midostaurin) is a devastating step backwards from the situation prior to the CADTH review. Th recommendation restricts access currently provided on an individual case-by-case basis and access accorded patients in Quebec.

While the summary of the response of patients with midostaurin experience accurately reflected variability across patients, it did not include the significant impact in symptom management, quality of life, and emotional well-being for those who did experience positive benefits. We reiterate:

"Benefits: 1. Severe reduction of bone and muscle pain. 2. Increased mobility - able to get out and socialize. 3. Dramatically reduced effect of Mast cell proliferation (results from bone marrow samples, reduced / eliminated skin blotches (very discolored spots on arms, legs and truck).4. Increased social activities.
Symptoms and Progression: 1. Reduced many critically blood parameters back to acceptable levels. 2. It has reduced SM effects significantly.
Rydapt Effects: 1. Allows patient to sleep better without pain (pain reduced by 70%) 2. More emotional 3. Overall major increase in quality of life."
"Makes life normal again."
"This drug allows individual to increase their quality of life, and not suffering with pain and throughout their extent of the disease. Better for family emotions and quality of life."
"I am glad to see all the red freckles disappear from my body, the hives on my face and torso almost non-appearing, and I am less itchy than before using Rydapt. It has helped with my self-esteem. I hope it will eventually cure my SM because frankly the dose is way too strong. My lifestyle was completely changed because of the tight schedule of pill taking and meal times to prevent nausea and vomiting."
"Benefits: hives and spots reduced = better body comfort. Quality of life is somewhat disrupted because of pill schedule. I now have to take anti- nausea meds 1 hour before eating and taking Rydapt. I lowered the dose to 3 capsules morning and evening instead of 4. I was just constantly vomiting. Now I only take anti-nausea meds 3 times per day and can function."

Despite the challenges of meeting the technical standards of a cost-effectiveness evaluation given the results from the Phase II clinical trials, we were nevertheless anticipating that CADTH would be able to appropriately balance the lack of long-term clinical outcome data against the serious nature of

aggressive systemic mastocytosis, the lack of effective alternative therapies, and the demonstrated benefit of Rydapt on symptom management and quality of life.

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

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
4	Summary	5-6	Expand to reflect the very positive benefits in symptom management and QoL for those who did benefit
4	Summary	7	Expand to reflect some patients experienced lessened side effects over time and/or able to mitigate SE with pre-treatment

3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the stakeholder would support this initial recommendation proceeding to final recommendation ("early conversion"), which would occur two business days after the end of the feedback deadline date.

☐ Support conversion to final recommendation.

Recommendation does not require reconsideration by pERC.

☒ Do not support conversion to final recommendation.

Recommendation should be reconsidered by pERC.

We acknowledge that the clinical trial data as well as the feedback from our patients who had experience with midostaurin reflected some level of uncertainty as to response rates and long-term outcomes in the broader population. However, we challenge the conclusion that there is not enough evidence of benefit relative to risks/adverse effects to make midostaurin available based on physician recommendation and monitoring. Midostaurin for aggressive SM is the exact situation for a "managed access" plan, used to determine appropriate use in many rare disease treatment scenarios.
We believe that there is sufficient "real world" evidence of the effectiveness of Rydapt with ASM patients for pERC to recommend a managed access scheme in a real-world setting based on physician recommendation, pre-treatment to manage side effects where warranted, and a monitoring program to track patient outcomes on an individualized basis, even the fact that symptoms are patient-specific. Set up a baseline of symptoms and quality of life (indiviidualizied), track patient responses and changes in identified symptoms, track side effects and response to pre-treatment protocols as well as direct interventions, and track quality of life (pre-defined and spontaneously experienced) outcomes using both a standardized scale as well as individualized qualitative indicators (patient-reported outcomes). These can be reviewed at regular (pre-defined) intervals and the rationale for continuance or discontinuance considered and implemented, if appropriate.

1 Instructions for Providing Feedback

a) The following stakeholders are eligible to submit feedback on the initial recommendation:
- The sponsor and/or the manufacturer of the drug under review;
- Patient groups who have provided input on the drug submission;
- Registered clinician(s) who have provided input on the drug submission; and
- CADTH's Provincial Advisory Group (PAG)

b) The following stakeholders are eligible to submit Feedback on the provisional algorithm:
    - The sponsor and/or the manufacturer of the drug under review;
    - Patient groups who have provided input on the drug submission;
    - Registered clinician(s) who have provided input on the drug submission; and
    - The Board of Directors of the Canadian Association of Provincial Cancer Agencies

- Feedback or comments must be based on the evidence that was considered by pERC in making the initial recommendation. No new evidence will be considered at this part of the review process.
- The template for providing stakeholder is located in section 3 of this document.
- The template must be completed in English. The stakeholder should complete those sections of the template where they have substantive comments and should not feel obligated to complete every section, if that section does not apply.
- Feedback on the initial recommendation should not exceed three pages in length, using a minimum 11-point font on 8 ½″ by 11″ paper. If comments submitted exceed three pages, only the first three pages of feedback will be provided to the pERC for their consideration.
- Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph). Opinions from experts and testimonials should not be provided. Comments should be restricted to the content of the initial recommendation, and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.
- References may be provided separately; however, these cannot be related to new evidence.
- *CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback must be disclosable and will be posted on the CADTH website*.
- The template must be filed with CADTH as a Microsoft Word document by the posted deadline.
- If you have any questions about the feedback process, please e-mail pcodrsubmissions@cadth.ca