CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

DEFERIPRONE (FERRIPROX)

(Chiesi Canada Corp.)

Indication: For the treatment of patients with transfusional iron overload due to sickle cell disease or other anemias.

January 06, 2023

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0741
Name of the drug and Indication(s)	Deferiprone (Ferriprox) for transfusional iron overload due to sickle cell disease (SCD) or other anemias
Organization Providing Feedback	FWG

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	☐
	No requested revisions	X☐

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.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0741-000
Brand name (generic)	FERRIPROX (deferiprone)
Indication(s)	For the treatment of patients with transfusional iron overload due to sickle cell disease (SCD) or other anemias.
Organization	Chiesi Canada Corp.
Contact information[a]	[redacted]

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

Chiesi Canada Corp. (Chiesi) agrees with CADTH's draft recommendation on FERRIPROX for the treatment of patients with transfusional iron overload due to sickle cell disease (SCD) or other anemias.

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	☐

Chiesi generally agrees that CADTH has considered the input provided but would like to reiterate the following explanations in response to the text identified below from CADTH's draft recommendation.

CADTH Recommendation	Chiesi Response
• The sponsor assumed equivalent clinical efficacy of deferiprone compared to DFO or DFX – i.e., all treatments are equally effective at chelating iron in patients with SCD and other anemias with transfusional iron overload. This assumption of equivalence is associated with uncertainty, given the limitations with the indirect comparison, but plausible according to clinical expert feedback obtained by CADTH.	The results of the NMA suggested that there is no statistically significant difference between DFP and DFO, or DFP and DFX in the reduction of LIC and SF. However, considering the study limitations, a level of uncertainty remains. Some of the main limitation in the analysis are: • The small sample size of the included studies • The heterogeneity between the study populations • The inconsistencies in the reported endpoints • The existence of non-mutually reported effect modifiers.
• The sponsor assumed patients receiving deferiprone experienced a slower decline in renal function compared to DFO or DFX. CADTH reviewed the real-world evidence and noted that evidence provided by the	The assumption was based on the analysis performed on using the real-world observational study of electronic medical records representing 46 US healthcare organisations, obtained from the TriNetX database between 1999 and 2021.

sponsor was insufficient to draw to conclusions on this claim. Clinical expert feedback noted that the this may be plausible, but there is no robust evidence supporting this assumption, and as such, assumption was highly uncertain.	The data showed that patients on deferiprone have a lesser detrimental impact on kidney function as measured by changes in eGFR and serum creatinine levels over time. However, we acknowledge that the due to the small sample size (n=65), the changes in renal function with deferiprone are not sufficiently large enough to reach statistical significance when compared against DFX and DFO.
• The sponsor's 3-health state Markov model is insufficient to capture the care pathway and may incorrectly estimate the total costs and QALYs of patients with SCD or other anemias. The sponsor's model also did not allow patients who failed the first ICT to receive subsequent ICTs; this assumption did not align with clinical practice based on feedback from the clinical expert consulted by CADTH, and overestimated any benefits associated with decline in renal function attributed to deferiprone.	Although we acknowledge that the three-state Markov model may overestimate the long-term health benefits and decline in patients' renal function, however this model was deemed to be most appropriate given the availability of trial and publicly accessible data for patients receiving subsequent ICTs. As such, splitting the health state by line of therapies will introduce considerable uncertainties to the cost-effectiveness model given the paucity of evidence. Based on the main assumption of the model of similar efficacy across treatment arms, expanding the model structure to include subsequent treatments is unlikely to change the overall model results.
• The sponsor's economic model did not consider all relevant comparators for patients with SCD or other anemias receiving chronic transfusion. Patients may receive multiple ICTs, or exchange transfusion which negates the need for ICT. The model was not flexible assess the cost-effectiveness of deferiprone in these situations.	Although combination therapies might be used in clinical practice, however, it is important to note that the company was not able to identify clinical data in the systemic literature searches for patients receiving combination ICTs. Therefore, the inclusion of such comparators in the cost-effectiveness model would require adopting assumptions around the clinical efficacy, which would introduce considerable uncertainties to the cost-effectiveness analysis results.
• The sponsor's assumption regarding ICT discontinuation due to causes other than renal impairment was not supported by any robust evidence. The clinical expert consulted by CADTH advised that the decision to stop ICT is dependent on iron burden, which can vary overtime.	For the first 12 months, treatment discontinuation for other than renal impairment was sourced from the clinical study report (CSR) of the LA38-0411 trial for DFP and DFO. As DFX was not included in the trial, rates of discontinuation for DFX were sourced from the RCT published by Vichinsky et al., 2007.[1] Given the short follow-up trial durations, and due to the paucity of data on long term treatment discontinuation, a decrease of 0.5% per cycle was assumed beyond month 12. Although, this assumption oversimplifies the treatment discontinuation in clinical practice, however, model results were not overly sensitive to

assumptions around long term treatment discontinuations.

Scenario	Description	$/QALY ICERs	
		DFP vs. DFO	DFP vs. DFX
Base case		**112,132**	**153,481**
Treatment discontinuations post 12 months	Assumed zero	188,936	255,356
	Assumed 0.1% per cycle	165,570	229,050
	Max threshold 25%	173,145	237,559
	Max threshold 50%	136,064	177,337

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

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

References

1. Vichinsky E, Onyekwere O, Porter J, et al. A randomised comparison of deferasirox versus deferoxamine for the treatment of transfusional iron overload in sickle cell disease. *Br J Haematol*. 2007;136(3):501-508. doi:10.1111/j.1365-2141.2006.06455.x