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CADTH DRUG REIMBURSEMENT REVIEW

Pharmacoeconomic Report

GLASDEGIB (DAURISMO)

(Pfizer Canada ULC)

Indication: in combination with low-dose cytarabine, for the treatment of newly diagnosed and previously untreated acute myeloid leukemia (AML) in adult patients who are age ≥75 years or who are not eligible to receive intensive induction chemotherapy.

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

AE	adverse event
AML	acute myeloid leukemia
AUC	area under the curve
AZA	azacitidine
BIA	budget impact analysis
BMB	bone marrow blasts
BSC	best supportive care
CGP	clinical guidance panel
ECOG	Eastern Cooperative Oncology Group
HR	hazard ratio
ICER	incremental cost-effectiveness ratio
ITC	indirect treatment comparison
LDAC	low-dose cytarabine
OCCI	Ontario Case Costing Initiative
OR	odds ratio
OS	overall survival
PFS-like	progression-free survival like
PPS	post-progression survival
QALY	quality-adjusted life year
QoL	quality of life
TTD	time-to-treatment discontinuation
WTP	willingness-to-pay

Executive Summary

The executive summary is comprised of two tables (Table 1: Background and Table 2: Economic) and a conclusion.

Table 1: Submitted for Review

Item	Description
Drug Product	Glasdegib (Daurismo), 25 mg and 100 mg tablet
Submitted Price	Glasdegib, $286.41 per 25 mg tablet; $572.82 per 100 mg tablet
Indication	In combination with low-dose cytarabine, for the treatment of newly diagnosed and previously untreated acute myeloid leukemia (AML) in adult patients who are aged ≥75 years or who are not eligible to receive intensive induction chemotherapy.
Health Canada Approval Status	NOC
Health Canada review pathway	Standard review
NOC Date	April 28, 2020
Reimbursement Request	As per indication.
Sponsor	Pfizer Canada Inc.
Submission History	Previously Reviewed: No

AML = acute myeloid leukemia; NOC = notice of compliance.

Table 2: Summary of Economic Evaluation

Component	Description
Type of Economic Evaluation	Cost-utility analysis Partitioned survival model
Target Population	Adult patients with newly diagnosed and previously untreated acute myeloid leukemia who are ineligible for intensive induction chemotherapy
Treatment	Glasdegib in combination with low-dose cytarabine (glasdegib + LDAC)
Comparators	Main population: Low-dose cytarabine (LDAC) alone 20 to 30 BMB" and >30% BMB subgroups: LDAC alone and azacitidine (AZA) alone
Perspective	Canadian publicly-funded health care payer
Outcomes	QALYs, LYs
Time Horizon	5 years
Key Data Source	BRIGHT AML 1003 trial and sponsor-submitted simulated and indirect treatment comparisons (STC/ITC) reporting overall survival (OS) and progression-free survival like (PFS-like)
Submitted Results for Base Case	Main Population • ICER = $177,065 per QALY (0.41 inc QALYs; $72,695 inc. costs) vs. LDAC Population 1 - 20% to 30% BMB • ICER for glasdegib + LDAC = $249,865 per QALY (0.60 inc. QALYs; $149, 919 inc. costs) vs. LDAC Population 2 - >30% BMB • ICER for glasdegib + LDAC = $155,645 per QALY (0.32 inc. QALYs; $50,408 inc. costs) vs. LDAC
Key Limitations	• Given the limitations associated with the sponsor's ITC, CADTH was unable to determine the comparative efficacy or cost-effectiveness of glasdegib + LDAC compared with AZA. • There was uncertainty associated with the use of a PFS-like health state given that this endpoint was not included as part of the BRIGHT AML 1003 trial and it is unknown to what extent the inclusion of partial responders in the non-remission health state biases cost-effectiveness results. • The sponsor applied a general chemotherapy cost code for the administration of AZA; however, it was unclear which modes of administration for treatment were included and if this accurately reflects the administration costs for AZA. Treatment administration costs were likely overestimated and biased results in favour of glasdegib + LDAC when compared with AZA. • Given the lack of quality of life data captured in the BRIGHT AML 1003 trial, the sponsor applied health state utility estimates from the published literature. CADTH considered these estimates to be associated with uncertainty given that the patient population (i.e., myelodysplastic syndrome) was not reflective of the patient population in the BRIGHT AML 1003 trial (i.e., acute myeloid leukemia). Further, the sponsor selected utilities were based on the time spent in transfusion dependence as opposed to remission status, the latter of which was only explored in the sponsor economic model using data from the BRIGHT AML 1003 trial. Given the uncertainty associated with health state utilities, conservative estimates were included in the CADTH base case. • The sponsor adjusted glasdegib + LDAC drug costs according to dose intensity (i.e., dose adjustments or drug interruption) which underestimated treatment costs. Further, the sponsor likely overestimated drug dose intensity for AZA, biasing results in favour of glasdegib + LDAC. • Due to the non-continuous nature of Kaplan-Meier curves, calculating point survival estimates was associated with challenges, specifically long plateaus or sudden drops in survival which potentially bias results in favour of glasdegib + LDAC. • The CGP highlighted that subsequent treatments were not reflective of clinical practice as a subset of patients would receive gilteritinib and the proportion of patients receiving AZA was likely overestimated.

Component	Description
CADTH Reanalysis Results	• CADTH reanalyses included: utilizing a parametric survival extrapolation for OS and PFS-like; utilizing a more conservative health state utility value for remission; revising subsequent treatment distributions; readjusting treatment administration costs for AZA to better reflect clinical practice; and, revising drug dose intensities for glasdegib + LDAC and AZA. The latter two limitations primarily affecting subsequent treatment in the CADTH base case and AZA as a comparator in exploratory analyses. <u>Main Population</u> • ICER for glasdegib + LDAC = $229,622 per QALY (0.36 inc. QALYs; $83,126 inc. costs) vs. LDAC • At a WTP threshold of $50,000 per QALY, a price reduction of 95% would be required

AZA = azacitidine; BMB = bone marrow blasts; ICER = incremental cost-effectiveness ratio; inc. = incremental; ITC = indirect treatment comparison; LDAC = low dose cytarabine; LY = life year; OS = overall survival; QALY= quality-adjusted life-year; PFS-like = progression-free survival like; STC = single treatment comparison; vs. = versus; WTP = willingness-to-pay.

Conclusions

Given the clinical review of evidence, there were multiple limitations associated with the sponsor's submitted indirect treatment comparison (ITC) meaning that CADTH was unable to determine the comparative efficacy between glasdegib + LDAC and AZA according to BMB subgroups. Therefore CADTH was unable to determine the cost-effectiveness between these treatments and focused base case results on the main population.

CADTH undertook reanalyses to address limitations that included: adjusting treatment administration costs for AZA to better reflect clinical practice; utilizing a more conservative health state utility for remission; revising drug dose intensities for glasdegib + LDAC and AZA; revising subsequent treatment distributions; and, utilizing a parametric survival function for overall survival and progression-free survival (PFS-like). There was uncertainty associated with the use of a PFS-like health state that could not be addressed by CADTH, specifically the classification of partial responding patients (with or without incomplete blood count) being considered as non-remission. The CGP indicated partial responder patients would likely be associated with an improved quality of life and lower healthcare resource utilization compared to non-responders, therefore it is uncertain what impact partial responding patients would have on cost-effectiveness results.

In the CADTH base case in the main population, glasdegib + LDAC was associated with an ICER of $229,622 per QALY gained compared with LDAC, with 0% of simulations resulting in glasdegib + LDAC being considered cost-effective at a WTP threshold of $50,000 per QALY gained. CADTH determined that a price reduction of 95% would be required for glasdegib + LDAC to be considered cost-effective at a willingness-to-pay (WTP) threshold of $50,000 per QALY.

In various scenario analyses, glasdegib + LDAC was sensitive to the target population explored due to variance in patient OS/PFS-like response. In the cytogenetic subgroups, glasdegib + LDAC was more cost-effective in patients with good/intermediate cytogenetic risk (ICER: $293,320 per QALY) compared to poor cytogenetic risk patients (ICER: $367,933 per QALY). As part of exploratory analyses where AZA was included in BMB reanalyses, CADTH investigated the impact of assuming equal efficacy between glasdegib + LDAC and AZA, which resulted in glasdegib + LDAC being dominated (i.e., more costly and less effective) by AZA for both BMB subgroups.

Based on the sponsor's submitted budget impact analysis, the total incremental cost is estimated to be $33,446,886 over the first three years for the main population. CADTH reanalyses suggest that the budget impact of introducing glasdegib to the market (based on revised market shares informed by the CGP which included a lower uptake of glasdegib + LDAC over the time horizon) was estimated to be $21,463,743 in the main population over the first three years. In scenario analyses, the use of the sponsor market share in CADTH reanalyses resulted in an estimated three-year budget impact of $63,084,041 in the main population.

Stakeholder Input Relevant to the Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 1: Cost Comparison Table

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 2: Submission Quality

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 3: Additional Information on the Submitted Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 4: Additional Details on the CADTH Reanalyses and Sensitivity Analyses of the Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

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Appendix 5: Submitted Budget Impact Analysis and CADTH Appraisal

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

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