Budget Impact Analysis of Revumenib for the Treatment of Relapsed or Refractory (R/R) *NPM1*-Mutated Acute Myeloid Leukemia (AML) in the United States

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INTRODUCTION

- *NPM1*-mutated (*NPM1*m) AML represents ~30% of all cases[1-3]
- Approximately 50% of adults with *NPM1*m AML will ultimately relapse following initial remission[4,5]
- Among patients with R/R *NPM1*m AML, ~20% did not initiate any AML treatment following first R/R episode, mostly due to death, highlighting a significant unmet need for effective salvage therapies[6]
- Revumenib, a first-in-class, oral, potent, and selective menin inhibitor, is used for treatment of R/R acute leukemia (AL) harboring a *KMT2A* translocation or R/R AML with an *NPM1*m in adult and pediatric patients 1 year and older
  - Revumenib is recommended in the National Comprehensive Cancer Network (NCCN) Guidelines® for treatment of R/R *KMT2A*-rearranged (*KMT2A*r) AL and R/R *NPM1*m AML[7]
- As payers increasingly focus on value-based care and outcomes, budget impact analysis is essential to inform access, coverage, and reimbursement decisions
- A previously developed budget impact model in R/R *KMT2A*r AL demonstrated that adding revumenib to a health plan's formulary was cost neutral, driven by lower drug administration- and adverse event (AE)-related costs compared with other available treatments[8]

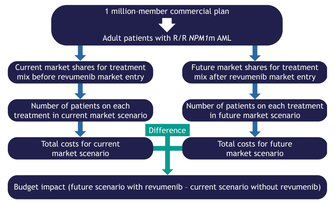
OBJECTIVE

- To develop a budget impact model from the US commercial payer perspective to estimate the financial impact of revumenib for treatment of adults with R/R *NPM1*m AML

METHODS

- A *de novo* budget impact model was created to estimate the 3-year financial impact of 2 scenarios: a formulary before entry of revumenib and a formulary after entry of revumenib for treatment of R/R *NPM1*m AML (**Figure 1**)

Figure 1. Budget impact model design comparing scenarios before and after market entry of revumenib for R/R *NPM1*m AML



AML, acute myeloid leukemia; *NPM1*m, *NPM1*-mutated; R/R, relapsed or refractory.

- Eligible population estimates were based on Surveillance, Epidemiology, and End Results (2017-2021) and published literature[1,3,9-19]
- No targeted therapies were approved for R/R *NPM1*m AML at the time of budget impact model development (August 4, 2025). Per NCCN Guidelines® for R/R AML, apart from revumenib, 6 representative therapies across key treatment classes were included in the budget impact model: gilteritinib (FLT3 inhibitor), enasidenib (IDH2 inhibitor), ivosidenib (IDH1 inhibitor), fludarabine, cytarabine, G-CSF, and idarubicin (FLAG-IDA; intensive chemotherapy), venetoclax + azacitidine (venetoclax-based low-intensity therapy), and azacitidine monotherapy (low-intensity therapy alone)
- **Table 1** lists hypothetical market share estimates for revumenib and other treatments for R/R AML:
  - In the scenario before market entry of revumenib, market shares for other treatments were based on the real-world study using COTA data, a US Oncology electronic health record database[20]
  - After market entry of revumenib, the model assumed a linear increase in increments of 5% in market share from 10% in Year 1 to 20% by Year 3, displacing existing treatments proportionally to their current market shares[8]

Table 1. Hypothetical R/R AML market share before and after revumenib market entry by year[8,20]

	Before revumenib market entry			After revumenib market entry		
Market share, %	Year 1	Year 2	Year 3	Year 1	Year 2	Year 3
Revumenib	0	0	0	10.0	15.0	20.0
Gilteritinib	24.5	24.5	24.5	22.0	20.8	19.6
Enasidenib	4.1	4.1	4.1	3.7	3.5	3.3
Ivosidenib	4.1	4.1	4.1	3.7	3.5	3.3
FLAG-IDA	15.3	15.3	15.3	13.8	13.0	12.2
Venetoclax + azacitidine	48.0	48.0	48.0	43.2	40.8	38.4
Azacitidine	4.1	4.1	4.1	3.7	3.5	3.3
Total	100	100	100	100	100	100

AML, acute myeloid leukemia; FLAG-IDA, fludarabine, cytarabine, G-CSF, and idarubicin; R/R, relapsed or refractory.

Clinical inputs

- Clinical inputs included treatment duration, event-free survival, overall survival, and rates of grade ≥3 AEs (including laboratory abnormalities) occurring in ≥5% of patients for any treatment. These inputs were informed by relevant clinical studies, US drug labels, and the AUGMENT-101 trial[21-27]
- Survival estimates were used to derive the proportion of patients who experienced disease progression or death over the time period, which were then used to estimate post-progression and end-of-life costs
- The analysis was based on the best available data for the respective treatments. Clinical inputs for revumenib were based on patients with R/R *NPM1*m AML from the phase 2 portion of the AUGMENT-101 trial. Clinical inputs for revumenib are not directly comparable with those for the other treatments, as they were sourced from distinct patient populations with different numbers of prior lines of therapy, biomarker profiles (eg, FLT3, IDH1, IDH2), and other baseline characteristics
  - Efficacy inputs were based on patients with R/R *NPM1*m AML for azacitidine, while efficacy inputs from broader R/R AML populations or from subgroups defined by other biomarkers (eg, FLT3, IDH1, IDH2) were used for other therapies

Cost inputs

- Cost components (2025 USD), which included drug acquisition and administration, hospitalization for FLAG-IDA (for infusion and recovery), management of grade ≥3 AEs, outpatient services, post-progression, and end-of-life care, were sourced from published literature and databases
  - Drug acquisition, administration, and outpatient costs were estimated as a function of treatment duration
  - As commonly done in hematologic oncology analyses, only grade ≥3 AEs were included in the analysis, assuming these AEs would incur significant health care resource utilization and associated costs
  - AE-related costs, post-progression costs, and end-of-life costs were applied as one-time costs based on rates of grade ≥3 AEs, disease progression, and death (**Table 2**)

Table 2. Budget impact model cost inputs for R/R *NPM1*m AML

Treatment	Acquisition cost per 28-day cycle[28]	Administration cost per 28-day cycle[29]	Outpatient cost per 28-day cycle[30,31,a]
Revumenib	$42,074[b]	$0	$6775
Gilteritinib	$27,047	$0	$6775
Enasidenib	$33,632	$0	$6775
Ivosidenib	$31,872	$0	$6775
FLAG-IDA	$6502	$2593	$3756
Venetoclax + azacitidine	Cycle 1: $14,254 Cycles 2+: $14,905	$664	$27,029
Azacitidine	$328	$664	$23,808
Hospitalization costs for FLAG-IDA[30,31]			$234,888
Post-discontinuation			
Post-progression costs[31,32]			$262,348
End-of-life costs[33,34]			$40,184

[a]Outpatient cost per cycle included costs for laboratory tests, physician visits, blood transfusions, and other costs incurred in the outpatient setting. For revumenib, enasidenib, and ivosidenib, outpatient costs were assumed to be the same as those for gilteritinib (oral) due to lack of data. Administration costs were sourced from the CMS Physician Fee Schedule based on HCPCS codes. [b]In the drug cost calculation, it was assumed that 90% of patients received 160 mg revumenib and 10% received 270 mg. The assumption that 10% of patients received the 270 mg dose is conservative, as all adult patients with R/R *NPM1*m AML in the phase 2 portion of the AUGMENT-101 trial received the 160 mg dose, and is consistent with the assumption used in the R/R *KMT2A*r budget impact model.[8]

AML, acute myeloid leukemia; CMS, Centers for Medicare & Medicaid Services; FLAG-IDA, fludarabine, cytarabine, G-CSF, and idarubicin; HCPCS, Healthcare Common Procedure Coding System; *KMT2A*r, *KMT2A*-rearranged; *NPM1*m, *NPM1*-mutated; R/R, relapsed or refractory.

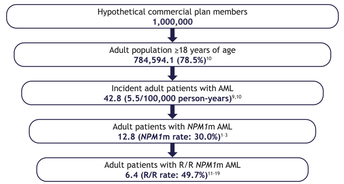
Analysis and model outputs

- Plan total and per-member per-month (PMPM) budgets were estimated for scenarios before and after revumenib market entry for treatment of R/R *NPM1*m AML, with the difference between scenarios used to estimate the net budget impact
- One-way sensitivity analyses (OWSAs) were conducted to test the robustness of the model. The OWSAs assumed a 20% variation or 95% confidence interval variation of each parameter, where available

RESULTS

- In a hypothetical 1 million-member commercial health plan, 6.4 patients with R/R *NPM1*m AML were estimated to be eligible annually for treatment with revumenib (**Figure 2**)
- Based on the estimated market share of revumenib, an estimated 0.6, 1.0, and 1.3 patients would initiate revumenib in Years 1, 2, and 3, respectively

Figure 2. Estimated R/R *NPM1*m AML population based on epidemiology input



AML, acute myeloid leukemia; *NPM1*m, *NPM1*-mutated; R/R, relapsed or refractory.

Base-case analysis

- The net budget impact of adding revumenib to the formulary was estimated to be $17,935 in savings over 3 years (**Figure 3**), with savings of $2405 in Year 1, $5764 in Year 2, and $9766 in Year 3 (**Table 3**)
  - These cost savings were primarily driven by lower drug administration costs, followed by additional savings in outpatient costs and AE-related costs (**Table 3**)
- Estimated PMPM differences were –$0.0002 in Year 1, –$0.0005 in Year 2, and –$0.0008 in Year 3 (**Table 3**), corresponding to an average PMPM difference of –$0.0005 over 3 years

Figure 3. Cumulative total plan costs and budget impact (2025 USD) before and after revumenib market entry over 3 years

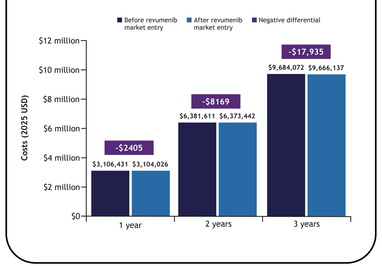


Table 3. Aggregated costs and budget impact (2025 USD) before and after revumenib market entry in Years 1 through 3

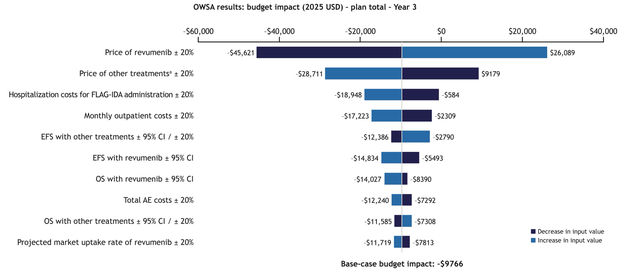
	Year 1			Year 2			Year 3		
	Revumenib market entry			Revumenib market entry			Revumenib market entry		
	Before	After	Differential[a]	Before	After	Differential[a]	Before	After	Differential[a]
Aggregated costs									
Drug acquisition	$445,181	$488,927	$43,746	$480,552	$544,441	$63,889	$484,369	$568,922	$84,552
Drug administration	$238,137	$214,323	-$23,814	$238,200	$202,473	-$35,727	$238,201	$190,564	-$47,637
Outpatient	$322,413	$304,383	-$18,029	$332,928	$305,124	-$27,804	$333,833	$296,549	-$37,284
AE	$324,581	$318,396	-$6184	$324,581	$315,304	-$9277	$324,581	$312,212	-$12,369
Post-progression	$1,600,064	$1,597,095	-$2969	$1,669,172	$1,667,622	-$1549	$1,674,312	$1,672,829	-$1482
End-of-life	$176,056	$180,901	$4845	$229,748	$234,452	$4704	$247,166	$251,619	$4454
Total	$3,106,431	$3,104,026	-	$3,275,180	$3,269,416	-	$3,302,461	$3,292,695	-
Budget impact of revumenib market entry									
Net budget impact	-	-	-$2405	-	-	-$5764	-	-	-$9766
PMPM costs	$0.2589	$0.2587	-$0.0002	$0.2729	$0.2725	-$0.0005	$0.2752	$0.2744	-$0.0008

[a]Differential may not equal the exact difference due to rounding.
AE, adverse event; PMPM, per-member per-month.

One-way sensitivity analyses

- The OWSAs indicated that the base-case results were robust, with the greatest sensitivity observed for the price of revumenib, followed by the prices of other treatments. These top 2 drivers remained consistent across the 3-year time horizon
- Subsequent key drivers of budget impact varied across the 3-year time horizon, including event-free survival with revumenib and hospitalization costs for FLAG-IDA administration (**Figure 4**)

Figure 4. One-way sensitivity analysis of total plan budget impact in Year 3: top 10 influential parameters



[a]In the scenario varying the "price of other treatments", the prices of all modeled treatments other than revumenib were varied simultaneously in a single OWSA.
AE, adverse event; CI, confidence interval; EFS, event-free survival; FLAG-IDA, fludarabine, cytarabine, G-CSF, and idarubicin; OS, overall survival; OWSA, one-way sensitivity analysis.

LIMITATIONS

- Projected market mix and revumenib uptake assumed in the budget impact model need to be validated with real-world data
- Because no other *NPM1*m-specific therapies were approved at model development, clinical inputs for comparator treatments (except azacitidine) were drawn from broader populations and are not directly comparable with revumenib

CONCLUSIONS

- Formulary inclusion of revumenib for adults with R/R *NPM1*m AML would provide patient access to a targeted therapy that addresses a significant unmet need while improving patient outcomes without increasing the overall financial burden
- Including revumenib in the formulary is expected to be cost neutral due to lower drug administration costs, with additional savings in outpatient costs and AE-related costs compared with other treatments for R/R *NPM1*m AML

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