Budget Impact of Zanubrutinib to Treat Relapsed or Refractory Marginal Zone Lymphoma from a Payer Perspective in the United States

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Background

- Marginal zone lymphoma (MZL) is a heterogeneous, rare subtype of B-cell non-Hodgkin lymphoma (NHL) with an annual incidence rate of 19.6 cases per 1,000,000 people in the United States (US)[1]
- Bruton tyrosine kinase (BTK) inhibition activity has demonstrated efficacy in the management of relapsed/refractory (R/R) MZL through mediation of B-cell proliferation, migration, and adhesion[2-4]
- On September 15, 2021, zanubrutinib (Brukinsa®), a BTK inhibitor, was granted accelerated by the US Food and Drug Administration (FDA) for the treatment of adult patients with R/R MZL who have received at least one anti-CD20-based regimen[5]
- The efficacy of zanubrutinib was examined in the phase 2 MAGNOLIA trial (NCT03846427) in adult patients with R/R MZL who have received at least one anti-CD20-based regimen[6]
- There are limited published studies evaluating the economic impact of treatments for R/R MZL

Objective

- To evaluate the budget impact of providing access to zanubrutinib for the treatment of adults with R/R MZL who have received at least one anti-CD20-based regimen from the US commercial and Medicare payer perspectives

Methods

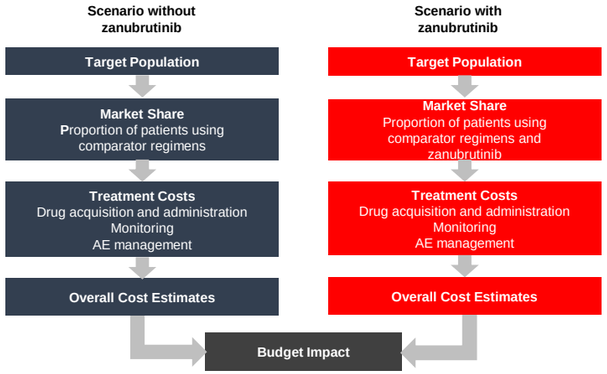
Structure

- A Microsoft Excel-based model was developed to compare two scenarios to estimate the economic impact of providing access to zanubrutinib for the treatment of R/R MZL in patients who have received at least one anti-CD20-based regimen over a time horizon of up to three years (**Figure 1**)
  - The first scenario was without access to zanubrutinib prior to approval, where patients could receive treatment with ibrutinib, rituximab monotherapy, rituximab+cyclophosphamide+doxorubicin+vincristine (R-CHOP) therapy, bendamustine with rituximab (B-R), or lenalidomide with rituximab (L-R)
  - The second scenario was after the introduction of zanubrutinib in addition to the regimens in the first scenario
- The target patient population included adult patients in a US health plan with R/R MZL who have received at least one prior anti-CD20-based regimen

Inputs and Assumptions

- The model assumed a hypothetical plan size of one million members of which 16.5% were covered by Medicare based on the proportion of the US population ≥65 years old[7]
- MZL incidence rates were 1.4 per 100,000 for patients <65 years and 10.5 per 100,000 for patients ≥65 years[1]
- Of the incident population, 76.9% were diagnosed and treated, of those treated 85% were assumed to receive anti-CD20 therapy, of which 51.4% had R/R MZL[8]
- Cost inputs included drug acquisition costs, drug administration costs, drug monitoring costs, and adverse event management costs (**Table 1**)
- Additional model assumptions are presented in **Table 2**

Figure 1. Budget Impact Model Structure



Abbreviations: AE – adverse event.

Table 1. Model Inputs for Treatment Costs and Duration

Regimen	Drug cost per Month*	Cost per Administration (Medicare/Commercial)	Monitoring Cost per Month (Medicare/Commercial)	AE Management per Month (Medicare/Commercial)	Duration of Therapy (Month)
Zanubrutinib	$13,693	N.A	$191/$425	$574/$559	12.0
Ibrutinib	$15,119	N.A	$191/$425	$689/$669	11.6
B-R	$14,728	$220/$635	$200/$472	$1,099/$1,064	5.5
R-CHOP	$7,450	$364/$1,068	$200/$472	$1,790/$1,792	4.1
R Monotherapy	$6,623	$148/$419	$200/$472	$213/$211	11.0
L-R	$38,692	$220/$635	$200/$472	$756/$757	11.0

Abbreviations: AE – adverse event; B – bendamustine; mg – milligram; L – lenalidomide; R – rituximab; R-CHOP – rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Outputs

- The model reported outputs as the incremental total budget impact, incremental per-member-per-year (PMPY) and per-member-per-month (PMPM) budget impact, and per-treated-member-per-year (PTMPY) and per-treated-member-per-month (PTMPM) budget impact for the health plan (**Figure 2**)

Sensitivity Analysis

- A one-way sensitivity analysis was completed by varying each input by ±10% to determine which variables had the greatest impact on the results (**Figure 3**)

Table 2. Model Input Category and Reference

Input Category	Sources and Assumptions
Acquisition Costs and Duration	• Drug acquisition costs calculated using wholesale acquisition price[9] • Clinical dosing and median duration of treatment based on prescribing information or trial publications[10-15]
Monitoring Costs	• Clinical monitoring and testing based on prescribing information or trial publications[10-15] • Frequencies for monitoring and testing based on assumptions • Costs were calculated from the CMS fee schedules or the National Fee Analyzer[16,17]
AE Management Costs	• AEs were selected for clinical relevance to MZL ○ These included neutropenia, other leukopenia, anemia, thrombocytopenia, fatigue, infection, diarrhea, atrial fibrillation, hypertension, secondary malignancy, and hemorrhage[10-12,15,18] • Related treatments and costs were adjusted for duration of treatment ○ Costs per AE were based on HCUP costs and inflated to 2021 US dollars using the medical care component of the CPI[10-12,15,18-20]
Market Dynamics	• Market shares calculated from available market insights[21] • Initial zanubrutinib uptake assumed to be 10% and increases 5% annually • Uptake of zanubrutinib assumed to come proportionally from all other treatment comparators

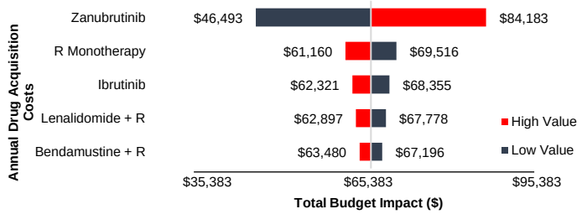
Abbreviations: AE – adverse event; CMS – Centers for Medicare & Medicaid Services; CPI – consumer price index; HCUP – Healthcare Cost and Utilization Project; MZL – marginal zone lymphoma; US – United States.

Figure 2. Incremental Annual Budget Impact by Year

Δ Total Cost	$65,338	$98,007	$130,767
Drug Acquisition	$70,015	$105,022	$140,029
Drug Administration	-$7,778	-$11,667	-$15,555
Monitoring	$667	$1,001	$1,334
AE Management	$2,434	$3,651	$4,868
Δ PMPM Cost	$0.005	$0.008	$0.011
Δ PTMPM Cost	$559	$838	$1,117

Abbreviations: Δ – change; AE – adverse event; PMPM – per member per month; PMPY – per member per year; PTMPM – per treated member per month; PTMPY – per treated member per year.

Figure 3. One-Way Sensitivity Analysis for Total Budget Impact in Year 1



Abbreviations: AE – adverse event; R – rituximab; R-CHOP – rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Results

Budget Impact

- In a hypothetical health plan with one million members, it was estimated that ten members would be treatment-eligible patients with R/R MZL
- Over three years, the incremental budget impact of providing patient access to zanubrutinib was $65,338 ($0.005 PMPM; $559 PTMPM) in year 1, $98,007 ($0.008 PMPM; $838 PTMPM) in year 2, and $130,676 ($0.011 PMPM; $1,117 PTMPM) in year 3 (**Figure 2**)

Sensitivity Analysis

- Results of the budget impact model were most sensitive to annual drug acquisition costs of zanubrutinib, rituximab monotherapy, and ibrutinib (**Figure 3**)

Limitations

- The model utilized inputs and assumptions to estimate budget impacts and are not intended to represent actual pricing or practice implementation, which may limit generalizability to specific health plans
- The population size and incidence of MZL were assumed to remain constant over the modeled time horizon
- Incident patients were assumed to initiate treatment at the beginning of the year in which they were diagnosed and treated for the median duration reported in trial publications or prescribing information; which may not reflect real-world trends
- Default medication doses are based on recommended dosing and administration of their respective product labels, which may not reflect real-world treatment patterns, adherence, or persistence

Conclusion

- Zanubrutinib offers an important therapeutic option for treating adults with R/R MZL who have received at least one anti-CD20-based regimen
- Allowing access to these patients is associated with a minimal budget impact to US health plans over a three-year time horizon

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