US Budget Impact Analysis of Bendamustine Ready-to-Dilute Products in Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma

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Background

- Chronic lymphocytic leukemia (CLL) is a subtype of B-cell non-Hodgkin lymphoma (NHL).[1]
- CLL is one of the most common leukemia in US adults with an estimated 21,040 new cases and 4,060 CLL-related deaths in 2020.[1]
- Indolent B-cell NHL (iNHL) is a less aggressively developing NHL of the B-cell origin.[1]
  - iNHL makes up approximately 30% of all NHL cases in the US, with an estimated 77,240 new cases and 19.940 NHL-related deaths in 2020.[1]
- Bendamustine (BND) is used to treat CLL and indolent, rituximab-refractory B-cell non-Hodgkin lymphoma.[2, 3]
  - BND is manufactured in ready-to-dilute formulations with differing infusion volumes, diluents, and durations.

Objectives

- The objective of this analysis was to estimate the budget impact of replacing BND large-volume, long-duration infusion (ie, Belrapzo™; BND-L) formulation with BND small-volume, short-duration infusion (ie, Bendeka®; BND-S).

Methods

Model

- An illustrative budget impact model (BIM) was developed, following ISPOR best practices,[4] to estimate facility perspective changes in drug and administration labor costs associated with a hypothetical shift from 50%/50% BND-L/BND-S use to exclusive BND-S use.
- The total facility budget impact was estimated for a 10,000-patient infusion facility, with an estimated 238 patients receiving BND for CLL or iNHL annually over a 1-year time horizon.

Input Parameters

- Patients expected to receive BND treatment for CLL or iNHL were determined based on national health system statistics, pertinent epidemiologic data, published real-world utilization data, and clinical practice guidelines (**Table 1**).[1, 5-15]

Table 1 Epidemiology and Estimation of Population Eligible for Bendamustine

Population	Estimated Proportion	Number	Source
Facility Total Annual Patient Count	100%	10,000	Yu (2016)[5], Richardson and Rouhana (2016)[6], and Bach (2014)[7]
Patients receiving bendamustine infusions for CLL	2.25%	225	ACS (2019)[8], Howlader et al (2019)[1], Ammann et al (2017)[9], Seymour et al (2019)[10], and NCCN (2019)[14]
Patients receiving bendamustine infusions for NHL	0.13%	13	ACS (2019)[8], Leukemia and Lymphoma Society (2019)[11], NCCN (2020) (15), Morrison et al (2019)[12], and Ren et al (2019)[13]
Total population that might receive bendamustine RTD		**238**	

Abbreviations: ACS=American Cancer Society; CLL=chronic lymphocytic leukemia; NCCN=National Comprehensive Cancer Network®; NHL=non-Hodgkin lymphoma; RTD=ready-to-dilute.

Table 2 Bendamustine Dosing per Patient by Indication

BND Indication	Treatment Dose	Calculated Dose*	Doses/Year	Total Dose/ Patient/ Year
CLL	100 mg/m^2	180 mg	12	2160 mg
NHL	120 mg/m^2	216 mg	16	3456 mg

*Based on a mean body surface area of 1.8 m^2.[2, 16-17]
Abbreviations: BND=bendamustine; CLL=chronic lymphocytic leukemia; NHL=non-Hodgkin lymphoma.

- Dosing and per-patient dose count (12 in CLL; 16 in iNHL) were based on product labeling[2-3] and a mean patient body surface area (BSA) of 1.8m^2 (**Table 2**).[16-17]

Table 3 Annual Bendamustine Acquisition Cost per Patient by Indication

Bendamustine Product	Indication	Doses/Year	WAC/mg	WAC/Patient/Year
BND-S	CLL	12	$24.74	$53,438.40
	NHL	16		$85,501.44
BND-L	CLL	12	$25.97	$56,095.20
	NHL	16		$89,752.32

Abbreviations: BND-L=bendamustine large-volume, long-duration infusion; BND-S=bendamustine small-volume, short-duration infusion; CLL=chronic lymphocytic leukemia; NHL=non-Hodgkin lymphoma; WAC=wholesale acquisition cost.

Table 4 Annual Admixture Diluent Acquisition Cost per Infusion

Bendamustine Product	Diluent for Product Admixture	Proportion of Diluent Use/ Patient Population	Diluent Cost/ Infusion*
BND-S	0.9% Sodium Chloride Injection, USP, 50 mL	75%	$1.99
	2.5% Dextrose/0.45% Sodium Chloride Injection, USP, 50 mL	5%	$5.60†
	5% Dextrose Injection, USP, 50 mL	20%	$2.15
BND-L	0.9% Sodium Chloride Injection, USP, 500 mL	95%	$3.33
	2.5% Dextrose/0.45% Sodium Chloride Injection, USP, 500 mL	5%	$5.60†

Note: The distribution of diluent utilization per facility is an assumption.
*Diluent acquisition costs represent the 25th percentile of products available on Red Book Online, recognizing that there are negotiated rates and many identical products on the market, accounting for lower acquisition costs.
†Red Book did not have a published cost for 2.5% Dextrose/0.45% Sodium Chloride Injection, USP, 500 mL; as such, the cost for this diluent is for a 1000-mL product.
Abbreviations: BND-L=bendamustine large-volume, long-duration infusion; BND-S=bendamustine small-volume, short-duration infusion; WAC=wholesale acquisition cost.

- Drug and diluent costs were derived from RED BOOK March 2020 (**Table 3** and **Table 4**).[18]
- Within a given facility, prescriber selection of diluent may vary by patient. As such, a default distribution was assigned per facility across FDA-approved diluents per product. This diluent distribution per facility is an assumption and includes patients receiving BND-S and BND-L for both FDA-approved indications (**Table 4**).

Table 5 Bendamustine Administration Labor Costs per Patient by Product and Indication

Bendamustine Product	Indication	Doses/Year	Infusion Time/Dose	Annual Infusion Labor Cost/ Patient*
BND-S	CLL	12	10 minutes	$75.48
	NHL	16	10 minutes	$100.64
BND-L	CLL	12	30 minutes	$226.44
	NHL	16	60 minutes	$603.84

*Infusion labor cost is assumed to be $37.74 per hour.[19]
Abbreviations: BND-L=bendamustine large-volume, long-duration infusion; BND-S=bendamustine small-volume, short-duration infusion; CLL=chronic lymphocytic leukemia; NHL=non-Hodgkin lymphoma.

- Administration labor costs were based on US Bureau of Labor Statistics data, using the hourly wage for nurses at specialty hospitals as a proxy for the infusion nurse wage at facilities that provide chemotherapy infusion services (**Table 5**).[19]

Analytic Approach

- Univariate sensitivity analyses were conducted. Parameters were varied individually in an attempt to reflect each parameter's true uncertainty, in accordance with the most recent ISPOR Budget Impact Analysis Principles of Good Practice.[4]

Results

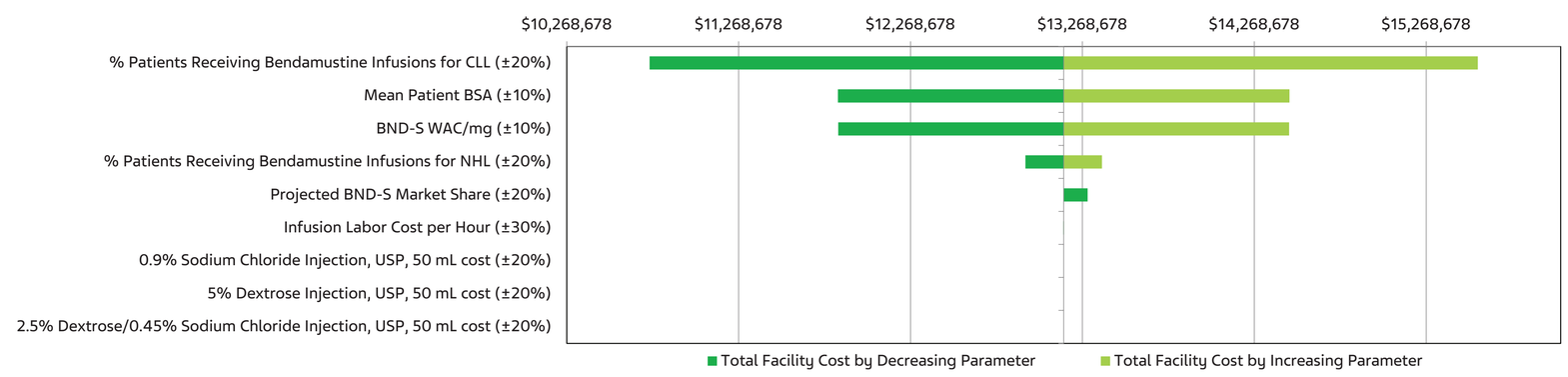
- The total estimated annual infusion facility incremental savings after the utilization shift were $348,579, resulting in $1464.61 savings per-BND-patient-per year (PBPPY; **Table 6**).
- Annual per-patient infusion labor costs per BND-S patient were $75.48 for CLL and $100.64 for iNHL; BND-L costs were $226.44 and $603.84, respectively (**Table 5**).
- The model was most sensitive to changes in CLL patient count, patient BSA, and BND-S treatment cost (**Figure 1**).

Table 6 Annual Facility Costs

Bendamustine Product	Current	Projected	Incremental
Total Costs*			
BND-S	$6,579,927	$13,159,855	$6,579,927
BND-L	$6,928,506	$0	–$6,928,506
Total Cost to Facility	**$13,508,434**	**$13,159,855**	**Savings of $348,579**
PBPPM Costs			
BND-S	$2303.90	$4607.79	$2303.89
BND-L	$2425.95	$0.00	–$2425.95
Total Cost to Facility	**$4729.85**	**$4607.79**	**Savings of $122.06**
PBPPY Costs			
BND-S	$27,646.75	$55,293.51	$27,646.76
BND-L	$29,111.37	$0.00	–$29,111.37
Total Cost to Facility	**$56,758.12**	**$55,293.51**	**Savings of $1464.61**

Note: Calculations aggregate facility costs for patients with CLL and NHL.
*Calculations are rounded to the nearest dollar.
Abbreviations: BND-L=bendamustine large-volume, long-duration infusion; BND-S=bendamustine small-volume, short-duration infusion; CLL=chronic lymphocytic leukemia; NHL=non-Hodgkin lymphoma; PBPPM=per bendamustine patient per month; PBPPY=per bendamustine patient per year.

Figure 1 One-Way Sensitivity Analyses for Year 1 Projected Annual Facility Costs



Note: BND-L parameters do not impact the results because there is no BND-L utilization in the future scenario (ie, all BND-L utilization shifts to BND-S).
Abbreviations: BND-L=bendamustine large-volume, long-duration infusion; BND-S=bendamustine small-volume, short-duration infusion; BSA=body surface area (in milligrams/square meter); CLL=chronic lymphocytic leukemia; mL=milliliter; NHL=non-Hodgkin lymphoma; USP=United States Pharmacopoeia; WAC=wholesale acquisition cost.

Conclusions

- This BIM estimated an annual savings of nearly $350,000 for 238 CLL and iNHL patients in a 10,000-patient infusion facility following a utilization shift from 50% use of each bendamustine product to 100% use of BND-S.
  - Savings were driven primarily by lower infusion costs associated with rapid infusion.
- BND-S also provides a clinical advantage over BND-L with the option to use a 5% dextrose diluent.[2-3]
- BND-S admixtures using 0.9% sodium chloride or 2.5% dextrose/0.45% sodium chloride are stable at room temperature twice as long as BND-L (6 hours vs 3 hours, respectively).[2-3]
- When drug acquisition costs are comparable, facilities retain savings associated with infusion labor cost differences once payers reimburse drug costs.
  - Estimated labor cost savings in this analysis reflect and are impacted by number of treated patients with CLL and iNHL, BSA of 1.8 m^2, and acquisition costs (ie, WAC) for bendamustine ready-to-dilute products.
  - Results vary according to real-world number of sequential infusions in one day and infusion time reimbursement rates to facilities.

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