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Budget Impact Analysis of Nefecon for the Treatment of Primary IgA Nephropathy in the United States

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Background

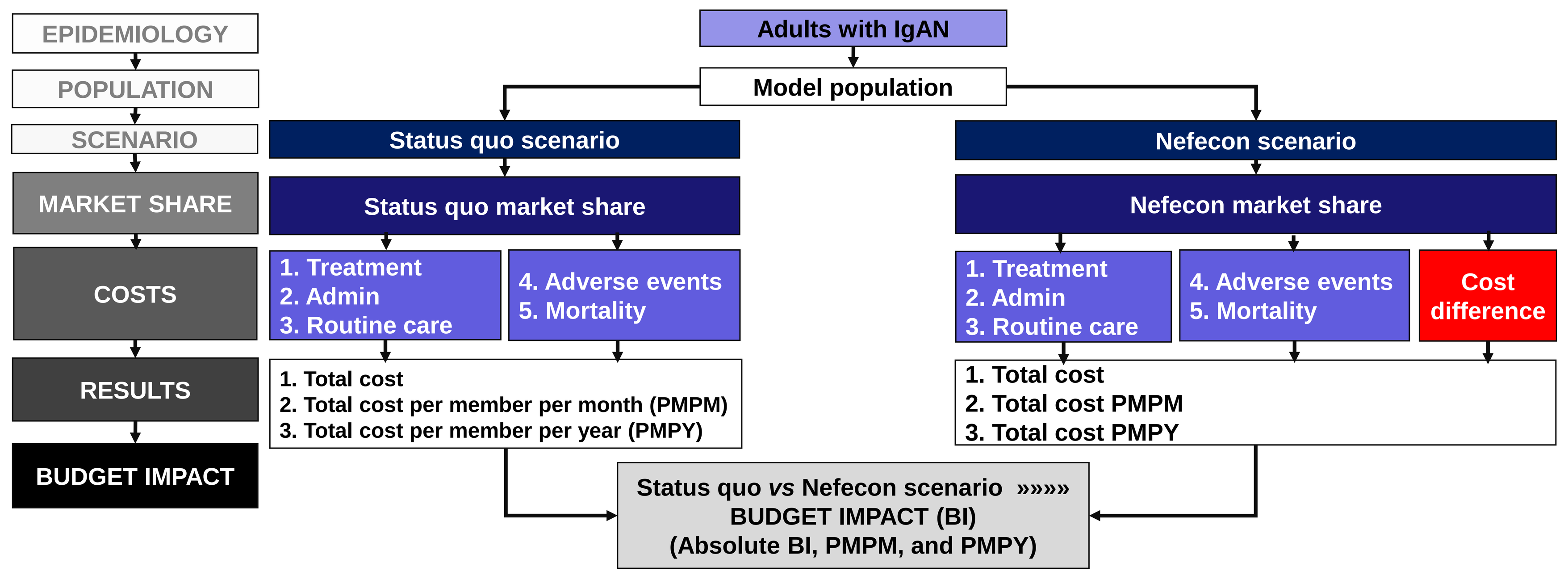
- Primary immunoglobulin A nephropathy (IgAN) is the most common type of primary glomerulonephritis globally, with an estimated US incidence of 1.29 per 100,000 people[1] and estimated US prevalence of 112,000 people in 2019.[2]
- IgAN is a rare progressive autoimmune disease that leads to chronic inflammation in the kidneys.[3] Over time, IgAN can lead to end-stage renal disease (ESRD). Studies found that 23% of patients with IgAN progressed to ESRD in 3.9 years[4] and 53% of patients with IgAN progressed to ESRD in 19 years.[5]
- Until recently, there were no approved disease-specific therapies available for IgAN and it was managed by best supportive care (BSC) that consists of blood pressure management, renin-angiotensin system (RAS) blockade with maximally tolerated dose of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARB) and lifestyle modification.[6]
- Evidence suggests a four-hit hypothesis to describe the pathogenesis of IgAN and its autoimmune disease mechanisms, where the first hit involves increased amounts of circulating galactose deficient IgA.[7]
- Nefecon is the developmental product name for a novel oral formulation of budesonide that is designed to deliver budesonide to an area of the ileum to target mucosal B cells, which are responsible for the production of galactose-deficient IgA1 antibodies, causing IgAN.[8,9]

Methods

A prevalence-based budget impact model was developed for the US to evaluate the economic impact of adding Nefecon to the formulary of a hypothetical commercial healthcare plan of one million members for adults with primary IgAN who are at risk of rapid disease progression over three years (base case analysis). Since there were no disease-specific therapies available prior to the FDA approval of the product, it was crucial to include all patients who would get treated, including incident and prevalent patients with IgAN. Therefore, a prevalence-based model was considered appropriate. The budget impact model structure is depicted in Figure 1.

- In the prevalence-based budget impact analysis, it was assumed that:
  - Existent patients (prevalent) and new patients (incident) enter the model at the beginning of each year
  - Patients stayed in the model until the model horizon was reached or until death, based on the survival rate from the NefIgArd trial data
- Two cost scenarios were evaluated in the model:
  - The status quo scenario without Nefecon where all patients receive best supportive care (BSC); and
  - The reimbursement scenario with Nefecon as an add-on therapy to BSC
- Comparators of Nefecon + RASi vs placebo + RASi were chosen to align with the NefIgArd trial, and with clinical practice in the US.
- The reimbursement scenario included an uptake projection consisting of increasing market shares for Nefecon in years 1, 2 and 3, stratified by chronic kidney disease (CKD) stage. In contrast, no patients were treated with Nefecon in the status quo scenario (0% market share) over the 3-year time horizon.

Figure 1. Model structure



Model Inputs

PATIENT FLOW

- In the base case analysis, only adult patients with IgAN with proteinuria ≥1 g and CKD stage 2 and 3 were considered eligible.
- Table 1 shows the granular inputs of patient flow.

DRUG COSTS

- The model included drug and drug administration costs (assumed at $14,160 per treatment cycle). (Table 2).
- In the model, treatment eligible patients received one round of Nefecon consisting of 9.25 months* based on market share assumptions.
- In the model, all patients with primary IgAN received continuous best supportive care.
- Costs of treatment used were calculated in monthly cycles.
- Administration costs associated with oral drugs were assumed to be $0 USD.
- Other costs used in the model are listed in Table 3 and Table 4. All costs are reported in US dollars and were inflated to 2022 values.

In the NefIgArd trial, treatment with Nefecon 16mg/day was administered for 9 months and was followed by 2-week tapering period with Nefecon 8 mg/day. However, the model assumed treatment with Nefecon 16 mg/ day for 9.25 months for simplicity.

Abbreviations: Admin: administration; AEs: adverse events; BI: budget impact; BSC: best supportive care; CKD: chronic kidney disease; CSR: Clinical Study Report; eGFR: glomerular filtration rate; FDA: Food and Drug Administration; IgAN: IgA nephropathy; PMPM: per member per month; PMPY: per member per year; PO: oral; RASi: renin angiotensin system inhibitors; SoC: standard of care; tx: treatment; UPCR: urine protein/creatinine ratio; UK: United Kingdom; US: United States; USD: United States dollar

Table 1.1. General population inputs

Parameter	Value	Source
Health plan population	1,000,000	Assumption
Annual population change	0.0%	Assumption
Adult population	78%	US Census Bureau, 2020[10]
Prevalent patients with IgAN	0.034%	Data extrapolated from Census.gov[2]
Annual incidence of primary IgAN (per 100,000)	1.29	Adapted from Table 3 in Kwon et al., 2021[1]

Table 1.2. Population inputs by subgroup

Parameter		Value	Source
Distribution of patients in the incident populations	CKD stage 2	22%	Adapted from Table 3 in Kwon et al., 2021 [1]
	CKD stage 3	26%	
Distribution of patients in the prevalent populations	CKD stage 2	13%	RealWorld Dynamix Exploring the Patient Journey IgA Nephropathy 2021 [11]
	CKD stage 3	32%	
Proportion of patients who have proteinuria ≥1 g at diagnosis of IgAN	Overall	65%	
Proportion of patients who have proteinuria ≥1 g in the prevalent populations	CKD stage 2	40%	Calliditas Therapeutics, data on file[9]
	CKD stage 3	55%	Calliditas Therapeutics, data on file[9]
One-year survival rates	Nefecon group	99.3%	Calliditas Therapeutics, data on file[9]
	SoC group	99.3%	Calliditas Therapeutics, data on file[9]

Table 2. Population inputs by subgroup

Payer	Drug	Admin route	Dose per admin (mg)	Admin per tx cycle	Cost /pack	Units /pack	Unit strength (mg)	Packs needed per tx cycle	Drug cost per tx cycle (USD)	Admin cost per tx cycle (USD)	Payer cost per tx cycle (USD)	Cost and dosing source
Commercial	Nefecon	PO	16	30	118	1	4	120.00	14,160	0	14,160	(8,12)

OTHER COSTS

Table 3. Health state costs

CKD stage	Annual cost	Cost year	Annual cost ($, inflation-adjusted)	% pts	Source
Stage 2	16,770	2016	19,484	22%	Golestaneh et al., 2017 (AJMC)[13], 2021 Spherix report[11]
Stage 3	35,195	2016	40,891	26%	Golestaneh et al., 2017 (AJMC)[13], 2021 Spherix report[11]

Table 4. Mortality costs (Cost of hospital care by period until death for people with CKD)

	UK costs	US costs	Cost year	Inflated
3 months at the end of life	6,048	15,434	2017	17,489

Source: Kerr,2017[14]
Note: 1.29 was used for currency conversion (June 2016) from xe.com[15](June 2017). 1.98 was used for UK to US end-of-life spending ratio from Bekelman et al.[16]

MARKET SHARE

- In the status quo scenario, the market share of Nefecon was 0% across all years.
- The reimbursement scenario included Nefecon as a new treatment option for eligible patients with IgAN and involved an increasing projected market uptake over 3 years at a different rate by CKD stage (Table 5).

Table 5. Market share

Treatment		Baseline	Year 1	Year 2	Year 3
CKD stage 2	Nefecon + RASi	0.0%	5.2%	15.2%	23.2%
	RASi alone	100.0%	94.8%	84.8%	76.8%
CKD stage 3	Nefecon + RASi	0.0%	5.6%	16.2%	24.8%
	RASi alone	100.0%	94.4%	83.8%	75.2%

Source: Based on analog research of recent orphan & rare disease launches in the US, Data on file.[9]

ADVERSE EVENTS

- The frequencies of adverse events (AEs) were sourced from the NefIgArd clinical trial for the safety analysis set over the median follow-up duration for the Nefecon 16 mg/day and placebo trial arms.
- The frequencies of AEs were transformed to monthly probabilities and applied to the number of months of treatment duration in the model.
- The frequencies of AEs were multiplied by the unit costs of inpatient and outpatient visits to obtain the monthly AE costs (Table 6 and 7).
- AEs experienced by patients which did not require hospitalizations were assumed to result in outpatient visits.

Table 6. Distribution of adverse event treatment setting

Treatment	% of AEs requiring inpatient admissions	% of AEs requiring outpatient visits	Source
Nefecon + RASi	4%	96%	Data on file[9]
Placebo + RASi	2%	98%	Data on file[9]

Table 7. Adverse event costs

Treatment	Cost	Source
Nefecon + RASi	$ 30.73	HCUPnet 2015/2017 Hospital Charges[17] and CMS (Physician Fee Schedule) with CPT code 99213[18]
Placebo + RASi	$ 3.76	

Note: AEs of SoC is assumed to be the same as placebo in the trial

LIMITATIONS

- Market share data are based on Calliditas Therapeutics US Inc., internal data, which may differ from real-world values given this is the first and only disease-specific treatment approved by the FDA in IgAN.
- There are limited data for US medical care costs in primary IgAN, which may introduce some uncertainties.
- While medical resource utilization data were based on published literature and studies in IgAN, these may not be fully aligned with the NefIgArd clinical trial population. As homogenous data sources are necessary for internal consistency, this gap may be considered a potential limitation of this analysis.
- A prevalence-based model is only appropriate when the treatment is novel as there is a large pool of eligible patients who have previously received no IgAN specific treatment. However, it is difficult to estimate the number of eligible patients undergoing treatment each year in a prevalence-based budget impact analysis. This is due to the relatively higher number of patients being included in the first few years due to the backlog of patients who have not previously had an approved treatment. Eventually, annual incident patients who require treatment will only be considered.

Results

- The number of patients estimated to receive Nefecon treatment in each year of the model horizon are presented in Table 8.
- The patient flow reflects the modeled market uptake.

BASE CASE: DRUG PLAN PERSPECTIVE

- Drug plan perspective considers solely the total costs of treatments. This excludes adverse events costs.
- In the status quo scenario, total drug costs incurred over 3 years for the treatment of IgAN was **$0**. It was because BSC costs which were in both scenarios, and therefore cancelled out. In the reimbursement scenario, the introduction of Nefecon for eligible patients with IgAN was associated with total drug costs of **$3,265,769** over 3 years (Table 9).
- For the drug plan perspective, absolute budget impact was **$3,265,769**, corresponding to a PMPM cost of $0.09 and a PMPY cost of **$1.09** over 3 years (Table 10).

HEALTHCARE SYSTEM PERSPECTIVE

- Healthcare system perspective considers the total costs of treatment, the routine medical costs, AE costs and the mortality costs.
- In the healthcare system perspective, the total drug costs are not different from drug plan perspective (Table 9).
- For the healthcare system perspective, the absolute budget impact was **$3,271,988**, corresponding to a PMPM cost of **$0.09** and a PMPY cost of **$1.09** over 3 years (Table 11).
- One-way deterministic sensitivity analyses were carried out to test the robustness of the model results. Inputs were selected for inclusion based on the perceived level of parameter uncertainty and included epidemiologic data and market share estimates (Table 12).
- Across all scenarios, greatest range of variance between optimistic and conservative scenarios totaled $255,884 ($3,146,512 to $3,402,396) for variations in the Nefecon uptake (CKD stage 3). Other scenarios' variances between upper and lower bounds ranged between $183,697 for the variation in the incidence of IgAN and $77,599 for Nefecon uptake (CKD stage 2) (Figure 2).

Table 8. Patient flow

	Year 1	Year 2	Year 3
Total population in plan	1,000,000	1,000,000	1,000,000
Adult population in plan	777,482	777,482	777,482
Prevalent IgAN adult population	266	266	266
Prevalent IgAN adult population with CKD 2 or 3	123	127	131
Prevalent IgAN adult population with CKD 2 or 3 and proteinuria >1 g	63	66	68
Total number of patients on TARPEYO™ treatment*	3	9	13

Note: The total may not match exactly due to rounding off
**The market uptake of Nefecon was estimated to be 5.2%, 15.2%, and 23.2% in adults with IgAN in CKD stage 2, and 5.6%, 16.2% and 24.8% in adults with IgAN in CKD stage 3 in years 1, 2, and 3, respectively. This uptake yielded 4, 12, and 16 patients entering a Nefecon treatment plan in year 1, 2, and 3, respectively.*

Table 9. Total drug costs in the status quo scenario and reimbursement scenario – US drug plan perspective

	Year 1	Year 2	Year 3	Total
Status quo scenario				
Total drug costs	$0	$0	$0	$0
Reimbursement scenario				
Total drug costs	$421,052	$1,207,741	$1,636,976	$3,265,769

Table 10. Overall budget impact of TARPEYO™ – US drug plan perspective

		Year 1	Year 2	Year 3	Total
Drug plan perspective	Absolute budget impact	$421,052	$1,207,741	$1,636,976	$3,265,769
	Cost PMPM	$0.04	$0.10	$0.14	$0.09
	Cost PMPY	$0.42	$1.21	$1.64	$1.09

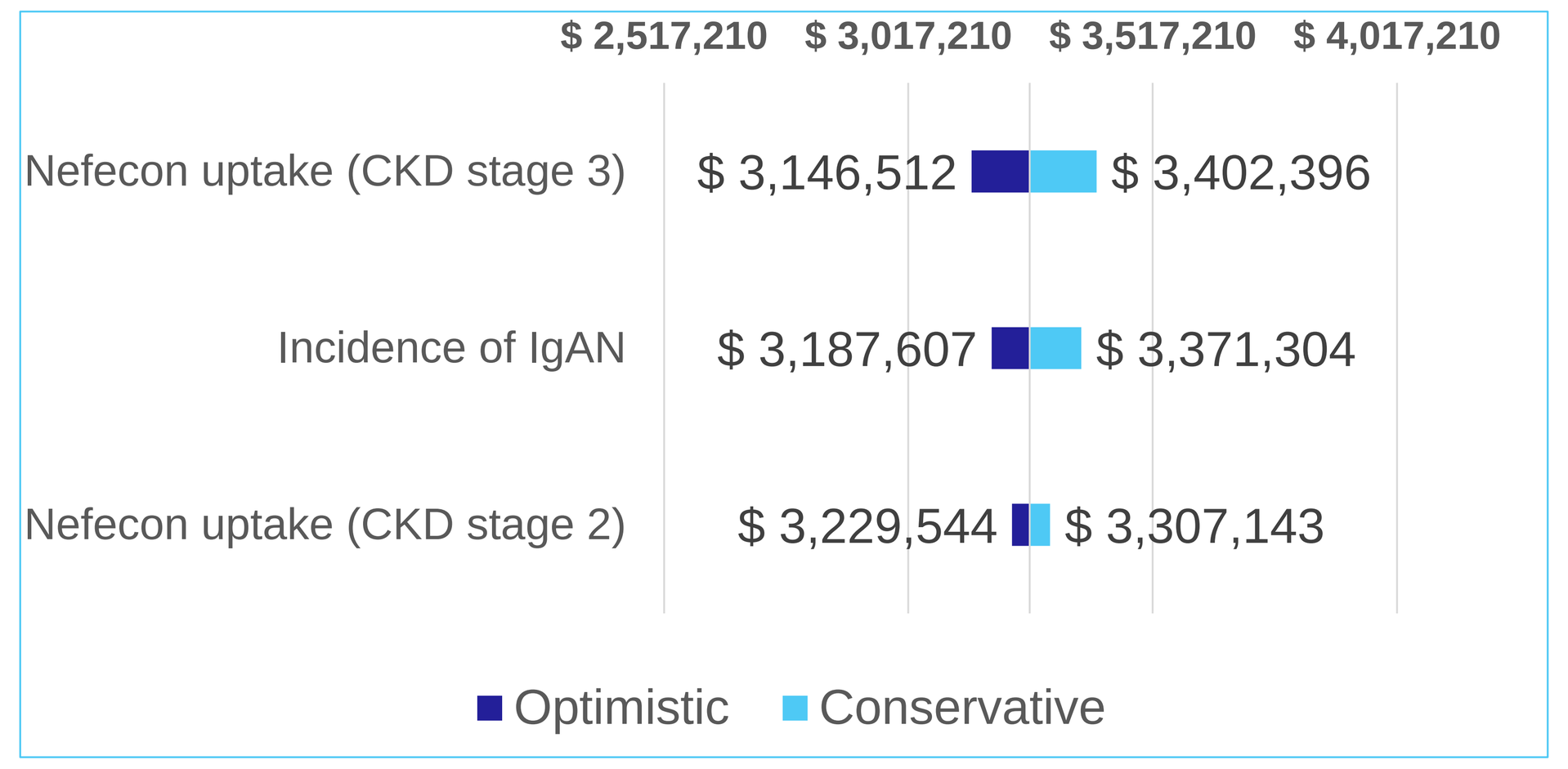
Table 11. Overall budget impact of TARPEYO™ – US healthcare system perspective

		Year 1	Year 2	Year 3	Total
Healthcare System Perspective	Absolute budget impact	$421,854	$1,210,041	$1,640,093	$3,271,988
	Cost PMPM	$0.05	$0.13	$0.18	$0.09
	Cost PMPY	$0.54	$1.56	$2.11	$1.09

Table 12. Results of one-way deterministic sensitivity analyses

	Variation	Lower bound	Base case	Upper bound	Note
Incidence of IgAN	SE (0.2)	-8.7%	0.0%	8.7%	Calculated from incidence rate
Nefecon uptake (CKD stage 2)	+/-10%	-5.4%	0.0%	6.2%	Weighted average from client inputs
Nefecon uptake (CKD stage 3)	+/-10%	-5.5%	0.0%	6.4%	

Figure 2. Results of one-way deterministic sensitivity analyses



Conclusions

- In summary, this budget impact model uses a robust methodological approach that yields overall expected cost estimates associated with the introduction of Nefecon from the perspective of a US commercial payer.
- In the base case analysis, the introduction of Nefecon, for adult patients with IgAN with proteinuria ≥1 g and CKD stage 2 and 3, was associated with a total cost increase in the drug plan perspective of **$3,265,769** with PMPM costs of **$0.09** and PMPY costs of **$1.09** for a hypothetical one-million-member commercial plan over 3 years.
- Findings suggest that the budget impact associated with the introduction of Nefecon is manageable and limited due to the low incidence of IgAN, well-defined patient population eligible for Nefecon treatment, and low costs associated with AE management.

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