Designing a Performance-Based Risk Sharing Arrangement for Aducanumab

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Background

- A recent coverage decision by the Center for Medicare and Medicaid Services (CMS) in the US approved the drug, Aducanumab, for Coverage with Evidence Development (CED)
- CED means CMS will pay for the drug only in the context of a clinical study to produce additional evidence on Aducanumab's effectiveness at slowing Alzheimer's disease progression. Currently, CMS pays the market price for Aducanumab, approximately $25,200 per patient annually, but due to CED, utilization is low.
- We consider a different approach that could have been taken by CMS and the drug manufacturer, a performance-based risk sharing arrangement (PBRSA), that would allow for broader coverage/utilization of Aducanumab but with a pricing structure tied to the effectiveness eventually observed in the clinical study already being conducted.
- **We focus on two hypothetical pricing structures that could have been established to pay for the drug under PBRSAs, both scenarios set the unit price as a function of the observed hazard ratio in future studies.**

Methods

- We adapted an existing model of Aducanumab's cost-effectiveness and budget impact[1], versus standard of care and combined with additional estimates of incidence and costs relevant to CMS[2].
- The model estimates the 5-year budget impact and total QALYs accrued with existing standard care and Aducanumab leaving the hazard ratio of progression uncertain.
- Using the standard of care budget impact as a baseline for 5-year spending and QALYs accrued for possible Aducanumab patients covered by CMS, we designed two dynamic pricing structures for Aducanumab that would change depending on what hazard ratio for progression was ultimately observed.
- **Scenario 1**: fixing CMSs total spending on this population at the 'status quo' spending (i.e., the 5-year spending on the cohort expected with no Aducanumab available)
  - In this scenario, each dollar that is saved by CMS over 5 years, goes to the manufacturer
- **Scenario 2:** each additional QALY accrued from using Aducanumab would be be valued at $150,000/QALY. Thus, we hold the QALYs expected from the status quo as fixed, and each additional QALY is paid to the manufacturer at a rate of $150,000/QALY.
  - In this scenario, each incremental QALY gained from using Aducanumab is valued at $150,000

Results

- If Aducanamab is not covered (effectively the status quo under CED), in our base budget impact model, the 5-year budget impact of caring for 1.4million CMS patients with pre-Alzheimer's who would potentially benefit from Aducanumab based on the label is $305.7billion, and the total QALYs expected to be earned by this group in 5 years is 3,572,324.
- In an alternate status quo, where CMS would have not done CED, but covered the drug and provided to all on label patients, spending, regardless of actually clinical efficacy ranging from 0.6-1.05 (roughly the confidence interval of progression from two prospective phase III trials[3]), spending would increase 100-108 billion over 5 years.
- PBRSA Scenario 1, yields value-based prices (per year of the drug) ranging from $2,623 at 0.6 hazard ratio to negative at hazard ratios above 0.85 and relatively modest revenue to the manufacturer <2 billion annually
- PBRSA Scenario 2, which rewards additional QALY accrual directly, increases manufacturer revenue at all hazard ratios compared to Scenario 1, and only yields negative value-based prices at a hazard ratio of 1 or above (i.e., no treatment effect).

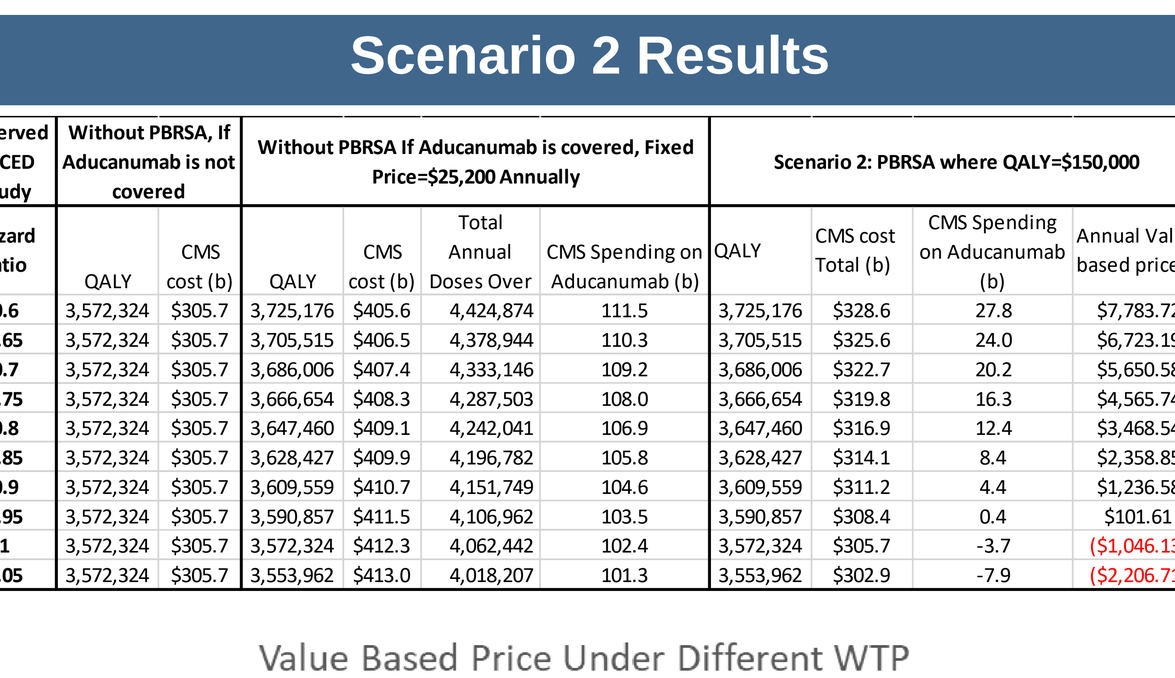
Scenario 1 Results

Observed in CED Study	Without PBRSA, If Aducanumab is not covered		Without PBRSA If Aducanumab is covered, Fixed Price=$25,200 Annually				Scenario 1: PBRSA Set to Cap CMS Spending at "Not Covered" Level			
Hazard ratio	QALY	CMS cost (b)	QALY	CMS cost (b)	Total Annual Doses Over	CMS Spending on Aducanumab (b)	QALY	CMS cost Total (b)	CMS Spending on Aducanumab (b)	Annual Value based price
0.6	3,572,324	$305.7	3,725,176	$405.6	4,424,874	111.5	3,725,176	$305.7	$11.6	$2,623.1
0.65	3,572,324	$305.7	3,705,515	$406.5	4,378,944	110.3	3,705,515	$305.7	$9.5	$2,180.8
0.7	3,572,324	$305.7	3,686,006	$407.4	4,333,146	109.2	3,686,006	$305.7	$7.5	$1,729.8
0.75	3,572,324	$305.7	3,666,654	$408.3	4,287,503	108.0	3,666,654	$305.7	$5.4	$1,270.0
0.8	3,572,324	$305.7	3,647,460	$409.1	4,242,041	106.9	3,647,460	$305.7	$3.5	$824.9
0.85	3,572,324	$305.7	3,628,427	$409.9	4,196,782	105.8	3,628,427	$305.7	$1.6	$371.5
0.9	3,572,324	$305.7	3,609,559	$410.7	4,151,749	104.6	3,609,559	$305.7	-$0.4	($90.5)
0.95	3,572,324	$305.7	3,590,857	$411.5	4,106,962	103.5	3,590,857	$305.7	-$2.3	($561.1)
1	3,572,324	$305.7	3,572,324	$412.3	4,062,442	102.4	3,572,324	$305.7	-$4.2	($1,040.4)
1.05	3,572,324	$305.7	3,553,962	$413.0	4,018,207	101.3	3,553,962	$305.7	-$6.0	($1,503.5)

Scenario 2 Results

Observed in CED Study	Without PBRSA, If Aducanumab is not covered		Without PBRSA If Aducanumab is covered, Fixed Price=$25,200 Annually				Scenario 2: PBRSA where QALY=$150,000			
Hazard ratio	QALY	CMS cost (b)	QALY	CMS cost (b)	Total Annual Doses Over	CMS Spending on Aducanumab (b)	QALY	CMS cost Total (b)	CMS Spending on Aducanumab (b)	Annual Value based price
0.6	3,572,324	$305.7	3,725,176	$405.6	4,424,874	111.5	3,725,176	$328.6	27.8	$7,783.72
0.65	3,572,324	$305.7	3,705,515	$406.5	4,378,944	110.3	3,705,515	$325.6	24.0	$6,723.19
0.7	3,572,324	$305.7	3,686,006	$407.4	4,333,146	109.2	3,686,006	$322.7	20.2	$5,650.58
0.75	3,572,324	$305.7	3,666,654	$408.3	4,287,503	108.0	3,666,654	$319.8	16.3	$4,565.74
0.8	3,572,324	$305.7	3,647,460	$409.1	4,242,041	106.9	3,647,460	$316.9	12.4	$3,468.54
0.85	3,572,324	$305.7	3,628,427	$409.9	4,196,782	105.8	3,628,427	$314.1	8.4	$2,358.85
0.9	3,572,324	$305.7	3,609,559	$410.7	4,151,749	104.6	3,609,559	$311.2	4.4	$1,236.58
0.95	3,572,324	$305.7	3,590,857	$411.5	4,106,962	103.5	3,590,857	$308.4	0.4	$101.61
1	3,572,324	$305.7	3,572,324	$412.3	4,062,442	102.4	3,572,324	$305.7	-3.7	($1,046.13)
1.05	3,572,324	$305.7	3,553,962	$413.0	4,018,207	101.3	3,553,962	$302.9	-7.9	($2,206.71)

Value Based Price Under Different WTP



Conclusions

- Our results highlight that alternate pricing arrangements like a PBRSA could increase utilization compared to CED at potentially similar budget impact for CMS.
- At most hazard ratios under scenario 2, spending would increase 10-20 billion dollars over 5 years, however this is much less than the 100+ billion if CMS covered all possible beneficiaries at market prices.
- Our analysis ignores legitimate complexity about initiating one of these contracts, including negotiating under uncertainty, adjudication, study design, how to deal with negative payment, and possible inadequacy of 5-year time horizon.
- Additionally, we assume no transaction/administrative costs, and that CMS could cover the drug and not determine their payment rate until many years in the future when definitive CED results were available.
- More work, and real-world implementation studies of this type of pricing structure warrant further study and may be necessary to handle budgets at CMS where numerous biologics with large patient populations are likely to come to marker over the next decade

References
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3. Knopman, David S., David T. Jones, and Michael D. Greicius. "Failure to demonstrate efficacy of aducanumab: An analysis of the EMERGE and ENGAGE trials as reported by Biogen, December 2019." Alzheimer's & Dementia 17.4 (2021): 696-701.