Underestimating the Value of an Intervention: The Case for Including Productivity in Value Assessments and Formulary Design

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ABSTRACT

BACKGROUND: Value assessment reports are increasingly being considered in health care coverage decisions. The inputs included and analytic methodologies underlying these reports should include all components of value.

OBJECTIVE: To determine whether and how productivity was included in a value assessment, compare the incremental cost per quality-adjusted life-year (cost/QALY) estimates with and without productivity, assess if inclusion of productivity changed the value category and estimate the direction and magnitude of change.

METHODS: We reviewed pharmaceutical value assessment reports published between March 2017 and July 2019 by the Institute for Clinical and Economic Review (ICER) to determine whether productivity was included and how it was reported (i.e., co-base case or scenario analysis). Within each report, we identified unique treatment comparisons for which modelers estimated an incremental cost/QALY. We categorized the incremental cost/QALY estimates using ICER's willingness-to-pay (WTP) categories and assessed if inclusion of productivity changed the value category (i.e., <\$50,000/QALY). For reports that included 2 numerical estimates, we assessed the direction and magnitude of change when productivity was included.

RESULTS: Of the 19 reports that evaluated pharmaceutical treatments, 18 (94.7%) included productivity. Two reports (11.1%) incorporated productivity in a co-base case analysis, and 16 included productivity in a scenario analysis. Across these 18 reports, there were 75 unique comparisons of pharmaceutical interventions. Across the 75 comparisons, 4 (5.3%), 3 (4.0%), 8 (10.6%), and 1 (1.3%) of the coverage decisions would change at the \$50,000/QALY, \$100,000/QALY, \$150,000/QALY, and \$500,000/QALY threshold, respectively. Sixty comparisons included 2 numerical cost/QALY estimates. The magnitude of change in the cost/QALY, after including productivity, ranged from -80.1% to 6.8%. The estimated value increased for 54 (72%), decreased for 5 (6.6%), and did not change for 1 (1.7%) of the comparisons.

CONCLUSIONS: Value assessment should capture the range of costs and benefits of an intervention. The exclusion of productivity costs can alter, often underestimating, the assessment of value. This may affect coverage decisions—inclusion or exclusion from the insurance benefit—based on these assessments. Value assessment reports intended to be used for health care decision making should include productivity and elevate its visibility by using base-case analyses rather than scenario analyses.

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What is already known about this subject

- Work productivity is an important patient-centered component of value that should be included in value assessments of health care interventions.
- Experts recommend that value assessments of health care interventions, based on cost-effectiveness analyses, should be conducted using a societal perspective, alongside the health care sector perspective, to capture the full range of costs and benefits that can drive value.

What this study adds

- Since March 2017, 18 of 19 (94.7%) pharmaceutical value assessment reports from the Institute for Clinical and Economic Review included productivity costs in the report, but only 2 (11.1%) included productivity in a primary (co-base case) analysis.
- Including productivity generally increased the estimated value of a treatment (decreased cost/QALY estimates) but varied in magnitude (-80.1% to 6.8%) and by disease type (orphan vs. nonorphan disease). The value category changed in 2 of 9 (22.2%) comparisons for treatments for orphan diseases and in 14 of 66 (21.2%) comparisons for treatments for nonorphan disease populations.
- To support appropriate patient access to treatments, it is important to include key factors such as productivity in value assessments that may be used by payers to inform coverage decisions in the United States.

As the United States moves toward a value-based payment health care system, there is growing discussion around how to define and measure value. In response to this measurement need, several value assessment frameworks have been developed each with different methods.¹ These frameworks now have real-world implications for patients, and payers, such as CVS, are beginning to use these value assessment frameworks to make coverage decisions.^{2,3} How might these decisions be affected by the exclusion (or inclusion) of a key component of value from the assessment?³

A key component of value often overlooked is productivity. The onset of a new health condition, or the deterioration of an individual's health status, can affect an individual's performance in the workforce or result in inefficient work or missed days from work due to ill-health. Medical treatments can have a positive or negative effect on an individual's health status

and hence affect productivity in a positive or negative manner. Employers often are already providing health insurance coverage for the employee, and expending additional resources to reallocate staff or to train new hires to account for an ill individual's time away from work increases health-related costs for employers.⁴ Therefore, any loss in productivity due to health comes at a cost to both the individual and his or her employer. Given this effect, assessments of the value of health interventions should include productivity.

One method to compare the value of a health intervention with treatment alternatives is cost-effectiveness analysis (CEA), which quantifies the result as an incremental cost-effectiveness ratio presented as dollars per quality-adjusted life-year (cost/QALY). The lower the incremental cost/QALY, the lower the cost to achieve an additional unit of benefit.⁵ To ensure the benefits and costs beyond the health care system are appropriately assessed, experts in health economics and policy have urged the inclusion of productivity in value assessment. The Second Panel on Cost-Effectiveness in Health & Medicine (Second Panel), a group of experts from academia, health care administration, and government who set the standards for reporting cost-effectiveness studies, recommended value assessments include a societal perspective, as a co-base case, which incorporates the effect on nonhealth sectors including productivity, educational achievement, housing, social services, and criminal justice.^{6,7} Other analyses have pointed out that exclusion of such measures can underestimate the value of an intervention.⁸

Underestimation of value can have important implications on the decisions made by policymakers and payers. These incremental cost/QALY figures are sometimes used to identify allocation of resources toward particular interventions and away from others through willingness-to-pay (WTP) thresholds. Although there is controversy around the use of these thresholds in the United States, the Institute for Clinical and Economic Review (ICER) uses a range of thresholds to make CEA-based judgments of value in its assessments: \$50,000, \$100,000, and \$150,000/QALY for most treatments and \$500,000/QALY for orphan drugs.^{9,10} In the United States, CVS has piloted a benefit design that allows formulary exclusions for treatments exceeding the \$100,000/QALY threshold.¹¹ New York State's Drug Utilization Review Board recommended a supplemental rebate for lumacaftor/ivacaftor (Orkambi, Vertex), a cystic fibrosis drug, based on ICER's \$150,000/QALY threshold.¹² Although these plans have been made public, other payers have not announced the use of a specific threshold. Survey research indicates that the percentage of U.S. payers following an ICER cost-effectiveness threshold, throughout the coverage and decision-making process, is growing.^{13,14}

Given the growing use of value assessments in payer decisions, we illustrate how, when productivity is included in value assessments, it can lead to different value categorizations and decisions, which can subsequently affect patient access to care.

Methods

To study the effect of including productivity on an assessment of value, we identified and reviewed all ICER value assessment reports published between March 2017 and July 2019 that focused on pharmaceutical treatments. This time period was chosen because ICER revised its assessment framework and began to quantitatively include work productivity in March 2017. Among the many existing value frameworks, ICER reports were chosen because the 2017 methodologic update provided a large volume of reports suitable for this analysis.¹⁵ One author extracted the data from ICER reports for this study (TK). Two authors reviewed the data before analysis (JG and KW).

Within each report, we identified unique treatment comparisons for which modelers estimated an incremental cost/QALY and noted how it was reported (e.g., co-base case or scenario analysis; see Appendix, available in online article). A co-base case, from the societal perspective, increases the consistency and comparability of evaluations across different patient populations and diseases.^{7,16} If the societal perspective is only taken in the scenario analysis, which was not consistently conducted, end-users may not capture the full effect of an intervention.

We then categorized the incremental cost/QALY estimates into categories created using ICER's WTP thresholds for orphan and nonorphan diseases:

- dominant: less costly, more effective
- < \$50,000/QALY
- \$50,000/QALY to < \$100,000/QALY
- \$100,000/QALY to < \$150,000/QALY
- \$150,000/QALY to < \$500,000/QALY
- > \$500,000/QALY (used only for ultrarare disease)
- dominated: more costly, less effective

We then assessed if the inclusion of productivity costs changed the value category. Finally, for those reports in which 2 numerical estimates of cost/QALY (i.e., incremental cost/QALY values that were not considered dominant or dominated) were provided, 1 with and 1 without productivity, we assessed the direction and estimated the magnitude of change.

Results

Of the 19 ICER reports evaluating pharmaceutical interventions published since March 2017, 18 (94.7%) provided an alternative perspective in which work productivity was considered. One report, regarding therapies for ovarian cancer, did not include work productivity. Two of the 18 reports (11.1%)—for childhood blindness and amyloidosis—were evaluated under ICER's modified framework for ultrarare diseases, which includes the calculation of a cost/QALY with work productivity as part of a co-base case analysis. The remaining 16 (88.8%) reports included work productivity as a scenario analysis.

FIGURE 1 Distribution of Cost/QALY Metrics Across WTP Thresholds (by Productivity Status and Disease Type)

QALY = quality-adjusted life-years; WTP = willingness-to-pay.

The inclusion of productivity changed the categorization of value using ICER's WTP threshold categories for both orphan and nonorphan diseases (Figure 1). Within the 18 reports, we found 75 unique comparisons of pharmaceutical interventions. With the inclusion of productivity, the distribution of cost/QALY estimates shifted to lower threshold (higher value) categories for 16 of the 75 (21.3%) unique treatment comparisons. At the lower and upper bounds of the distribution for nonorphan diseases, little effect was found when excluding or including productivity costs on the dominant (18.18% vs. 19.7%, respectively) and dominated (3.03% vs. 3.03%) WTP categories. We saw a small increase in the number of interventions that fell between cost savings and the \$50,000/QALY category (1.5% vs. 6.1%) and a small decrease in the number of interventions that fell between \$50,000/QALY and \$100,000/QALY (9.1% vs. 7.6%) once productivity was included. Using the \$150,000/QALY threshold, 40.9% of cost/QALY estimates fell below the \$150,000/QALY threshold when productivity was not included but increased to 57.58% of all cost/QALY estimates after productivity costs were incorporated.

For orphan diseases, in which value assessments include the \$500,000/QALY threshold in addition to the \$50,000/QALY-\$150,000/QALY thresholds, we found fewer changes with the majority of the cost/QALY estimates remaining above the \$500,000/QALY threshold (88.89% vs. 77.78%).

The value category changed in 2 of 9 (22.2%) comparisons for treatments for orphan diseases and in 14 of 66 (21.2%) comparisons for treatments for nonorphan disease populations.

Across the 75 comparisons, 4 (5.3%), 3 (4%), 8 (10.6%), and 1 (1.3%) of the coverage decisions would change at the \$50,000/QALY, \$100,000/QALY, \$150,000/QALY, and \$500,000/QALY threshold, respectively.

Although the inclusion of productivity generally improved the assessment of value, this was not uniform across all treatment comparisons. We calculated a percentage difference (Figure 2) among the 60 comparisons in which 2 numerical cost/QALY estimates were provided (1 with and 1 without productivity). For 54 (90.0%) of the 60 comparisons, inclusion of productivity costs improved the estimated value, decreasing

FIGURE 2 Change (%) in Cost/QALY with Inclusion of Productivity Costs

Note: This graph includes unique comparisons in which there were 2 numerical cost/QALY estimates used to calculate a percentage change (n=60). Multiple treatment comparisons within a single report are indicated using a number. For example, there were 2 unique treatment comparisons for chronic migraine (erenumab vs. no preventive treatment; fremanezumab vs. no preventive treatment).

^aIndicates a comparison in which the percentage change in cost/QALY led to a change in WTP threshold categorization.

NHL = non-Hodgkin leukemia; QALY = quality-adjusted life-year; WTP = willingness-to-pay.

the incremental cost/QALY by -0.5% to -80.1%. For 5 (8.3%) comparisons, the incremental cost/QALY increased by 0.1% to 6.8% representing a decrease in value. For 1 (1.7%) comparison, there was no change.

For 16 of these 60 (26.7%) comparisons, including productivity changed the ICER value category. These changes occurred across various therapeutic areas—chronic migraine, vision loss, arthritis, psoriasis, endometriosis, and peanut allergies (see footnoted conditions in Figure 2).

Discussion

The effects of poor health are felt beyond the health care sector.¹⁷⁻¹⁹ Our review highlights that work productivity can and does have an effect on the assessment of value. Although the magnitude of change varied widely, most of the comparisons in our analysis saw an improvement in value—or a reduction in cost/QALY—when productivity was included. With the recent focus on value assessment to inform formulary coverage decisions, this can have a tangible effect on patient access.

Although several nonhealth care sectors can be affected by health interventions, this study focused on productivity costs given the data most consistently and systematically provided in ICER reports. By focusing solely on productivity costs, we

were able to include a larger number of comparisons as part of our analytic sample and ensure an appropriate comparison between cost/QALY estimates. The decision to formally include productivity in an analysis from the societal perspective was a prominent change as part of the methodologic revisions to ICER's framework and provided the opportunity to analyze this component of value.^{14,15}

Incorporating the costs and benefits of work productivity has challenges. For example, the report on ovarian cancer did not include any analyses from a societal perspective. The report states that “given the typically advanced age [of] and severity of disease” in ovarian cancer patients, there was “limited evidence on indirect costs, employment levels, and time missed at work.”²⁰ However, for some women, as noted in the ICER report, ovarian cancer can occur in their 30s and 40s when they are “immersed in careers, civic engagement, or parenting.”²⁰ Limited evidence available to estimate the productivity costs is a pervasive issue. Several existing instruments and databases already collect the type of data necessary to calculate productivity costs; however, additional efforts are necessary to fill gaps in data.^{21,22} Future efforts to identify therapeutic areas in which productivity has the greatest effect could inform targeted data collection efforts. Although an important

component of CEA methodology, experts have cautioned about the potential drawbacks of estimating and including productivity. Using the WTP approach could result in double counting of the value of productivity in the incremental cost/QALY estimate—in the estimation of costs in the numerator and in the estimation of utility, or the quality component of the QALY, in the denominator.²³ Additionally, whereas most models, including those developed by ICER, use the human capital approach to value productivity, the friction cost approach may provide a more accurate estimation of net productivity loss when a new, healthy employee is hired in place of an employee in ill-health.²³

Although health economists agree productivity costs should be included as a co-base case in value assessments, how these costs are presented in the final reports matters. Some modelers include productivity in a co-base case analysis from the societal perspective, consistent with the recommendations of the Second Panel. For example, ICER's ultrarare disease framework uses this approach. Models by the Innovation and Value Initiative also use a broad societal approach.²⁴ However, in most of the reports we reviewed, ICER included productivity as a scenario analysis, which is not included in report summaries. This limits the visibility of productivity estimates to end-users, potentially excluding important costs and benefits from the decision-making process for payers.

The effect of changes in an individual's work productivity extend beyond the individual. Employers face the costs of replacing a sick employee and experience the business effect of lost work time due to an employee in ill-health.²⁵ Previous research has quantified this potential productivity loss borne by employers when employees experience a range of health conditions.²⁶ In the U.S. health care system, employers also play a significant role in paying for health care benefits and an increasing role in employee wellness.²⁵ If they face these costs for their employees and health plans are making benefit design decisions using value assessments, it follows employers would want productivity to be factored into those assessments.²⁷

This review demonstrates that leaving productivity out of assessments can underestimate the value of a therapeutic intervention. For payers using ICER's WTP thresholds as a criterion for determining coverage, decisions on what to cover and for whom could change, subsequently affecting patient access to therapies.

Limitations

Our review of value assessment reports has some limitations worth noting. First, we were limited to the conditions and comparisons covered in the existing reports. Inclusion of productivity in specific clinical conditions and comparisons (i.e., migraines or vision loss) changed the value of the intervention but may not hold true in other clinical contexts.

Second, our review and conclusions were constrained by the data and evidence used in the reports to estimate productivity. Using different data sources or studies may yield different cost/QALY estimates. Although we note the risks of underestimating value using cost/QALY estimates, the overestimation of value may lead to an alternate allocation of resources that may similarly affect coverage. Payers have finite resources with which to provide coverage and an accurate estimate of value is important to ensure the appropriate allocation of those resources.

Third, ICER's value assessment reports are specific to the context of the U.S. health care system and may not be generalizable to international settings. Fourth, the value assessment reports in this review focus on pharmaceutical products. Understanding the value of various health interventions is beneficial to a broad audience; however, the application of value assessments in the United States has largely focused on pharmaceutical products.

Finally, in reports for select therapeutic areas, such as opioid use disorder, vision loss, and amyloidosis, modelers incorporated nonhealth care factors in addition to productivity in the analysis from the societal perspective. Although we cannot isolate the effect of productivity on the value estimate in these cases, it emphasizes the importance of measuring value holistically and the effects of health or ill-health beyond clinical outcomes.

Conclusions

We found productivity costs were often included in an alternative, rather than primary, assessment of value in cost-effectiveness analysis-based value assessment reports. Overall, when included, productivity costs and benefits generally increased the estimated value of an intervention although the magnitude varied widely. Although the formal use of value thresholds in benefit design is in its early stages and effect on coverage decisions may vary with choice of threshold, the potential role of productivity in assigning value to pharmaceutical therapies is important.

Payers, facing the reality of finite resources, are increasingly looking to quantitative metrics found in value assessment reports to help inform benefit design. Because the inclusion of productivity, valued by both patients and employers, might change the determination of value, it is critical that value assessment reports intended to be used for health care decision-making both include productivity and ensure its visibility by using co-base case analysis rather than scenario analysis. Health plans using assessments that exclude productivity risk inappropriate restrictions on patient access to treatments that have been undervalued. To support value-based access to treatments, it is important to include key factors such as productivity in value assessments that may be used by payers to inform coverage decision.

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APPENDIX List of Treatment Comparisons Across All Reports

#	Disease/ Condition	Drug/ Intervention	Comparator	Cost/QALY (without productivity)	Cost/QALY (with productivity)	Changes ICER Threshold Category?	% Change	Base Case vs. Scenario	Model Perspective	ICER Thresholds for Comparison
1	Chronic Migraine	erenumab	no preventive treatment	\$90,000	\$50,000	Y	-44.40%	Scenario	Health system	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
2	Chronic Migraine	fremanezumab	no preventive treatment	\$120,000	\$80,000	Y	-33.30%	Scenario	Health system	
3	Episodic Migraine	erenumab	no preventive treatment	\$150,000	\$110,000	N	-26.70%	Scenario	Health system	
4	Episodic Migraine	fremanezumab	no preventive treatment	\$150,000	\$110,000	N	-26.70%	Scenario	Health system	
5	Cystic Fibrosis - Gaiting & Residual Function Mutations	ivacaftor	best supportive care	\$956,762	\$952,061	N	-0.50%	Scenario	Health system and societal	\$50,000/QALY, \$100,000/QALY, \$150,000/QALY, \$200,000/QALY, \$300,000/QALY and \$500,000/ QALY
6	Cystic Fibrosis - Homozygous for F508del Mutation	lumacaftor/iva- caftor	best supportive care	\$890,739	\$885,140	N	-0.60%	Scenario	Health system and societal	
7	Cystic Fibrosis - Homozygous for F508del Mutation	texacaftor/iva- caftor	best supportive care	\$974,348	\$968,744	N	-0.60%	Scenario	Health system and societal	
8	Cystic Fibrosis - Heterozygous for F508del Mutation	ivacaftor	best supportive care	\$941,110	\$936,633	N	-0.50%	Scenario	Health system and societal	
9	Cystic Fibrosis - Heterozygous for F508del Mutation	texacaftor/iva- caftor	best supportive care	\$840,568	\$835,987	N	-0.50%	Scenario	Health system and societal	
10	Pediatric B-ALL (Peds CAR-T)	tisagenlecleucel	chemotherapy	\$45,871	\$46,875	N	2.20%	Scenario	Third-Party Payer	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
11	Adults with NHL (Adult CAR-T)	axicabtagene ciloleucel	chemotherapy	\$136,078	\$137,717	N	1.20%	Scenario	Third-Party payer	
12	Tardive Dyskinesia	valbenazine	placebo	\$752,080	\$728,000	N	-3.20%	Scenario	Health System	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
13	Tardive Dyskinesia	deutetrabenazine	placebo	\$1,100,773	\$1,077,000	N	-2.20%	Scenario	Health system	
14	Blindness - 15 year olds	voritegene neparvovec	standard of care	\$643,800	\$480,100	Y	-25.40%	Co-base case	Health System and Societal	\$50,000/QALY, \$100,000/QALY, \$150,000/QALY, \$250,000/QALY and \$500,000/ QALY
15	Blindness - 3 year olds	voritegene neparvovec	standard of care	\$287,915	\$135,331	Y	-53.00%	Co-base case	Health system and societal	

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APPENDIX List of Treatment Comparisons Across All Reports (continued)

#	Disease/ Condition	Drug/ Intervention	Comparator	Cost/QALY (without productivity)	Cost/QALY (with productivity)	Changes ICER Threshold Category?	% Change	Base Case vs. Scenario	Model Perspective	ICER Thresholds for Comparison
16	Amyloidosis	inotersen	best supportive care	\$1,730,000	\$1,730,000	N	0.00%	Co-base case	Health system and societal	\$50,000/QALY, \$100,000/QALY, \$150,000/QALY and \$500,000/ QALY
17	Amyloidosis	patisiran	best supportive care	\$835,000	\$853,000	N	2.10%	Co-base case	Health system and societal	
18	Arthritis	rituximab	cDMARD	\$198,056	\$159,880	N	-23.80%	Scenario	Health System	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
19	Arthritis	abatacept (iv)	cDMARD	\$191,317	\$152,784	N	-25.20%	Scenario	Health System	
20	Arthritis	abatacept (sc)	cDMARD	\$225,853	\$188,200	N	-20.00%	Scenario	Health System	
21	Arthritis	tocilizumab (iv)	cDMARD	\$183,949	\$145,555	Y	-26.30%	Scenario	Health System	
22	Arthritis	tocilizumab (sc)	cDMARD	\$168,660	\$130,522	Y	-29.20%	Scenario	Health System	
23	Arthritis	tofacitinib	cDMARD	\$271,749	\$232,738	N	-16.70%	Scenario	Health System	
24	Arthritis	adalimumab	cDMARD	\$232,644	\$193,763	N	-20.10%	Scenario	Health System	
25	Arthritis	certolizumab pegol	cDMARD	\$209,736	\$169,724	N	-23.50%	Scenario	Health System	
26	Arthritis	etanercept	cDMARD	\$212,021	\$173,345	N	-22.30%	Scenario	Health System	
27	Arthritis	golimumab (sc)	cDMARD	\$222,380	\$183,025	N	-21.50%	Scenario	Health System	
28	Arthritis	golimumab (iv)	cDMARD	\$204,212	\$165,380	N	-23.40%	Scenario	Health System	
29	Arthritis	infliximab	cDMARD	\$202,824	\$164,194	N	-23.50%	Scenario	Health System	
30	Arthritis	rituximab	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
31	Arthritis	abatacept (iv)	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
32	Arthritis	abatacept (sc)	adalimumab	\$163,376	\$137,017	Y	-19.20%	Scenario	Health System	
33	Arthritis	tocilizumab (iv)	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
34	Arthritis	tocilizumab (sc)	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
35	Arthritis	tofacitinib	adalimumab	More costly, less effective	More costly, less effective	N	N/A	Scenario	Health System	
36	Arthritis	certolizumab pegol	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
37	Arthritis	etanercept	adalimumab	\$119,233	\$81,481	Y	-46.30%	Scenario	Health System	
38	Arthritis	golimumab (sc)	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
39	Arthritis	golimumab (iv)	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	
40	Arthritis	infliximab	adalimumab	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health System	

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APPENDIX List of Treatment Comparisons Across All Reports (continued)

#	Disease/ Condition	Drug/ Intervention	Comparator	Cost/QALY (without productivity)	Cost/QALY (with productivity)	Changes ICER Threshold Category?	% Change	Base Case vs. Scenario	Model Perspective	ICER Thresholds for Comparison
41	Prostate Cancer	apalutamide + ADT	continued ADT	\$67,924	\$67,924	N	0.00%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
42	Prostate Cancer	enzalutamide + ADT	continued ADT	\$84,000	\$83,333	N	-0.80%	Scenario	Health Sector	
43	Psoriasis	adalimumab	non-targeted treatment	\$164,000	\$141,000	Y	-16.30%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
44	Psoriasis	apremilast	non-targeted treatment	\$135,000	\$111,000	N	-21.60%	Scenario	Health Sector	
45	Psoriasis	brodalumab	non-targeted treatment	\$131,000	\$109,000	N	-20.20%	Scenario	Health Sector	
46	Psoriasis	certolizumab pegol	non-targeted treatment	\$188,000	\$165,000	N	-13.90%	Scenario	Health Sector	
47	Psoriasis	etanercept	non-targeted treatment	\$175,000	\$151,000	N	-15.80%	Scenario	Health Sector	
48	Psoriasis	guselkumab	non-targeted treatment	\$161,000	\$139,000	Y	-15.80%	Scenario	Health Sector	
49	Psoriasis	infliximab	non-targeted treatment	\$134,000	\$111,000	N	-20.70%	Scenario	Health Sector	
50	Psoriasis	ixekizumab	non-targeted treatment	\$142,000	\$120,000	N	-18.30%	Scenario	Health Sector	
51	Psoriasis	secukinumab	non-targeted treatment	\$145,000	\$123,000	N	-17.80%	Scenario	Health Sector	
52	Psoriasis	ustekinumab	non-targeted treatment	\$169,000	\$146,000	Y	-15.70%	Scenario	Health Sector	
53	Endometriosis	elagolix 200 mg twice daily (long-run)	no active treat- ment	\$81,000	\$48,900	Y	-65.60%	Scenario	Health Sector	
54	Hemophilia A in >12 years old	emicizumab	no prophylaxis	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health Sector	
55	Hemophilia A in > 12 years old	emicizumab	BPA prophylaxis	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health Sector	
56	Hemophilia A in <12 years old	emicizumab	no prophylaxis	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health Sector	
57	Hemophilia A in <12 years old	emicizumab	BPS prophylaxis	Less costly, more effective	Less costly, more effective	N	N/A	Scenario	Health Sector	
58	Asthma	omalizumab	Standard of care	\$325,000	\$303,000	N	-7.26%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
59	Asthma	mepolizumab	Standard of Care	\$344,000	\$320,000	N	-7.50%	Scenario	Health Sector	
60	Asthma	reslizumab	Standard of Care	\$391,000	\$364,000	N	-7.42%	Scenario	Health Sector	
61	Asthma	benralizumab	Standard of Care	\$371,000	\$342,000	N	-8.48%	Scenario	Health Sector	
62	Asthma	dupilumab	Standard of Care	\$351,000	\$327,000	N	-7.34%	Scenario	Health Sector	

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APPENDIX List of Treatment Comparisons Across All Reports *(continued)*

#	Disease/ Condition	Drug/ Intervention	Comparator	Cost/QALY (without productivity)	Cost/QALY (with productivity)	Changes ICER Threshold Category?	% Change	Base Case vs. Scenario	Model Perspective	ICER Thresholds for Comparison
63	Hereditary Angioedema	Cinryze	No Prophylaxis	\$5,954,000	\$4,367,000	N	-36.34%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY, \$150,000/QALY, \$250,000/QALY and \$500,000/ QALY
64	Hereditary Angioedema	Haegarda	No Prophylaxis	\$328,000	\$257,000	N	-27.63%	Scenario	Health Sector	
65	Hereditary Angioedema	Lanadelumab	No Prophylaxis	\$1,108,000	\$1,189,000	N	6.81%	Scenario	Health Sector	
66	Opioid Use Disorder	Vivitrol	Generic SL Buprenorphine/ Naloxone)	More costly, less effective	More costly, less effective	N	N/A	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
67	Opioid Use Disorder	Probuphine	Generic SL Buprenorphine/ Naloxone)	\$265,000	less costly, more effective	Y	N/A	Scenario	Health Sector	
68	Spinal Muscular Atrophy	Spinraza	Best supportive care	\$1,112,000	\$1,124,000	N	1.08%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY, \$150,000/QALY, \$200,000/QALY, \$300,000/QALY and \$500,000/ QALY
69	Spinal Muscular Atrophy	Zolgensma	Best supportive Care	\$243,000	\$238,000	N	-2.06%	Scenario	Health Sector	
70	Peanut Allergy	AR101 oral immunotherapy + avoidance	Avoidance	\$88,000	\$27,000	Y	-69.32%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
71	Peanut Allergy	Viaskin Peanut + avoidance	Avoidance	\$216,000	\$155,000	N	-28.24%	Scenario	Health Sector	
72	Peanut Allergy	AR101 oral immunotherapy + avoidance	Avoidance	\$88,000	Range \$24,500 - \$17,500	Y	(-72.1% to -80.1%)	Scenario	Health Sector	
73	Peanut Allergy	Viaskin Peanut + avoidance	Avoidance	\$216,000	Range \$140,000 - \$100,000	Y	(-35.1% to -53.7%)	Scenario	Health Sector	
74	Multiple Sclerosis (Overall SPMS population)	Siponimod	Best supportive care	\$1,150,000	\$1,140,000	N	-0.87%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY
75	Treatment- Resistant Depression	Esketamine nasal spray + background antidepressant	Background anti- depressant alone	\$198,000	\$188,000	N	-5.05%	Scenario	Health Sector	\$50,000/QALY, \$100,000/QALY and \$150,000/ QALY

ADT = androgen deprivation therapy; B-ALL = B-cell acute lymphoblastic leukemia; BPA = bisphenol A; BPS = best practice statement; cDMARD = conventional disease-modifying antirheumatic drugs; ICER = incremental cost-effectiveness ratio; iv = intravenous; NHL = non-Hodgkin leukemia; QALY = quality-adjusted life-year; sc = subcutaneous.