Appendix A
Assumptions and inputs for traditional cost-effectiveness ratios

Table of contents

Contents

A1 – Trikafta

Literature

- Tice JA, Kuntz KM, Wherry K, Chapman R, Seidner M, Pearson SD, Rind DM. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value; Final Evidence Report and Meeting Summary. Institute for Clinical and Economic Review, September 23, 2020. https://icer.org/wp-content/uploads/2020/08/ICER_CF_Final_Report_092320.pdf

Commentary

- We used the Population 4 scenario from Tice et al. (2020), which models treatment with Trikafta beginning at age 12. Other scenarios in the report involved treatments outside the scope of this case study—specifically, Kalydeco beginning at 6 months (Populations 1 and 3) and Orkambi beginning at 2 years (Population 2).

A1.1 Annual undiscounted drug cost

- Intervention: $311,741 — from Tice et al. (2020), Table 5.5 ("Drug cost inputs"), column "Annual drug cost."
- Comparator: $0 — per Tice et al. (2020), p. E7: "The comparator for each population is best supportive care (BSC) and, where applicable, the other interventions with an indication for that population." Table 5.9 confirms the cost of BSC as zero.

A1.2 Total undiscounted cost

- Intervention: $13,455,000.
- Comparator: $3,449,000.
- Values are from Tice et al. (2020), Table E2 ("Total cost"), section "Population 4."

A1.3 Total undiscounted life years

- Intervention: 40.32.
- Comparator: 26.22.
- Values are from Tice et al. (2020), Table ES2 ("Total Life Years"), section "Population 4."

A1.4 Total undiscounted QALYs

- Intervention: 28.38.
- Comparator: 17.21.
- Values are from Tice et al. (2020), Table E2 ("Total QALYs"), section "Population 4."

A1.5 Annual undiscounted non-drug cost

- Intervention: $21,964 — calculated as total undiscounted cost ($13,455,000; see A1.2) divided by total life years (40.32; see A1.3), minus annual drug cost ($311,741; see A1.1).
- Comparator: $131,541 — calculated as total undiscounted cost ($3,449,000; see A1.2) divided by total life years (26.22; see A1.3).

A1.6 Average utility weight

- Intervention: 0.70 — total undiscounted QALYs (28.38; see A1.4) divided by total life years (40.32; see A1.3).
- Comparator: 0.66 — total undiscounted QALYs (17.21; see A1.4) divided by total life years (26.22; see A1.3).

A1.7 Duration of drug use (Tufts calculator only)

- Intervention: 40.32 years — patients were assumed to receive Trikafta throughout their lifetime, corresponding to the total life expectancy (see A1.3).
- Comparator: Not applicable (see A1.1).

A1.8 Analysis time horizon

- Tufts calculator: Lifetime (see A1.3).
- GCEA calculator: 70 years (personal communication, Richard Xie, No Patient Left Behind, August 19, 2025).

A2 – Xtandi

Literature

- Wilson L, Tang J, Zhong L, et al. New therapeutic options in metastatic castration-resistant prostate cancer: Can cost-effectiveness analysis help in treatment decisions? J Oncol Pharm Pract. 2014;20(6):417–425. doi:10.1177/1078155213509505

Commentary

- The authors did not discount costs or effects, stating: "No discounting was used due to the short time-horizon." However, we applied discounting because outcomes accrue to future cohorts over time (see Appendix A2.1).

A2.1 Undiscounted drug cost for 18 months

- Intervention: $62,266 — from Wilson et al. (2014), Table 2 ("Costs used in the decision model"), row "Drug costs – enzalutamide."
- Comparator: $47,577 — from the same table, row "Drug costs – abiraterone."
- Table 2 provides model inputs for an 18-month time horizon. The article explains: "A model time-horizon of 18 months was used for costs and outcomes and to model lifetime survival. No discounting was used due to the short time-horizon (Figure 1)." Therefore, it is reasonable to assume the costs in Table 2 reflect an 18-month period.

A2.2 Total undiscounted cost

- Intervention: $129,769.
- Comparator: $116,700.
- Values are from Wilson et al. (2014), Table 5.

A2.3 Total undiscounted life years

- Intervention: 1.50.
- Comparator: 1.47.
- Values are from Wilson et al. (2014), Table 4, row "LE overall."

A2.4 Total undiscounted QALYs

- Intervention: 0.73.
- Comparator: 0.70.
- Values are from Wilson et al. (2014), Table 5.

A2.5 Annual undiscounted drug cost

- Intervention: $41,511 — $62,266 ÷ 1.5 years (see A2.1).
- Comparator: $31,718 — $47,577 ÷ 1.5 years (see A2.1).

A2.6 Annual undiscounted non-drug cost

- Intervention: $45,002 — total cost ($129,769; see A2.2) ÷ life years (1.5; see A2.3), minus annual drug cost ($41,511; see A2.5).
- Comparator: $47,670 — total cost ($116,700; see A2.2) ÷ life years (1.47; see A2.3), minus annual drug cost ($31,718; see A2.5).

A2.7 Average utility weight

- Intervention: 0.49 — total QALYs (0.73; see A2.4) ÷ total life years (1.5; see A2.3).
- Comparator: 0.48 — total QALYs (0.70; see A2.4) ÷ total life years (1.47; see A2.3).

A2.8 Duration of drug use (Tufts calculator only)

- Patients were assumed to receive treatment throughout their lifetime. Thus, the duration of drug use equals total life expectancy (see A2.3).
- Intervention: 1.5 years.
- Comparator: 1.47 years.

A2.9 Analysis time horizon

- Tufts calculator: Total undiscounted life years modeled (see A2.3).
- GCEA calculator: 10 years (personal communication, Richard Xie, No Patient Left Behind, August 19, 2025).

A3 – Vyndaqel

Literature

- Kazi DS, Bellows BK, Baron SJ, et al. Cost-Effectiveness of Tafamidis Therapy for Transthyretin Amyloid Cardiomyopathy. Circulation. 2020;141(15):1214–1224. doi:10.1161/CIRCULATIONAHA.119.045093

Commentary

- No additional comments.

A3.1 Annual undiscounted drug cost

- Intervention: $225,000 — from Kazi et al. (2020), Table 1 ("Input Parameters"), row "Tafamidis therapy, USD per year."
- Comparator: $0 — the article states, "We evaluated the effect of tafamidis compared with no disease-specific ATTR-CM treatment ('usual care')."

A3.2 Total discounted drug cost

- Intervention: $1,086,000 — from Kazi et al. (2020), Table 2 ("Base Case Results"), row "Spending on Tafamidis."
- Comparator: $0 — see A3.1.

A3.3 Total discounted cost

- Intervention: $1,262,000.
- Comparator: $126,000.
- Values are from Kazi et al. (2020), Table 2 ("Base Case Results").

A3.4 Total undiscounted life years

- Intervention: 5.43.
- Comparator: 3.46.
- Values are from Kazi et al. (2020), Table 2 ("Base Case Results"), row "Survival, life years (undiscounted)."

A3.5 Total discounted QALYs

- Intervention: 3.48.
- Comparator: 2.19.
- Values are from Kazi et al. (2020), Table 2 ("Base Case Results"), row "Quality-adjusted survival, QALYs (discounted)."

A3.6 Total discounted non-drug cost

- Intervention: $176,000 — total discounted cost ($1,262,000; see A3.3) minus discounted drug cost ($1,086,000; see A3.2).
- Comparator: $126,000 — total discounted cost ($126,000; see A3.3) minus discounted drug cost ($0; see A3.2).

A3.7 Annual undiscounted non-drug cost

- Intervention: $34,570 — assumes a discounted non-drug cost of $176,000 (see A3.6), a 3% discount rate, and a 5.43-year duration (see A3.4). Converted to an annual value using the Excel formula: $PMT(0.03, 5.43, -176000, ,1)$
- Comparator: $37,749 — assumes a discounted non-drug cost of $126,000 (see A3.6), a 3% discount rate, and a 3.46-year duration (see A3.4). Converted to an annual value using the same method.

A3.8 Average utility weight

- Intervention: 0.68 — based on total discounted QALYs (3.48; see A3.5), a duration of 5.43 life years (see A3.4), and a 3% discount rate. Calculated using the Excel PMT function to derive annual QALYs and, hence, the average utility weight (see A3.7).
- Comparator: 0.66 — based on total discounted QALYs (2.19; see A3.5), a duration of 3.46 life years (see A3.4), and a 3% discount rate. Calculated using the same method (see A3.7).

A3.9 Duration of drug use (Tufts calculator only)

- Intervention: 5.43 years — assumes treatment for the full lifetime (undiscounted life years; see A3.4).
- Comparator: Not applicable (see A3.1).

A3.10 Analysis time horizon

- Tufts calculator: Lifetime (see A3.4).
- GCEA calculator: 30 years (personal communication, Richard Xie, No Patient Left Behind, August 19, 2025).

A4 – Ibrance

Literature

- Mamiya H, Tahara RK, Tolaney SM, Choudhry NK, Najafzadeh M. Cost-effectiveness of palbociclib in hormone receptor–positive advanced breast cancer. Ann Oncol. 2017;28(8):1825–1831. doi:10.1093/annonc/mdx201

Commentary

- We assumed that the duration of drug use equals progression-free survival (PFS). Supplement S1 of Mamiya et al. indicates that patients switched to second-line treatment once their disease progressed.
- The intervention arm included both palbociclib and letrozole. As the article explains: "Treatment-naïve patients were assigned to PAL (125 mg/day for 3 weeks, followed by 1 week off) plus LET (2.5 mg daily) or LET as first-line endocrine therapy."

A4.1 Annual undiscounted drug cost

- Intervention: $136,940 — calculated as the 4-week cost of palbociclib ($9,850) plus the 4-week cost of letrozole ($655), multiplied by the number of 4-week periods in a year (365 ÷ 7 ÷ 4).
- Comparator: $8,538 — calculated as $655 × (365 ÷ 7 ÷ 4).
- Values are from Mamiya et al. (2017), Table 1 ("Input parameters"), rows "LET/4 week" and "PAL/4 week."

A4.2 Total discounted cost

- Intervention: $372,761.
- Comparator: $128,435.
- Values are from Mamiya et al. (2017), Table 2, section "Patients who had not received any endocrine treatment," rows "PAL+LET" and "LET."

A4.3 Total undiscounted life years

- Intervention: 3.15 — based on a median overall survival of 37.8 months (Table S3, "Median overall survival on palbociclib + letrozole"), divided by 12.
- Comparator: 2.775 — based on 33.3 months (Table S3, "Median overall survival on letrozole"), divided by 12.

A4.4 Total undiscounted progression-free survival (PFS) years

- Intervention: 1.69 — from Table S3, "Median progression-free survival on palbociclib + letrozole as first-line endocrine therapy," reported as 20.3 months (20.3 ÷ 12).
- Comparator: 0.83 — from Table S3, "Median progression-free survival on letrozole as first-line endocrine therapy," reported as 10.0 months (10.0 ÷ 12).

A4.5 Total discounted QALYs

- Intervention: 2.13.

- Comparator: 1.82.
- Values are from Mamiya et al. (2017), Table 2, section "Patients who had not received any endocrine treatment," rows "PAL+LET" and "LET."

A4.6 Total discounted drug cost

- Intervention: $229,317 — calculated assuming an annual drug cost of $136,940 (see A4.1), a 1.69-year PFS period (see A4.4), and a 3% discount rate, using the Excel formula:
- $PV(0.03, 1.69, -136940, , 1)$
- Comparator: $7,133 — calculated assuming an annual drug cost of $8,538 (see A4.1), a 0.83-year PFS period (see A4.4), and a 3% discount rate, using the same method.

A4.7 Total discounted non-drug cost

- Intervention: $143,444 — total discounted cost ($372,761; see A4.2) minus discounted drug cost ($229,317; see A4.6).
- Comparator: $121,302 — total discounted cost ($128,435; see A4.2) minus discounted drug cost ($7,133; see A4.6).

A4.8 Annual undiscounted non-drug cost

- Intervention: $46,993 — assumes lifetime non-drug costs of $143,444 (see A4.7), 3.15 years of use (see A4.3), and a 3% discount rate. Calculated using the Excel PMT function (see A3.7).
- Comparator: $44,863 — assumes lifetime non-drug costs of $121,302 (see A4.7), 2.775 years of use (see A4.3), and a 3% discount rate. Calculated using the same method.

A4.9 Average utility weight

- Intervention: 0.70 — based on total discounted QALYs (2.13; see A4.5), duration of 3.15 life years (see A4.3), and a 3% discount rate. Calculated using the Excel PMT function (see A3.7).
- Comparator: 0.67 — based on total discounted QALYs (1.82; see A4.5), duration of 2.775 life years (see A4.3), and a 3% discount rate. Calculated using the same method.

A4.10 Duration of drug use (Tufts calculator only)

- Intervention: 1.69 years.
- Comparator: 0.83 years.
- We assumed patients use each drug throughout the PFS period (see Commentary and A4.4).

A4.11 Analysis time horizon

- Tufts calculator: Lifetime (see overall survival in A4.3).
- GCEA calculator: 10 years (personal communication, Richard Xie, No Patient Left Behind, August 19, 2025).

A5 – Eylea

Literature

- Brown GC, Brown MM, Rapuano S, Boyer D. Cost-Utility Analysis of VEGF Inhibitors for Treating Neovascular Age-Related Macular Degeneration. Am J Ophthalmol. 2020;218:225–241. doi:10.1016/j.ajo.2020.05.029

Commentary

- The model used an 11-year time horizon, which was also the assumed lifetime for both the intervention and the comparator.
- The authors did not report total QALYs for either the intervention or the comparator. Instead, they reported incremental QALY gains relative to the baseline for both arms. Taking the difference between the incremental QALY gains does not affect the delta QALY calculation.

A5.1 Total discounted cost

- Intervention: $61,811.
- Comparator: $14,772.
- Values are from Brown et al. (2020), Table 4, row "Total direct ophthalmic medical cost per average patient."

A5.2 Ratio of total drug cost to total cost

- Intervention: 79.3%.
- Comparator: 27.4%.
- Values are from Brown et al. (2020), Table 4, row "Bilateral drug cost/direct ophthalmic medical cost per average patient."

A5.3 Total discounted drug cost

- Intervention: $49,016 — computed as $61,811 × 79.3% (see A5.1–A5.2).
- Comparator: $4,048 — computed as $14,772 × 27.4% (see A5.1–A5.2).

A5.4 Total discounted non-drug cost

- Intervention: $12,795 — computed as $61,811 × 20.7% (one minus 79.3%; see A5.2).
- Comparator: $10,724 — computed as $14,772 × 72.6% (one minus 27.4%; see A5.2).

A5.5 Annual undiscounted drug cost (average over 11 years)

- Intervention: $4,456 — $49,016 ÷ 11 life-years (see A5.3 and Commentary).
- Comparator: $368 — $4,048 ÷ 11 life-years (see A5.3 and Commentary).

A5.6 Annual undiscounted non-drug cost (average over 11 years)

- Intervention: $1,163 — $12,795 ÷ 11 life-years (see A5.4 and Commentary).
- Comparator: $975 — $10,724 ÷ 11 life-years (see A5.4 and Commentary).

A5.7 Total discounted incremental QALYs

- Intervention: 1.380.
- Comparator: 1.339.
- Values are from Brown et al. (2020), Table 9, "Societal cost perspective, Combined-eye model," columns "Aflibercept" and "Bevacizumab."

A5.8 Average utility weight (derived)

- Intervention: 0.1448.
- Comparator: 0.1405.
- These values were calculated using the Excel PMT function, assuming the total discounted incremental QALYs in A5.7, an 11-year duration, and a 3% discount rate. The rationale for using incremental rather than total QALYs is described at the start of Appendix A5. See Appendix A3.7 for the calculation method.

A5.9 Duration of drug use (Tufts calculator only)

- Assumed to be 11 years for both arms; see Commentary.

A5.10 Analysis time horizon

- Tufts calculator: Duration of drug use (A5.9).
- GCEA calculator: 11 years (personal communication, Richard Xie, No Patient Left Behind, August 19, 2025).

Notes for Excel functions

Excel PMT Function

Calculates the periodic nominal payment assuming a specified interest rate, number of periods, initial principal, amount still owed following the last payment, and a payment type (beginning or end of period).

1. Source: https://support.microsoft.com/en-us/office/pmt-function-0214da64-9a63-4996-bc20-214433fa6441
2. Syntax: $PMT(rate, nper, pv, [fv], [type])$
3. Arguments:
   - $rate$ (required) – interest rate per period; equivalently, the rate used to discount future income and payments.
   - $nper$ (required) – number of payment periods.
   - pv (required) – The present value of the amount borrowed at time zero (also known as the principal.
   - fv (optional) – The future value attained following the last payment. If fv is omitted, PMT assumes its value to be zero. That is, it assumes that the value of the repayments equals pv.
   - $Type$ (optional) – Indicates when payments are due (0: end of period; 1: beginning of period).

Excel PV function

Calculates the present value of a series of payments, minus a future value remaining following the last payment, assuming a specified interest rate, a specified number of periods, a nominal payment each period, and a payment type (beginning or end of period).

Calculates the present value of a stream of periodic payments.

1. Source: https://support.microsoft.com/en-us/office/pv-function-23879d31-0e02-4321-be01-da16e8168cbd
2. Syntax: $PV(rate, nper, pmt, [fv], [type])$
3. Arguments:
   - $rate$ (required) – interest rate per period; equivalently, the rate used to discount future income and payments.
   - $nper$ (required) – number of payment periods.
   - pmt (required) – The nominal payment made during each period.
   - fv (optional) – The future value attained following the last payment. If fv is omitted, PV assumes its value to be zero.
   - $Type$ (optional) – Indicates when payments are due (0: end of period; 1: beginning of period).