**Comparative cost-effectiveness of CIC prescription drug therapies and usual care.** Results are displayed according to different responder endpoints based on availability of data in integrated analyses. For this analysis, efficacy outcomes were extracted for each endpoint from recent network meta-analyses and systematic reviews4,5,7 and verified against relevant source data (FDA approval documents, integrated analyses, and clinical trials). Costs are rounded to the nearest whole US dollar ($). The primary responder definition used in our primary analysis was the most rigorous endpoint and associated with the highest ICERs (i.e. the least cost-effectiveness) compared to other endpoints. The “increase of ≥1 CSBM per week from baseline” endpoint resulted in the lowest ICERs (i.e. the greatest cost-effectiveness).

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| --- | --- | --- | --- | --- | --- |
| **Strategy** | **Total cost ($/year)** | **Total effectiveness (QALY gained) over 12 weeks** | **Incremental cost ($)** | **Incremental effectiveness (QALY)** | **ICER**  **($/QALY-gained)** |
| *Insurer perspective* | | | | | |
| **Usual care** | $569 | 0.188 | Reference | Reference | Reference |
| **Plecanatide 3mg daily**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks with sustained response for the last ≥3/4 weeks7 | $1,506 | 0.193 | $937 additional cost | +0.005 | $187,276/QALY-gained |
| **Prucalopride 2mg**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks (defined as Alternative Endpoint A in Table 51 of FDA multi-discipline review)3  ≥3 CSBM per week averaged over 12 weeks (defined as primary FDA responder endpoint for prucalopride in Table 52 of FDA multi-discipline review)3  Increase of ≥1 CSBM per week from baseline averaged over 12 weeks (Table 54 of FDA multi-discipline review)3 | $1,519  $1,471  $1,365 | 0.191  0.191  0.191 | $950 additional cost  $902 additional cost  $796 additional cost | +0.003  +0.003  +0.003 | $333,910/QALY-gained  $211,276/QALY-gained  $107,606/QALY-gained |
| **Linaclotide 145mcg daily**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks7  ≥3 CSBM/wk for ≥9/12 weeks8  Increase of ≥1 CSBM/wk from baseline for ≥9/12 weeks8,9 | $1,554  $1,554  $1,461 | 0.191  0.191  0.191 | $985 additional cost  $985 additional cost  $892 additional cost | +0.003  +0.003  +0.003 | $309,968/QALY-gained  $309,968/QALY-gained  $132,924/QALY-gained |
| **Linaclotide 72mcg daily**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks7 | $1,584 | 0.191 | $1,015 additional cost | +0.003 | $345,401/QALY-gained |
| **Lubiprostone 24mcg twice daily\***  Increase of ≥3 SBM/wk averaged over 4 weeks compared to baseline (Table 9 of FDA multi-discipline review)6 | $1,187 | 0.196 | $618 additional cost | +0.009 | $72,053/QALY-gained |
| *Patient perspective* | | | | | |
| **Usual care** | $3,154 | 0.188 | Reference | Reference | Reference |
| **Linaclotide 145mcg daily**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks7  ≥3 CSBM/wk for ≥9/12 weeks8  Increase of ≥1 CSBM/wk from baseline for ≥9/12 weeks8,9 | $2,772  $2,772  $2,257 | 0.191  0.191  0.191 | $382 saved  $382 saved  $897 saved | +0.003  +0.003  +0.003 | Dominates usual care  Dominates usual care  Dominates usual care |
| **Linaclotide 72mcg daily**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks7 | $2,827 | 0.191 | $327 saved | +0.003 | Dominates usual care |
| **Plecanatide 3mg daily**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks with sustained response for the last ≥3/4 weeks7 | $2,617 | 0.193 | $537 saved | +0.005 | Dominates usual care |
| **Prucalopride 2mg**  ≥3 CSBM/wk + increase ≥1 CSBM/wk compared to baseline for ≥9/12 weeks (defined as Alternative Endpoint A in Table 51 of FDA multi-discipline review)3  ≥3 CSBM per week averaged over 12 weeks (defined as primary FDA responder endpoint for prucalopride in Table 52 of FDA multi-discipline review)3  Increase of ≥1 CSBM per week from baseline averaged over 12 weeks (Table 54 of FDA multi-discipline review)3 | $2,698  $2,512  $1,841 | 0.191  0.191  0.191 | $456 saved  $642 saved  $1,313 saved | +0.003  +0.003 | Dominates usual care  Dominates usual care  Dominates usual care |
| **Lubiprostone 24mcg twice daily\***  Increase of ≥3 SBM/wk averaged over 4 weeks compared to baseline (Table 9 of FDA multi-discipline review)6 | $2,037 | 0.196 | $1,117 saved | +0.009 | Dominates usual care |

\*Lubiprostone is reported for comparison to usual care but is not intended for comparison against other treatments due to differences in trial design. CIC=chronic idiopathic constipation; QALY=quality-adjusted life year; ICER=incremental cost-effectiveness ratio; FDA=Food and Drug Administration; CSBM=complete spontaneous bowel movement; SBM=spontaneous bowel movement; wk=week.