## **Supplemental**

Supplemental Table 1. Key Utility Estimatesa

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Unit** | **Value** | **Source** | **Notes** |
|  |  |  |  |  |
| **Bleed Utilities** |  |  |  |  |
| **Pettersson Score ≤ 12** |  |  |  |  |
| No bleed | daily utility | 0.83 | Fischer 2016 [42] |  |
| Non-joint bleed | daily utility | 0.66 | Neufeld 2012 [43] |  |
| Joint bleed | daily utility | 0.54 | Mazza 2016 [44] | Mazza reports a 0.12 decrement for joint bleeds; applied to non-joint bleed utility |
| **Pettersson Score > 12 and ≤ 21** |  |  |  |
| No bleed | daily utility | 0.79 | Fischer 2016 [42] |  |
| Non-joint bleed | daily utility | 0.63 | Calculation | Applied a percent change decrement associated with progressing joint damage; calculated percent difference between “No bleed” state with a PS≤12 and “No bleed” state PS>12 and ≤21 |
| Joint bleed | daily utility | 0.51 | Calculation |
| **Pettersson Score > 21 and ≤ 39** |  |  |  |
| No bleed | daily utility | 0.73 | Fischer 2016 [42] |  |
| Non-joint bleed | daily utility | 0.58 | Calculation | Applied a percent change decrement associated with progressing joint damage; calculated percent difference between “No bleed” state with a PS>12 and ≤21 and “No bleed” state PS>21 and ≤39 |
| Joint bleed | daily utility | 0.47 | Calculation |
| **Pettersson Score > 39** |  |  |  |
| No bleed | daily utility | 0.72 | Fischer 2016 [42] |  |
| Non-joint bleed | daily utility | 0.57 | Calculation | Applied a percent change decrement associated with progressing joint damage; calculated percent difference between “No bleed” state with a PS>21 and ≤39 and “No bleed” state PS>39 |
| Joint bleed | daily utility | 0.47 | Calculation |
| **Utility Decrements** |  |  |  |  |
| **FVIII infusion** | per infusion | −0.0004 | Matza 2015 [45] | Applied per discounted infusion of FVIII  |
| **Joint replacement surgery** | weekly utility | −0.39 | Ballal 2008 [46] |  |

aAll utilities are assumed to be equal between both treatment arms.

Supplemental Table 2. 10-Year Model Horizon Resultsa,b

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| --- | --- | --- | --- |
| **Outcome** | **Valoctocogene roxaparvovec** | **Prophylaxis** | **Valoctocogene roxaparvovec vs Prophylaxis** |
|   |   |   |   |
| Discounted Total Cost, $ | 3,469,487 (27,704) | 8,502,702 (24,878) | -5,033,215 (30,450) |
| Total Bleed Events (All) | 17 (0) | 51 (1) | -33 (1) |
| Total Joint Bleed Events | 6 (0) | 32 (0) | -26 (1) |
| Total Non-Joint Bleed Events | 11 (0) | 19 (0) | -8 (0) |
| Discounted Total Infusions | 287 (5) | 1,640 (2) | -1,353 (5) |
| Discounted LYs | 8.532 (0.008) | 8.532 (0.008) | 0 (0) |
| Discounted QALYs | 6.875 (0.007) | 6.370 (0.006) | 0.504 (0.002) |

aAll values are reported as mean (Monte Carlo standard error).

bScenario analysis reduces the model time-horizon to 10 years. All other parameters, including bleed rates, reflect the model base case.

Supplemental Table 3. Increased Utility for Valoctocogene Roxaparvovec across All Health States Resultsa,b

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome** | **Valoctocogene roxaparvovec** | **Prophylaxis** | **Valoctocogene roxaparvovec vs Prophylaxis** |
|   |   |   |   |
| Discounted Total Cost, $ | 16,656,470 (81,490) | 23,466,845 (87,259) | -6,810,374 (47,786) |
| Total Bleed Events (All) | 186 (2) | 229 (3) | -43 (1) |
| Total Joint Bleed Events | 112 (2) | 144 (2) | -33 (1) |
| Total Non-Joint Bleed Events | 75 (1) | 85 (1) | -10 (0) |
| Discounted Total Infusions | 5,572 (26) | 7,379 (25) | -1,808 (10) |
| Discounted LYs | 23.565 (0.051) | 23.565 (0.051) | 0 (0) |
| Discounted QALYs | 18.340 (0.039) | 17.318 (0.038) | 1.022 (0.005) |

aAll values are reported as mean (Monte Carlo standard error).

bScenario analysis assigns an additional 0.02 utility increase to valoctocogene roxaparvovec patients across all health states, reflecting reduced concerns of spontaneous bleed events and general relief from chronic disease management. All other parameters, including bleed rates, reflect the model base case.

Supplemental Table 4. Emicizumab Comparator Arm Resultsa,b

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome** | **Valoctocogene roxaparvovec** | **Emicizumab** | **Valoctocogene roxaparvovec vs Emicizumab** |
|   |   |   |   |
| Discounted Total Cost, $ | 13,488,412 (64,957) | 18,249,581 (69,385) | -4,761,169 (37,106) |
| Total Bleed Events (All) | 186 (2) | 229 (3) | -43 (1) |
| Total Joint Bleed Events | 112 (2) | 144 (2) | -33 (1) |
| Total Non-Joint Bleed Events | 75 (1) | 85 (1) | -10 (0) |
| Discounted Total Infusions | 1,251 (7) | 1,612 (8) | -361 (3) |
| Discounted LYs | 23.565 (0.051) | 23.565 (0.051) | 0 (0) |
| Discounted QALYs | 18.793 (0.041) | 18.497 (0.040) | 0.296 (0.004) |

aAll values are reported as mean (Monte Carlo standard error).

bScenario analysis only alters the cost ($148.80 per mg; dose of 3.0 mg/kg) and injection frequency (biweekly) of the comparator arm to reflect the treatment regimen for emicizumab-kxwh. All other parameters, including bleed rates, reflect the model base case (with standard half-life FVIII prophylaxis comparator).

Supplemental Table 5. Extended Half-life Prophylaxis Comparator Arm Resultsa,b

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| --- | --- | --- | --- |
| **Outcome** | **Valoctocogene roxaparvovec** | **Extended Half-life Prophylaxis** | **Valoctocogene roxaparvovec vs Extended Half-life Prophylaxis** |
|   |   |   |   |
| Discounted Total Cost, $ | 17,403,698 (85,395) | 24,682,895 (91,471) | -7,279,197 (50,305) |
| Total Bleed Events (All) | 186 (2) | 229 (3) | -43 (1) |
| Total Joint Bleed Events | 112 (2) | 144 (2) | -33 (1) |
| Total Non-Joint Bleed Events | 75 (1) | 85 (1) | -10 (0) |
| Discounted Total Infusions | 3,843 (18) | 5,073 (18) | -1,230 (7) |
| Discounted LYs | 23.565 (0.051) | 23.565 (0.051) | 0 (0) |
| Discounted QALYs | 18.358 (0.039) | 17.790 (0.039) | 0.569 (0.005) |

aAll values are reported as mean (Monte Carlo standard error).

bScenario analysis alters the cost ($103.50 per kg; dose of 50 IU/kg) and injection frequency (twice weekly) of the comparator arm to reflect the treatment regimen for extended half-life prophylaxis. All other parameters, including bleed rates, reflect the model base case (with standard half-life FVIII prophylaxis comparator).