**Supplementary Material**

**Cost-effectiveness Analysis of Secukinumab in Ankylosing Spondylitis from the Canadian Perspective**

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Table S1 Population inputs to define baseline characteristics

|  |  |  |
| --- | --- | --- |
| **Input**  | **Mean** | **SD** |
| Percentage male  | 69.5% | N/A |
| Age (years) | 42.37 | N/A |
| Weight (kg)  | 78.20 | 16.882 |

N/A= not applicable; SD=standard deviation

Source: MEASURE 1 and MEASURE 2 study pooled trial data (data not published).

Table S2 Drug dosing, mode of administration and number of doses in each treatment period in AS patients

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  | Number of Doses |
| Administration | Drug | Dose | First 3 Months | Months 4-6 | Subsequent 3-month Periods |
| Subcutaneous | Secukinumab1 | 150 mg | 7.00 | 3.00 | 3.00 |
| Adalimumab2 | 40 mg | 7.00 | 6.00 | 6.52 |
| Certolizumab pegol3 | 200 mg | 10.00 | 6.00 | 6.52 |
| Etanercept4 | 50 mg | 13.00 | 13.00 | 13.04 |
| Golimumab5 | 50 mg | 3.00 | 3.00 | 3.00 |
| Intravenous | Infliximab6 | 5 mg/kg | 3.00 | 2.00 | 1.63 |

AS: Ankylosing spondylitis; mg:milligrams

Table S3 BASDAI 50 Response at 3 Months for biologic-naïve AS patients7

|  |  |  |
| --- | --- | --- |
| **Administration** | **Treatment**  | **BASDAI 50 Response** |
| Subcutaneous | Secukinumab | 41.53% |
| Certolizumab pegol | 44.20% |
| Etanercept | 36.80% |
| Adalimumab | 48.85% |
| Golimumab | 47.20% |
| Intravenous | Infliximab | 44.20% |

AS: Ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index;

Data for Certolizumab pegol and infliximab were not available and were assumed equivalent to the lowest biologic in the network meta-analysis

Table S4 Short-term changes in BASDAI and BASFI at 3 months in Biologic-naïve AS patients

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Secukinumab** | **Certolizumab pegol** | **Etanercept** | **Adalimumab** | **Infliximab** | **Golimumab** |
| Change in BASDAI | Responders\* | -4.60 | -5.57 | -4.47 | -4.56 | -7.94 | -5.32 |
| Non responders | -1.01 | -1.28 | -1.02 | -0.81 | -1.82 | -1.37 |
| Change in BASFI | Responders | -3.75 | -3.59 | -3.44 | -3.15 | -3.96 | -4.07 |
| Non responders | -1.17 | -0.89 | -0.85 | -0.78 | -0.98 | -0.71 |

AS: Ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index. \*Responders are those that showed BASDAI 50 response at 3 month.

Source: Biologic-naïve change in BASDAI data were not available for SEC and CER P and were assumed equivalent to the average of other biologics in the network meta-analysis. Biologic-naïve change in BASFI data for CER P was not available and were assumed equivalent to the average of other biologics in the network meta-analysis (excluding secukinumab).

Table S5 Long-term changes in BASFI for secukinumab and comparators in biologic-naïve AS patients

|  |  |
| --- | --- |
| **Input**  | **Mean** |
| Annual rate of mSASSS change for mSASSS ≥ 10 for all biologics | 1.4408 |
| BASFI change associated with 1 unit change in mSASSS  | 0.0578 |
| Biologic treatment effect on mSASSS progression for comparators | 0.4208 |
| Biologic treatment effect on mSASSS progression for secukinumab a | 0.1539 |
| Time to treatment effect (years)  | 0b |

AS: Ankylosing spondylitis; BASFI = Bath Ankylosing Spondylitis Functional Index; mSASSS = modified Stoke Ankylosing Spondylitis Spine Score.

a This figure was calculated using the overall background progression rate of 0.98 units/year from Ramiro,2013 study9 and MEASURE 1 week 104 mSASSS progression figure of 0.3.8

b Based on input from clinical expert.

Table S6 Annual treatment specific biologic withdrawal rates

|  |  |  |  |
| --- | --- | --- | --- |
| Administration | Drug | Year 1 | Year 2+ |
| Subcutaneous | Secukinumab | 15.3% | 1.6% |
| Adalimumab10, 11 | 13.0% | 9.3% |
| Certolizumab pegol12 | 12.6% | 11.0% |
| Etanercept13,14 | 25.1% | 25.1% |
| Golimumab15 | 15.1% | 6.2% |
| Intravenous | Infliximab11,16 | 2.1% | 15.7% |

Source: Secukinumab from MEASURE 1 and MEASURE 2 clinical study report (data not published)

Table S7 Outpatient medical support costs for all biologics

|  |  |  |
| --- | --- | --- |
| **Input**  | **Mean** | **Unit** |
| Specialist visit17 | CAD 22.56 | Per visit |
| Full blood count18 | CAD 9.26 | Per test |
| Erythrocyte sedimentation rate19 | CAD 10.93 | Per test |
| Liver function test18 | CAD 14.63 | Per test |
| Urea and electrolytes18 | CAD 6.00 | Per test |
| Chest radiograph20 | CAD 40.11 | Per test |
| Tuberculosis Heaf test 21 | CAD 16.44 | Per test |
| Antinuclear antibodies22 | CAD 24.53 | Per test |
| DNA test22 | CAD 20.83 | Per test |

DNA = deoxyribonucleic acid; CAD=Canadian Dollar

Table S8 Adverse event rates over a 3-month period

|  |  |  |  |
| --- | --- | --- | --- |
| **Administration** | **Drug**  | **Serious Infection** | **Malignancy** |
| Subcutaneous | Secukinumab (MEASURE 1 & 2 trial) | 0.16% | 0.0015% |
| Adalimumab23 | 0.35% | 0.12% |
| Certolizumab pegol12 | 0.67% | 0.00% |
| Etanercept13 | 0.00% | 0.00% |
| Golimumab15 | 0.19% | 0.03% |
| Intravenous | Infliximab16  | 0.52% | 0.13% |

Source: Secukinumab from Novartis data on file (data not published)

Serious infections considered included tuberculosis or other serious infection, such as such as septicemia, bronchopneumonia, kidney or unitary tract infection, lower respiratory disease, or bronchitis.

Table S9 Utility weight inputs used in the model to calculate QALYs

|  |  |  |
| --- | --- | --- |
| **Parameter** | **MEASURE 1 & 2 data** | **Mcleod,2007**24 |
| Intercept |  0.9610 | 0.8772 |
| BASFI coefficient |  -0.0330 | -0.0323 |
| BASDAI coefficient |  -0.0442 | -0.0384 |
| Male coefficient |  -0.0111 | -0.0279 |
| Age coefficient |  -0.0005 | 0.0017 |

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index

For base-case analysis, utilities calculated from MEAURE 1 and MEASURE 2 trials are included (data not published). For alternative scenario analysis, utilities obtained from McLeod et al. 2007 are included.

Table S10 Adverse event disutilities

|  |  |  |
| --- | --- | --- |
| **Adverse event** | **Disutility** | **Source** |
| **Serious infection** | -0.156 | Stevenson,201625 |
| **Malignancy** | -0.017 | Sullivan and Ghushchyan, 200626 |

Serious infections disutility applied for 1 month. Disutility for malignancy was assumed to be applied for 1 year

Table S11 Age related annual mortality rates27

| **Age (years)** | **Male** | **Female** | **Age (years)** | **Male** | **Female** |
| --- | --- | --- | --- | --- | --- |
| 18 | 0.00064 | 0.0003 | 54 | 0.00470 | 0.00295 |
| 19 | 0.00071 | 0.0003 | 55 | 0.00516 | 0.00322 |
| 20 | 0.00078 | 0.0003 | 56 | 0.00568 | 0.00353 |
| 21 | 0.00082 | 0.0003 | 57 | 0.00624 | 0.00386 |
| 22 | 0.00083 | 0.0003 | 58 | 0.00686 | 0.00423 |
| 23 | 0.00082 | 0.0003 | 59 | 0.00755 | 0.00464 |
| 24 | 0.00079 | 0.0003 | 60 | 0.00830 | 0.00510 |
| 25 | 0.00075 | 0.0003 | 61 | 0.00914 | 0.00560 |
| 26 | 0.00073 | 0.0003 | 62 | 0.01005 | 0.00615 |
| 27 | 0.00072 | 0.00031 | 63 | 0.01106 | 0.00677 |
| 28 | 0.00073 | 0.00033 | 64 | 0.01217 | 0.00745 |
| 29 | 0.00074 | 0.00035 | 65 | 0.01340 | 0.00821 |
| 30 | 0.00077 | 0.00038 | 66 | 0.01475 | 0.00905 |
| 31 | 0.00081 | 0.00041 | 67 | 0.01624 | 0.00999 |
| 32 | 0.00086 | 0.00045 | 68 | 0.01788 | 0.01102 |
| 33 | 0.0009 | 0.00049 | 69 | 0.01969 | 0.01218 |
| 34 | 0.00096 | 0.00053 | 70 | 0.02168 | 0.01347 |
| 35 | 0.00101 | 0.00058 | 71 | 0.02388 | 0.01490 |
| 36 | 0.00108 | 0.00063 | 72 | 0.02630 | 0.01650 |
| 37 | 0.00115 | 0.00068 | 73 | 0.02898 | 0.01828 |
| 38 | 0.00123 | 0.00074 | 74 | 0.03193 | 0.02028 |
| 39 | 0.00131 | 0.00081 | 75 | 0.03518 | 0.02250 |
| 40 | 0.00141 | 0.00088 | 76 | 0.03877 | 0.02499 |
| 41 | 0.00151 | 0.00096 | 77 | 0.04273 | 0.02777 |
| 42 | 0.00163 | 0.00104 | 78 | 0.04711 | 0.03088 |
| 43 | 0.00176 | 0.00114 | 79 | 0.05193 | 0.03437 |
| 44 | 0.00191 | 0.00124 | 80 | 0.05726 | 0.03828 |
| 45 | 0.00207 | 0.00135 | 81 | 0.06314 | 0.04267 |
| 46 | 0.00225 | 0.00147 | 82 | 0.06963 | 0.04760 |
| 47 | 0.00245 | 0.00160 | 83 | 0.07680 | 0.05313 |
| 48 | 0.00268 | 0.00175 | 84 | 0.08471 | 0.05935 |
| 49 | 0.00293 | 0.00190 | 85 | 0.09345 | 0.06634 |
| 50 | 0.00322 | 0.00208 | 86 | 0.10311 | 0.07421 |
| 51 | 0.00354 | 0.00226 | 87 | 0.11378 | 0.08308 |
| 52 | 0.00389 | 0.00247 | 88 | 0.12556 | 0.09308 |
| 53 | 0.00427 | 0.00270 | 89 | 0.13858 | 0.10435 |
| 90 | 0.15297 | 0.11708 | 101 | 0.34856 | 0.32078 |
| 91 | 0.16852 | 0.13112 | 102 | 0.36799 | 0.34270 |
| 92 | 0.18490 | 0.14622 | 103 | 0.38718 | 0.36455 |
| 93 | 0.20204 | 0.16236 | 104 | 0.40601 | 0.38612 |
| 94 | 0.21988 | 0.17950 | 105 | 0.42436 | 0.40726 |
| 95 | 0.23440 | 0.19754 | 106 | 0.44214 | 0.42778 |
| 96 | 0.25251 | 0.21631 | 107 | 0.45925 | 0.44755 |
| 97 | 0.27115 | 0.23596 | 108 | 0.47562 | 0.46646 |
| 98 | 0.29020 | 0.25639 | 109 | 0.49120 | 0.48440 |
| 99 | 0.30953 | 0.27744 | 110 | 1.00000 | 1.00000 |
| 100 | 0.32903 | 0.29896 |  |  |  |

Table S12 Disease specific and adverse event related mortality inputs considered in the analysis

|  |  |
| --- | --- |
| **Input**  | **Relative Risk** |
| **Disease specific mortalitya** |
| Male  | 1.63 |
| Female  | 1.38 |
| **Adverse event related mortalityb** |
| Tuberculosis  | 1.65 |
| Other serious infection  | 1.65 |
| Malignancy |  |
| 1 Year  | 1.41 |
| 2 Years  | 1.41 |

Disease-specific mortality data obtained from Bakland, 201128

Mortality data for adverse event obtained from Abuabara, 201029

a Relative risk of mortality in AS patients compared to general population; b Relative risk of mortality in AS patients having adverse event compared to AS patients not having adverse event

Table S13 Sensitivity analysis inputs for biologic-naive base-case population

| **Variable** | **Base case** | **Lower Bound** | **Upper Bound** | **Distribution used in Probabilistic sensitivity analysis** |
| --- | --- | --- | --- | --- |
| Discount rate - costs | 1.50% | 0.0% | 5.0% | Not varied |
| Discount rate - outcomes | 1.50% | 0.0% | 5.0% | Not varied |
| Baseline BASDAI | 6.75 | 5.40 | 8.10 | Not varied |
| Baseline BASFI | 6.38 | 5.10 | 7.65 | Not varied |
| Baseline BASDAI responders: Secukinumab | 6.23 | 4.98 | 7.47 | Not varied |
| Baseline BASDAI responders: Certolizumab pegol | 6.23 | 4.98 | 7.47 | Not varied |
| Baseline BASDAI responders: Etanercept | 6.23 | 4.98 | 7.47 | Not varied |
| Baseline BASDAI responders: Adalimumab | 6.23 | 4.98 | 7.47 | Not varied |
| Baseline BASDAI responders: Infliximab | 6.23 | 4.98 | 7.47 | Not varied |
| Baseline BASDAI responders: Golimumab | 6.23 | 4.98 | 7.47 | Not varied |
| Baseline BASDAI responders: Conventional care | 6.34 | 5.07 | 7.61 | Not varied |
| Baseline BASDAI non-responders: Secukinumab | 6.90 | 5.52 | 8.28 | Not varied |
| Baseline BASDAI non-responders: Certolizumab pegol | 6.90 | 5.52 | 8.28 | Not varied |
| Baseline BASDAI non-responders: Etanercept | 6.90 | 5.52 | 8.28 | Not varied |
| Baseline BASDAI non-responders: Adalimumab | 6.90 | 5.52 | 8.28 | Not varied |
| Baseline BASDAI non-responders: Infliximab | 6.90 | 5.52 | 8.28 | Not varied |
| Baseline BASDAI non-responders: Golimumab | 6.90 | 5.52 | 8.28 | Not varied |
| Baseline BASDAI non-responders: Conventional care | 6.88 | 5.50 | 8.25 | Not varied |
| Baseline BASFI responders: Secukinumab | 5.69 | 4.55 | 6.83 | Not varied |
| Baseline BASFI responders: Certolizumab pegol | 5.69 | 4.55 | 6.83 | Not varied |
| Baseline BASFI responders: Etanercept | 5.69 | 4.55 | 6.83 | Not varied |
| Baseline BASFI responders: Adalimumab | 5.69 | 4.55 | 6.83 | Not varied |
| Baseline BASFI responders: Infliximab | 5.69 | 4.55 | 6.83 | Not varied |
| Baseline BASFI responders: Golimumab | 5.69 | 4.55 | 6.83 | Not varied |
| Baseline BASFI responders: Conventional care | 5.77 | 4.62 | 6.93 | Not varied |
| Baseline BASFI non-responders: Secukinumab | 6.83 | 5.47 | 8.20 | Not varied |
| Baseline BASFI non-responders: Certolizumab pegol | 6.83 | 5.47 | 8.20 | Not varied |
| Baseline BASFI non-responders: Etanercept | 6.83 | 5.47 | 8.20 | Not varied |
| Baseline BASFI non-responders: Adalimumab | 6.83 | 5.47 | 8.20 | Not varied |
| Baseline BASFI non-responders: Infliximab | 6.83 | 5.47 | 8.20 | Not varied |
| Baseline BASFI non-responders: Golimumab | 6.83 | 5.47 | 8.20 | Not varied |
| Baseline BASFI non-responders: Conventional care | 6.38 | 5.10 | 7.65 | Not varied |
| Annual rate of MSASSS change for MSASSS≥10 - Secukinumab | 1.440 | 1.152 | 1.728 | Normal |
| Annual rate of MSASSS change for MSASSS≥10 - TNFs | 1.440 | 1.152 | 1.728 | Normal |
| BASFI change with 1 unit change in MSASSS | 0.057 | 0.046 | 0.068 | Normal |
| Treatment effect on progression - Secukinumab | 0.153 | 0.122 | 0.184 | Normal |
| Treatment effect on progression - TNFs | 0.420 | 0.336 | 0.504 | Normal |
| Relative risk BASDAI response: Second line | 1.00 | 0.80 | 1.20 | Not varied |
| Relative risk Δ BASDAI: Second line | 1.00 | 0.80 | 1.20 | Not varied |
| Relative risk Δ BASFI: Second line | 1.00 | 0.80 | 1.20 | Not varied |
| Discontinuation year 1: Secukinumab | 15.3% | 12.3% | 18.4% | Normal |
| Discontinuation year 1: Certolizumab pegol | 12.6% | 10.1% | 15.1% | Normal |
| Discontinuation year 1: Etanercept | 25.1% | 20.1% | 30.2% | Normal |
| Discontinuation year 1: Adalimumab | 13.0% | 10.4% | 15.7% | Normal |
| Discontinuation year 1: Infliximab | 2.1% | 1.7% | 2.6% | Normal |
| Discontinuation year 1: Golimumab | 15.1% | 12.1% | 18.1% | Normal |
| Discontinuation year 2: Secukinumab | 1.6% | 1.3% | 2.0% | Normal |
| Discontinuation year 2: Certolizumab pegol | 11.0% | 8.8% | 13.2% | Normal |
| Discontinuation year 2: Etanercept | 25.1% | 20.1% | 30.2% | Normal |
| Discontinuation year 2: Adalimumab | 9.3% | 7.5% | 11.2% | Normal |
| Discontinuation year 2: Infliximab | 15.7% | 12.6% | 18.9% | Normal |
| Discontinuation year 2: Golimumab | 6.2% | 4.9% | 7.4% | Normal |
| Drug acquisition cost: Secukinumab | CAD 822.50 | CAD 658.00 | CAD 987.00 | Not varied |
| Drug acquisition cost: Certolizumab pegol | CAD 664.51 | CAD 531.61 | CAD 797.41 | Not varied |
| Drug acquisition cost: Etanercept | CAD 405.99 | CAD 324.79 | CAD 487.18 | Not varied |
| Drug acquisition cost: Adalimumab | CAD 769.97 | CAD 615.98 | CAD 923.96 | Not varied |
| Drug acquisition cost: Infliximab | CAD 987.56 | CAD 790.05 | CAD 1,185.07 | Not varied |
| Drug acquisition cost: GOL | CAD 1,555.17 | CAD 1,244.14 | CAD 1,866.20 | Not varied |
| Subcutaneous therapy training | CAD 0.00 | CAD 0.00 | CAD 0.00 | Normal |
| IV administration | CAD 0.00 | CAD 0.00 | CAD 0.00 | Normal |
| Cost equation intercept | CAD 2,413.31 | CAD 1,930.65 | CAD 2,895.98 | Log-normal |
| BASFI coefficient | 0.40 | 0.32 | 0.48 | Normal |
| Tuberculosis cost | CAD 57,181.60 | CAD 45,745.28 | CAD 68,617.93 | Gamma |
| Other serious infection cost | CAD 21,661.56 | CAD 17,329.25 | CAD 25,993.87 | Gamma |
| Malignancy cost | CAD 29,662.47 | CAD 23,729.97 | CAD 35,594.96 | Gamma |
| GP visit cost | CAD 21.90 | CAD 17.52 | CAD 26.28 | Gamma |
| Specialist visit cost | CAD 21.90 | CAD 17.52 | CAD 26.28 | Gamma |
| Full blood count cost | CAD 8.99 | CAD 7.19 | CAD 10.78 | Gamma |
| Erythrocyte sedimentation rate cost | CAD 10.61 | CAD 8.49 | CAD 12.73 | Gamma |
| Liver function test cost | CAD 14.20 | CAD 11.36 | CAD 17.04 | Gamma |
| Urea and electrolytes test cost | CAD 5.83 | CAD 4.66 | CAD 7.00 | Gamma |
| Chest radiograph cost | CAD 38.94 | CAD 31.15 | CAD 46.73 | Gamma |
| Tuberculosis Heaf test cost | CAD 15.96 | CAD 12.77 | CAD 19.15 | Gamma |
| Antinuclear antibodies cost | CAD 23.82 | CAD 19.06 | CAD 28.58 | Gamma |
| DNA double-stranded test cost | CAD 20.22 | CAD 16.18 | CAD 24.26 | Gamma |
| Serious infection probability: Secukinumab | 0.16% | 0.13% | 0.20% | Beta |
| Serious infection probability: Certolizumab pegol | 0.67% | 0.54% | 0.81% | Beta |
| Serious infection probability: Etanercept | 0.00% | 0.00% | 0.00% | Beta |
| Serious infection probability: Adalimumab | 0.35% | 0.28% | 0.42% | Beta |
| Serious infection probability: Infliximab | 0.52% | 0.41% | 0.62% | Beta |
| Serious infection probability: Golimumab | 0.19% | 0.15% | 0.23% | Beta |
| Serious infection probability: Conventional care | 0.00% | 0.00% | 0.00% | Beta |
| Malignancy probability: Secukinumab | 0.00% | 0.00% | 0.00% | Beta |
| Malignancy probability: Certolizumab pegol | 0.00% | 0.00% | 0.00% | Beta |
| Malignancy probability: Etanercept | 0.00% | 0.00% | 0.00% | Beta |
| Malignancy probability: Adalimumab | 0.12% | 0.10% | 0.15% | Beta |
| Malignancy probability: Infliximab | 0.13% | 0.10% | 0.15% | Beta |
| Malignancy probability: Golimumab | 0.03% | 0.02% | 0.04% | Beta |
| Malignancy probability: Conventional care | 0.00% | 0.00% | 0.00% | Beta |
| AS mortality relative risk - males | 1.63 | 1.30 | 1.96 | Log-normal |
| AS mortality relative risk - females | 1.38 | 1.10 | 1.66 | Log-normal |
| Tuberculosis mortality relative risk | 1.65 | 1.32 | 1.98 | Not varied |
| Other serious infection mortality relative risk | 1.65 | 1.32 | 1.98 | Not varied |
| Malignancy relative risk: Year 1 | 1.41 | 1.13 | 1.69 | Not varied |
| Malignancy relative risk: Year 2 | 1.41 | 1.13 | 1.69 | Not varied |
| Utility intercept | 0.961 | 0.77 | 1.15 | Normal |
| Utility BASFI coefficient | -0.0330 | -0.0264 | -0.0396 | Normal |
| Utility BASDAI coefficient | -0.0442 | -0.0354 | -0.0530 | Normal |
| Utility male coefficient | -0.0111 | -0.0089 | -0.0133 | Normal |
| Utility age coefficient | -0.0005 | -0.0004 | -0.0006 | Normal |
| Serious infection disutility: Year 1 | -0.1560 | -0.1248 | -0.1872 | Normal |
| Serious infection disutility: Year 2 | 0.0000 | 0.0000 | 0.0000 | Normal |
| Serious infection disutility: Years 3+ | 0.0000 | 0.0000 | 0.0000 | Normal |
| Malignancy disutility | -0.0174 | -0.0139 | -0.0209 | Normal |
| BASDAI 50 at 3 months: Secukinumab | 41.53% | 15.21% | 73.77% | Normal |
| BASDAI 50 at 3 months: Certolizumab pegol | 44.20% | 19.27% | 72.44% | Normal |
| BASDAI 50 at 3 months: Etanercept | 36.80% | 14.92% | 65.89% | Normal |
| BASDAI 50 at 3 months: Adalimumab | 48.85% | 38.43% | 59.37% | Normal |
| BASDAI 50 at 3 months: Infliximab | 44.20% | 19.27% | 72.44% | Normal |
| BASDAI 50 at 3 months: Golimumab | 47.20% | 28.39% | 66.85% | Normal |
| BASDAI 50 at 3 months: Conventional care | 16.73% | 13.07% | 21.17% | Normal |
| 3-month responder BASDAI change: Secukinumab | -4.602 | -2.982 | -6.222 | Normal |
| 3-month responder BASDAI change: Certolizumab pegol | -5.569 | -4.010 | -7.127 | Normal |
| 3-month responder BASDAI change: Etanercept | -4.474 | -2.743 | -6.206 | Normal |
| 3-month responder BASDAI change: Adalimumab | -4.562 | -3.970 | -5.155 | Normal |
| 3-month responder BASDAI change: Infliximab | -7.941 | -5.836 | -10.046 | Normal |
| 3-month responder BASDAI change: Golimumab | -5.316 | -4.004 | -6.629 | Normal |
| 3-month responder BASDAI change: Conventional care | -3.061 | -2.404 | -3.718 | Normal |
| 3-month non-responder BASDAI change: Secukinumab | -1.007 | -0.652 | -1.361 | Normal |
| 3-month non-responder BASDAI change: Certolizumab pegol | -1.275 | -0.886 | -1.575 | Normal |
| 3-month non-responder BASDAI change: Etanercept | -1.025 | -0.608 | -1.375 | Normal |
| 3-month non-responder BASDAI change: Adalimumab | -0.806 | -0.837 | -1.087 | Normal |
| 3-month non-responder BASDAI change: Infliximab | -1.819 | -1.290 | -2.220 | Normal |
| 3-month non-responder BASDAI change: Golimumab | -1.368 | -0.906 | -1.500 | Normal |
| 3-month non-responder BASDAI change: Conventional care | -0.701 | -0.539 | -0.833 | Normal |
| 3-month responder BASFI change: Secukinumab | -3.748 | -2.294 | -5.202 | Normal |
| 3-month responder BASFI change: Certolizumab pegol | -3.594 | -2.211 | -4.978 | Normal |
| 3-month responder BASFI change: Etanercept | -3.444 | -1.914 | -4.975 | Normal |
| 3-month responder BASFI change: Adalimumab | -3.145 | -2.622 | -3.668 | Normal |
| 3-month responder BASFI change: Infliximab | -3.965 | -2.119 | -5.811 | Normal |
| 3-month responder BASFI change: Golimumab | -4.072 | -2.816 | -5.327 | Normal |
| 3-month responder BASFI change: Conventional care | -1.627 | -0.945 | -2.308 | Normal |
| 3-month non-responder BASFI change: Secukinumab | -1.174 | -0.718 | -1.629 | Normal |
| 3-month non-responder BASFI change: Certolizumab pegol | -0.886 | -0.651 | -1.465 | Normal |
| 3-month non-responder BASFI change: Etanercept | -0.849 | -0.555 | -1.442 | Normal |
| 3-month non-responder BASFI change: Adalimumab | -0.775 | -0.778 | -1.089 | Normal |
| 3-month non-responder BASFI change: Infliximab | -0.977 | -0.624 | -1.710 | Normal |
| 3-month non-responder BASFI change: Golimumab | -0.712 | -0.781 | -1.477 | Normal |
| 3-month non-responder BASFI change: Conventional care | -0.401 | -0.258 | -0.629 | Normal |

AS=Ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; DNA: deoxy ribonucleic acid; GP=general practitioner; IV=intravenous; MSASSS= modified stoke ankylosing spondylitis spinal score

Table S14 List of published studies evaluating cost-effectiveness of biologics in AS

| **Publication year** | **Population** | **Country of focus** | **Model type** | **Comparators** | **Key results** |
| --- | --- | --- | --- | --- | --- |
| 201730 | Active AS unresponsive to conventional treatment | Turkey | Markov model | Secukinumab, certolizumab pegol, etanercept, adalimumab and infliximab | Biologic-naïve: cost for secukinumab € 4,644-9134 lower than others and Experienced population: cost for secukinumab € 7,641-15,297 lower than othersBiologic-naïve: 0.20-0.86 QALYs gained with secukinumab treatmentExperienced population: 0.26-1.06 QALYs gained with secukinumab |
| 201731 | AS | Colombia | Markov model | TNF-α inhibitors | Incremental QALYs for secukinumab vs.certolizumab pegol: 0.099etanercept: 0.164adalimumab: 0.046Incremental costs for secukinumab vs.certolizumab pegol: -$28,472,133etanercept: -$27,696,705adalimumab: -$39,077,037 |
| 201732 | Active AS responding inadequately to conventional treatment | UK | Markov model | Secukinumab, etanercept, etanercept biosimilar, infliximab | ICER for secukinumab vs.etanercept originator: 10,173 per QALY gainedetanercept biosimilar: 11,417 per QALY gained |
| 201733 | Active AS responding inadequately to conventional treatment | UK | Combined decision tree/Markov state-transition model | Secukinumab, anti-TNF therapies | Biolgic-naïve: Secukinumab dominated adalimumab and infliximab and ICER was less than £20,000 per QALY gained vs. certolizumab pegol and etanercept.Biologic experienced: ICER for secukinumab vs. conventional care: £4,817 per QALY gained |
| 201734 | AS | Bulgaria | Not reported | SecukinumabEtanerceptInfliximabAdalimumabGolimumabCertolizumab Pegol | Secukinumab dominated certolizumab pegol, etanercept, adalimumab, golimumab and was cost-effective in comparison to infliximab considering WTP threshold of three times GDP per capita in Bulgaria (ICER: 27 552 BGN/QALY) |
| 201635 | AS | Russia | Not reported | AdalimumabCertolizumab PegolEtanerceptGolimumabInfliximab | Secukinumab had the lowest ICER 35 in comparison to all other biologics |

AS=ankylosing spondylitis; BGN=Bulgarian lev; GDP=gross domestic product; ICER=incremental cost effectiveness ratio; QALY= quality adjusted life years; TNF=tumor necrosis factor; UK=United Kingdom; WTP=willingness to pay

**Figure S1 One-way sensitivity analysis among biologic naïve population**

**SEC vs CER P**

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**SEC vs ETN branded**

****

**SEC vs ETN BS**

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**SEC vs ADA**

****

**SEC vs INF**

****

**SEC vs INF BS**

****

**SEC vs GOL**

****

ADA = adalimumab; CER P = certolizumab pegol; ETN = etanercept; ETN BS = etanercept biosimilar; GOL = golimumab; INF = infliximab; INF BS = infliximab biosimilar; SEC = secukinumab

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index;

# References

1. Health Canada. PRODUCT MONOGRAPH COSENTYX® 2017 [cited 16th April 2018]. Available from: https://pdf.hres.ca/dpd\_pm/00040683.PDF.

2. Health Canada. PRODUCT MONOGRAPH HUMIRA® 2018 [16th April 2018]. Available from: https://pdf.hres.ca/dpd\_pm/00044463.PDF.

3. Health Canada. PRODUCT MONOGRAPH CIMZIA® 2017 [16th April 2018]. Available from: https://pdf.hres.ca/dpd\_pm/00040019.PDF.

4. Health Canada. PRODUCT MONOGRAPH Enbrel. 2018.

5. Health Canada. PRODUCT MONOGRAPH SIMPONI® 2018 [16th April 2018]. Available from: https://pdf.hres.ca/dpd\_pm/00044615.PDF.

6. Health Canada. PRODUCT MONOGRAPH REMICADE® 2018 [16th April 2018].

7. D. Baeten PM, V. Strand, I. McInnes, H. Thom, S. Kanters, E. Palaka, K. Gandhi, H. Richards, S. Jugl. Secukinumab for the treatment of ankylosing spondylitis: comparative effectiveness results VERSUS CURRENTLY LICENSED BIOLOGICS FROM A NETWORK META-ANALYSIS Annals of the Rheumatic Diseases. 2016;75 (supplement 2):809.

8. Corbett M SM, Jhunti G, Rice S, Spackman E, Sideris E, et al. . TNF-alpha inhibitors for ankylosing spondylitis and axial spondyloarthritis without radiographic evidence of ankylosing spondylitis (including a review of technology appraisal 143 and technology appraisal 233) CRD/CHE Technology Assessment Group (Centre for Review and Dissemination/Centre for Health Economics) University of York. 2014.

9. Ramiro S, Stolwijk C, van Tubergen A, van der Heijde D, Dougados M, van den Bosch F, et al. Evolution of radiographic damage in ankylosing spondylitis: a 12 year prospective follow-up of the OASIS study. Annals of the rheumatic diseases. 2013;74(1):52-9.

10. Sieper J, van der Heijde D, Dougados M, Brown LS, Lavie F, Pangan AL. Early response to adalimumab predicts long-term remission through 5 years of treatment in patients with ankylosing spondylitis. Annals of the rheumatic diseases. 2012;71(5):700-6.

11. van der Heijde D, Kivitz A, Schiff MH, Sieper J, Dijkmans BA, Braun J, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis and rheumatism. 2006;54(7):2136-46.

12. Sieper J, Landewe R, Rudwaleit M, van der Heijde D, Dougados M, Mease PJ, et al. Effect of certolizumab pegol over ninety-six weeks in patients with axial spondyloarthritis: results from a phase III randomized trial. Arthritis Rheumatol. 2015;67(3):668-77.

13. Dougados M, Braun J, Szanto S, Combe B, Geher P, Leblanc V, et al. Continuous efficacy of etanercept in severe and advanced ankylosing spondylitis: results from a 12-week open-label extension of the SPINE study. Rheumatology (Oxford, England). 2012;51(9):1687-96.

14. Navarro-Sarabia F, Fernandez-Sueiro JL, Torre-Alonso JC, Gratacos J, Queiro R, Gonzalez C, et al. High-dose etanercept in ankylosing spondylitis: results of a 12-week randomized, double blind, controlled multicentre study (LOADET study). Rheumatology (Oxford, England). 2011;50(10):1828-37.

15. Deodhar A, Braun J, Inman RD, van der Heijde D, Zhou Y, Xu S, et al. Golimumab administered subcutaneously every 4 weeks in ankylosing spondylitis: 5-year results of the GO-RAISE study. Annals of the rheumatic diseases. 2015;74(4):757-61.

16. Braun J, Baraliakos X, Listing J, Fritz C, Alten R, Burmester G, et al. Persistent clinical efficacy and safety of anti-tumour necrosis factor alpha therapy with infliximab in patients with ankylosing spondylitis over 5 years: evidence for different types of response. Annals of the rheumatic diseases. 2008;67(3):340-5.

17. Ontario Ministry of Health and Long-Term Care. Schedule of Benefits Physician Services Under the Health Insurance Act 2014 [4th August 2014]. Available from: http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv\_mn.html

18. Pan F, Brazier NC, Shear NH, Jivraj F, Schenkel B, Brown R. Cost utility analysis based on a head-to-head Phase 3 trial comparing ustekinumab and etanercept in patients with moderate-to-severe plaque psoriasis: a Canadian perspective. Value Health. 2011;14(5):652-6.

19. Ministry of Health Province of British Columbia, Schedule of Fees - For the Laboratory Services Outpatient [Internet]. 2015 [cited 07/15/2016]. Available from: http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/laboratory-services/schedule\_of\_fees\_-\_laboratory\_services\_payment\_schedule.pdf.

20. Coyle D, Judd M, Blumenauer B, Cranney A, Maetzel A, Tugwell P, et al. Infliximab and etanercept in patients with rheumatoid arthritis: a systematic review and economic evaluation. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA), 2006 Contract No.: Technology Issue Report 64.

21. Canada Communicable Disease Report 2007 [Internet]. Publich health agnency of Canada. [Acccessed on 12/28/2016]. Available from: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/index-eng.php. .

22. Man A, Shojania K, Phoon C, Pal J, de Badyn MH, Pi D, et al. An evaluation of autoimmune antibody testing patterns in a Canadian health region and an evaluation of a laboratory algorithm aimed at reducing unnecessary testing. Clinical rheumatology. 2013;32(5):601-8.

23. Sieper J, van der Heijde D, Dougados M, Brown LS, Lavie F, Pangan AL. Early response to adalimumab predicts long-term remission through 5 years of treatment in patients with ankylosing spondylitis. Annals of the rheumatic diseases. 2012;71(5):700-6.

24. McLeod C, Bagust A, Boland A, Dagenais P, Dickson R, Dundar Y, et al. Adalimumab, etanercept and infliximab for the treatment of ankylosing spondylitis: a systematic review and economic evaluation. Health Technology Assessment (Winchester, England). 2007;11(28):1-158, iii-iv.

25. Stevenson M, Archer R, Tosh J, Simpson E, Everson-Hock E, Stevens J, et al. Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for the treatment of rheumatoid arthritis not previously treated with disease-modifying antirheumatic drugs and after the failure of conventional disease-modifying antirheumatic drugs only: systematic review and economic evaluation. Health Technol Assess. 2016;20(35):1-610.

26. Sullivan PW, Ghushchyan V. Preference-Based EQ-5D index scores for chronic conditions in the United States. Medical decision making : an international journal of the Society for Medical Decision Making. 2006;26(4):410-20.

27. Statistics Canada. Probability of dying by age and sex, Canada, 2007/2009 period [Internet] http://www.statcan.gc.ca/pub/91-209-x/2013001/article/11785/c-g/desc/desc02-eng.htm [cited 08/19/2016].

28. Bakland G, Gran JT, Nossent JC. Increased mortality in ankylosing spondylitis is related to disease activity. Annals of the rheumatic diseases. 2011;70(11):1921-5.

29. Abuabara K, Azfar RS, Shin DB, Neimann AL, Troxel AB, Gelfand JM. Cause-specific mortality in patients with severe psoriasis: a population-based cohort study in the U.K. Br J Dermatol. 2010;163(3):586-92.

30. Sarioz F, Ozdemir O, Direk S, Cavusoglu Sezen S, Barutcugil M. Secukinumab is dominant vs. TNF-inhibitors in the treatment of active ankylosing spondylitis: Results from a Turkish cost-effectiveness model. Value in Health. 2017;20(9):A534.

31. Romero Prada ME, Roa Cardenas NC, Serrano GY, Huerfano LM. Cost-utility analysis of secukinumab use versus tnf-a inhibitors, in patients with ankylosing spondilytis. Value in Health. 2017;20(9):A938-A9.

32. Marzo-Ortega H, Halliday A, Jugl S, Mokashi S, Gunda P, Graham C, et al. The cost-effectiveness of secukinumab versus tumour necrosis factor a inhibitor biosimilars for ankylosing spondylitis in the UK. Rheumatology (United Kingdom). 2017;56:ii92.

33. Emery P, Van Keep M, Beard SM, Graham CN, Miles L, Jugl SM, et al. Cost-effectiveness of secukinumab for the treatment of active ankylosing spondylitis in the UK. Value in Health. 2017;20(9):A534.

34. Djambazov S, Vekov T. Incremental cost-effectiveness analysis of biological drug therapies for the treatment of ankylosing spondylitis in Bulgaria, 2016. Value in Health. 2017;20(5):A221.

35. Fedyaev D, Derkach EV. Cost-effectiveness analysis of different biologic agents for ankylosing spondylitis treatment in Russia. Value in Health. 2016;19(7):A539.