Supplementary Table 1: Patient demographic characteristics and prescriber specialty

|  | | Apremilast | Methotrexate | All | *P* Value |
| --- | --- | --- | --- | --- | --- |
| N (%) | | 3,288 (56.1) | 2,572 (43.9) | 5,860 (100) |  |
| Age, years | Mean (SD) [Median] | 49.2 (12.9) [51] | 49.5 (13.2) [51] | 49.3 (13.1) | 0.289 |
|  |  |  |  |  | 0.512 |
| 18-30 | no. (%) | 307 (9.3) | 235 (9.1) | 542 (9.2) |  |
| 31-64 | no. (%) | 2,739 (83.3) | 2,127 (82.7) | 4,866 (83.0) |  |
| 65+ | no. (%) | 242 (7.4) | 210 (8.2) | 452 (7.7) |  |
| Female | no. (%) | 1772 (53.9) | 1417 (55.1) | 3189 (54.4) | 0.360 |
| Geographic region |  |  |  |  |  |
| Midwest | no. (%) | 627 (19.1) | 539 (21.0) | 1,166 (19.9) | <0.001 |
| Northeast | no. (%) | 689 (21.0) | 335 (13.0) | 1,024 (17.5) |  |
| South | no. (%) | 1,023 (31.1) | 932 (36.2) | 1,955 (33.4) |  |
| West | no. (%) | 303 (9.2) | 295 (11.5) | 598 (10.2) |  |
| Unknown | no. (%) | 646 (19.6) | 471 (18.3) | 1,117 (19.1) |  |
| Insurance type |  |  |  |  |  |
| Commercial | no. (%) | 2,956 (89.9) | 2,311 (89.9) | 5,267 (89.9) | 0.949 |
| Medicare supplemental | no. (%) | 332 (10.1) | 261 (10.1) | 593 (10.1) |  |
| Index year |  |  |  |  |  |
| 2015 | no. (%) | 1,015 (30.9) | 982 (38.2) | 1,997 (34.1) | <0.001 |
| 2016 | no. (%) | 1,029 (31.3) | 803 (31.2) | 1,832 (31.3) |  |
| 2017 | no. (%) | 923 (28.1) | 634 (24.7) | 1,557 (26.6) |  |
| 2018 | no. (%) | 321 (9.8) | 153 (5.9) | 474 (8.1) |  |
| Prescriber specialty |  |  |  |  |  |
| Dermatologist | no. (%) | 1,542 (46.9) | 1,183 (46.0) | 2,725 (46.5) | <0.001 |
| Rheumatologist | no. (%) | 83 (2.5) | 572 (22.2) | 655 (11.2) |  |
| Primary care/PA/NP | no. (%) | 400 (12.2) | 196 (7.6) | 596 (10.2) |  |
| Other/Unknown | no. (%) | 1,263 (38.4) | 621 (24.1) | 1,884 (32.2) |  |
| Days of follow-up | Mean (SD) [Median] | 829.8 (326.9) [781] | 845.2 (328.4) [797] | 836.6 (327.6) [788] | 0.073 |
|  |  |  |  | 0.008 |
| 1Y-<2Y | no. (%) | 1,485 (45.2) | 1,107 (43.0) | 2,592 (44.2) |  |
| 2Y-<3Y | no. (%) | 996 (30.3) | 841 (32.7) | 1,837 (31.3) |  |
| 3Y-<4Y | no. (%) | 692 (21.0) | 501 (19.5) | 1,193 (20.4) |  |
| 4Y+ | no. (%) | 115 (3.5) | 123 (4.8) | 238 (4.1) |  |

Supplementary Table 2: Baseline comorbidities

|  | | Apremilast | Methotrexate | All | *P* Value |
| --- | --- | --- | --- | --- | --- |
| N | | 3,288 | 2,572 | 5,860 |  |
| Charlson comorbidity index (CCI) | Mean (SD) [Median] | 0.6 (1.2) [0] | 0.5 (1.1) [0] | 0.6 (1.1) [0] | 0.121 |
|  |  |  |  |  | 0.144 |
| 0 | no. (%) | 2,274 (69.2) | 1,792 (69.7) | 4,066 (69.4) |  |
| 1 | no. (%) | 606 (18.4) | 496 (19.3) | 1,102 (18.8) |  |
| 2 | no. (%) | 159 (4.8) | 128 (5.0) | 287 (4.9) |  |
| 3+ | no. (%) | 249 (7.6) | 156 (6.1) | 405 (6.9) |  |
| No. of chronic conditions | Mean (SD) [Median] | 3.6 (2.1) [3] | 3.7 (2.1) [4] | 3.7 (2.1) [3] | 0.077 |
| PsA | no. (%) | 438 (13.3) | 505 (19.6) | 943 (16.1) | <0.001 |
| Cardiovascular disease | no. (%) | 329 (10.0) | 260 (10.1) | 589 (10.1) | 0.897 |
| Diabetes | no. (%) | 508 (15.5) | 357 (13.9) | 865 (14.8) | 0.093 |
| Metabolic syndrome | no. (%) | 25 (0.8) | 26 (1.0) | 51 (0.9) | 0.305 |
| Obesity | no. (%) | 614 (18.7) | 485 (18.9) | 1099 (18.8) | 0.859 |
| Anxiety | no. (%) | 412 (12.5) | 348 (13.5) | 760 (13.0) | 0.258 |
| Depression | no. (%) | 326 (9.9) | 303 (11.8) | 629 (10.7) | 0.022 |
| Non-alcoholic fatty liver disease | no. (%) | 102 (3.1) | 61 (2.4) | 163 (2.8) | 0.092 |
| Chronic kidney disease | no. (%) | 68 (2.1) | 41 (1.6) | 109 (1.9) | 0.183 |
| Hyperlipidemia | no. (%) | 1,186 (36.1) | 900 (35.0) | 2,086 (35.6) | 0.392 |
| Hypertension | no. (%) | 578 (17.6) | 515 (20.0) | 1093 (18.7) | 0.017 |
| Periodontitis | no. (%) | 1 (0.0) | 0 (0.0) | 1 (0.0) | 0.376 |
| Serious infection | no. (%) | 52 (1.6) | 37 (1.4) | 89 (1.5) | 0.657 |

Supplementary Table 3: Baseline medication use

|  | | Apremilast | Methotrexate | All | *P* Value |
| --- | --- | --- | --- | --- | --- |
| N | | 3,288 | 2,572 | 5,860 |  |
| Anti-diabetic medications | no. (%) | 433 (13.2) | 304 (11.8) | 737 (12.6) | 0.122 |
| Lipid lowering medications | no. (%) | 890 (27.1) | 644 (25.0) | 1534 (26.2) | 0.080 |
| Anti-hypertensive medications | no. (%) | 1267 (38.5) | 1030 (40.0) | 2297 (39.2) | 0.239 |
| Pain Medications | no. (%) | 1354 (41.2) | 1259 (49.0) | 2613 (44.6) | <0.001 |
| Glucocorticoids | no. (%) | 866 (26.3) | 935 (36.4) | 1801 (30.7) | <0.001 |
| Phototherapy | no. (%) | 1 (0.0) | 1 (0.0) | 2 (0.0) | 0.864 |

Supplementary Table 4: Baseline healthcare utilization, and costs

|  | | Apremilast | Methotrexate | All | *P* Value |
| --- | --- | --- | --- | --- | --- |
| N | | 3,288 | 2,572 | 5,860 |  |
| Any baseline inpatient hospitalizations | no. (%) | 218 (6.6) | 166 (6.5) | 384 (6.6) | 0.787 |
| Any baseline ED visits | no. (%) | 496 (15.1) | 483 (18.8) | 979 (16.7) | <0.001 |
| No. of baseline office visits | Mean (SD) [Median] | 12.8 (13.8) [8] | 11.7 (12.3) [8] | 12.3 (13.2) [8] | 0.002 |
| Baseline total healthcare costs | Mean (SD) [Median] | $10,509 (26,679.6) [4,324] | $8,882 (17,296.8) [3,845] | $9,795 (23,049.3) [4,123] | 0.005 |

Supplementary Table 5: Number of index medication fills before biologic initiation during the 1-year follow-up period

|  | | **Apremilast Users Who Initiating Biologic in 1 Year** | **Methotrexate Users Who Initiating Biologic in 1 Year** |
| --- | --- | --- | --- |
| N | | 467 | 785 |
| **No. of index medication fills before biologic initiation** | Mean (SD) [Median] | 3.87 (2.51) [3] | 3.50 (2.57) [3] |

Supplementary Table 6: First biologic medication used during the 1-year follow-up period among apremilast patients who initiated biologic

| First biologic use | Frequency | Percent | Cumulative Frequency | Cumulative Percent |
| --- | --- | --- | --- | --- |
| Adalimumab | 210 | 44.97 | 210 | 44.97 |
| Ustekinumab | 113 | 24.20 | 323 | 69.16 |
| Secukinumab | 68 | 14.56 | 391 | 83.73 |
| Etanercept | 35 | 7.49 | 426 | 91.22 |
| Ixekizumab | 26 | 5.57 | 452 | 96.79 |
| Guselkumab | 9 | 1.93 | 461 | 98.72 |
| Golimumab | 3 | 0.64 | 464 | 99.36 |
| Infliximab | 2 | 0.43 | 466 | 99.79 |
| Certolizumab Pegol | 1 | 0.21 | 467 | 100.00 |

Supplementary Table 7: First biologic medication used during the 1-year follow-up period among methotrexate patients who initiated biologic

| First biologic use | Frequency | Percent | Cumulative Frequency | Cumulative Percent |
| --- | --- | --- | --- | --- |
| Adalimumab | 515 | 65.61 | 515 | 65.61 |
| Etanercept | 127 | 16.18 | 642 | 81.78 |
| Ustekinumab | 66 | 8.41 | 708 | 90.19 |
| Secukinumab | 39 | 4.97 | 747 | 95.16 |
| Infliximab | 13 | 1.66 | 760 | 96.82 |
| Certolizumab Pegol | 8 | 1.02 | 768 | 97.83 |
| Ixekizumab | 8 | 1.02 | 776 | 98.85 |
| Guselkumab | 7 | 0.89 | 783 | 99.75 |
| Abatacept | 1 | 0.13 | 784 | 99.87 |
| Golimumab | 1 | 0.13 | 785 | 100.00 |

Supplementary Table 8: Biologic initiation adjusted results

|  | Cox Regression  Risk of Biologic Initiation in 1-Year Follow-up | | Logistic Regression  Any Biologic Use in 1-Year Post Index | |
| --- | --- | --- | --- | --- |
| HR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age groups (Ref: 65+) |  |  |  |  |
| 18-30 | 2.48 (1.76 - 3.47) | <0.001 | 2.71 (1.86 - 3.94) | <0.001 |
| 31-64 | 2.23 (1.67 - 2.98) | <0.001 | 2.45 (1.79 - 3.35) | <0.001 |
| Female (Ref: Male) | 0.86 (0.77 - 0.96) | 0.008 | 0.85 (0.74 - 0.96) | 0.012 |
| Geographic region (Ref. West) |  |  |  |  |
| Midwest | 1.07 (0.87 - 1.32) | 0.516 | 1.09 (0.86 - 1.39) | 0.476 |
| Northeast | 0.81 (0.65 - 1.02) | 0.068 | 0.80 (0.62 - 1.03) | 0.088 |
| South | 1.01 (0.83 - 1.22) | 0.951 | 1.00 (0.80 - 1.25) | 0.990 |
| Unknown | 1.03 (0.83 - 1.28) | 0.801 | 1.04 (0.81 - 1.34) | 0.761 |
| Index year (Ref: 2018) |  |  |  |  |
| 2015 | 1.08 (0.86 - 1.37) | 0.498 | 1.09 (0.84 - 1.43) | 0.510 |
| 2016 | 1.12 (0.89 - 1.41) | 0.323 | 1.12 (0.86 - 1.46) | 0.382 |
| 2017 | 0.97 (0.77 - 1.23) | 0.819 | 0.96 (0.73 - 1.25) | 0.755 |
| Prescriber specialty (Ref: Primary care/PA/NP) |  |  |  |  |
| Dermatologist | 1.01 (0.82 - 1.23) | 0.958 | 1.01 (0.80 - 1.27) | 0.946 |
| Rheumatologist | 1.31 (1.03 - 1.65) | 0.027 | 1.37 (1.03 - 1.81) | 0.028 |
| Other/Unknown | 0.94 (0.76 - 1.16) | 0.560 | 0.92 (0.73 - 1.17) | 0.512 |
| Baseline comorbidities of interest (Yes vs No) |  |  |  |  |
| PsA | 1.17 (1.01 - 1.36) | 0.042 | 1.20 (1.01 - 1.44) | 0.044 |
| Depression | 1.01 (0.84 - 1.21) | 0.896 | 1.03 (0.84 - 1.27) | 0.776 |
| Hypertension | 0.99 (0.85 - 1.16) | 0.938 | 0.99 (0.83 - 1.19) | 0.941 |
| Baseline medication use (Yes vs No) |  |  |  |  |
| Pain medication | 1.22 (1.08 - 1.37) | 0.001 | 1.25 (1.09 - 1.44) | 0.002 |
| Glucocorticoids | 0.97 (0.86 - 1.10) | 0.615 | 0.97 (0.84 - 1.11) | 0.638 |
| Baseline HCRU and Costs |  |  |  |  |
| Any ED visits (yes vs no) | 1.07 (0.92 - 1.24) | 0.380 | 1.07 (0.90 - 1.27) | 0.458 |
| No. of baseline office visits | 1.00 (0.99 - 1.00) | 0.480 | 1.00 (0.99 - 1.00) | 0.417 |
| Total healthcare costs, per $1,000 | 1.00 (1.00 - 1.00) | 0.146 | 1.00 (1.00 - 1.00) | 0.092 |
| Apremilast vs Methotrexate | 0.45 (0.40 - 0.51) | <0.001 | 0.42 (0.37 - 0.48) | <0.001 |

**Abbreviations**: HR, hazard ratio; OR, odds ratio; CI, confidence interval; Ref., reference; PA, physician assistant; NP, nurse practitioner; PsO, psoriasis; HCRU, healthcare resource utilization; ED, emergency department.