## Summary of the incidence of adverse events (AEs) in clinical studies of patients with inflammatory diseases taking an FDA-approved biosimilar (n=474) vs. its reference TNF inhibitor (n=470)

**Note:** No statistically significant safety differences between the agents were found in any category contained within this table

| | Biosimilar n (%) | Reference Biologic n (%) |
|---|---|---|
| **Patients with ≥1 AE** | 295 (62.2) | 311 (66.2) |
| **Patients with ≥1 severe AE** | 17 (3.6) | 12 (2.6) |
| **Patients who discontinued due to an AE** | 28 (5.9) | 21 (4.5) |
| **Deaths** | 2 (0.4) | 1 (0.2) |

Huizinga TWJ et al. *Rheumatol Ther.* 2021;8:41.

## Characteristics and costs of comparative efficacy trials for all TNF inhibitor biosimilars approved in the United States as of October 2019

| Number | | Median (Interquartile Range) | | |
|---|---|---|---|---|
| Trials | Biosimilar products | Patients enrolled, # | Treatment duration, wk | Estimated cost, $US million |
| 10 | 9 | 564 (526–606) | 61 (52–78) | 19.0 (14.0–32.8) |

Moore TJ et al. *JAMA Intern Med*. 2021;181:52.

## Quality differences identified between a reference TNF inhibitor, etanercept, used to treat inflammatory diseases and two of its FDA-approved biosimilars, etanercept-ykro and etanercept-szzs. The data come from various non-clinical comparative studies conducted to support approval of the biosimilars.

**Note:** Detection of a difference does not necessarily indicate the difference is clinically meaningful.

| | Difference from Reference Biologic (Etanercept)? | |
|---|---|---|
| **Type of Study** | **etanercept-ykro** | **etanercept-szzs** |
| **Formulation** | Yes | Yes |
| **Receptor Binding** | Yes | No |
| **Biological Activities** | Yes | Yes |

Bielsky MC et al. *Drug Discov Today*. 2020;25:1910.

## Primary pharmacokinetic endpoints for a reference TNF inhibitor, infliximab, used to treat inflammatory diseases vs. its biosimilar, infliximab-dyyb, in a randomized, single-dose, phase I study.

**Note:** The FDA defines pharmacokinetic equivalence for a biosimilar to be when the geometric mean ratio for the area under the concentration-time curve and maximal concentration between the biosimilar and its reference biologic both fall within the log-transformed range of 80-125%.

| Parameter | Geometric mean | | GMR% | 90% CI |
|---|---|---|---|---|
| | Biosimilar Infliximab-dyyb | Ref. Biologic Infliximab | | |
| $C_{max}$ | 132.29 | 125.95 | 105.03 | 100.64–109.62 |
| AUC | 32,526.76 | 31,949.76 | 101.81 | 96.36–107.56 |

**Abbreviations:** AUC, area under the concentration-time curve from time zero to last quantifiable concentration; $C_{max}$, maximum serum concentration; GMR, geometric mean ratio of biosimilar to reference biologic.

FDA guidance
Park et al. *Expert Rev Clin Immunol*. 2015;11 Suppl 1:25.

## Similarity of safety profiles, including side effect profiles, for five FDA-approved biosimilars used to treat inflammatory diseases, relative to their reference TNF inhibitor, adalimumab. Data compiled from multiple clinical studies.

| Biosimilar | Safety similarity? |
|---|---|
| **Adalimumab-atto** | Yes |
| **Adalimumab-bwwd** | Yes |
| **Adalimumab-adbm** | Yes |
| **Adalimumab-adoz** | Yes |
| **Adalimumab-fkjp** | Yes |

Bielsky MC et al. *Drug Discov Today*. 2020;25:1910.

## Antidrug antibodies to (1) the infliximab reference biologic vs (2) an infliximab biosimilar in 250 patients with rheumatic disorders who were being treated with the infliximab reference biologic.

| Antidrug antibodies? | Infliximab | Infliximab-dyyb |
|---|---|---|
| Yes | 126 | 126 |
| No | 124 | 124 |

Ruiz-Argüello MB et al. *Ann Rheum Dis*. 2016;75:1693.

# Information about FDA biosimilar approvals for reference biologics used to treat inflammatory arthritis, as of October 2021.

| Reference Biologic | Biosimilar Name | Approval Date | U.S. Market Status |
|---|---|---|---|
| **Etanercept** | Etanercept-szzs | August 30, 2016 | Not Available |
| | Etanercept-ykro | April 25, 2019 | Not Available |
| **Adalimumab** | Adalimumab-atto | September 23, 2016 | Not Available |
| | Adalimumab-adbm | August 25, 2017 | Not Available |
| | Adalimumab-adaz | October 30, 2018 | Not Available |
| | Adalimumab-bwwd | July 23, 2019 | Not Available |
| | Adalimumab-afzb | November 15, 2019 | Not Available |
| | Adalimumab-fkjp | July 9, 2020 | Not Available |
| **Infliximab** | Infliximab-dyyb | April 5, 2016 | Available |
| | Infliximab-qbtx | December 13, 2017 | Not Available |
| | Infliximab-abda | April 21, 2017 | Available |
| | Infliximab-axxq | December 6, 2019 | Available |
| **Rituximab** | Rituximab-abbs | November 28, 2018 | Available |
| | Rituximab-pvvr | July 23, 2019 | Available |
| | Rituximab-arrx | December 17, 2020 | Available |

FDA

Gherghescu I et al. *Pharmaceutics*. 2021;13:48.

## Medicare Part D prescription drug plan requirements for infliximab and its biosimilars, as of September 2018

| | Medicare Advantage (%) n=837 | Standalone (%) n=117 |
|---|---|---|
| Prior authorization for reference biologic and biosimilars | 89 | 98 |
| Prior authorization for reference biologic only | 0 | 0 |
| Prior authorization for biosimilars only | 1 | 0 |
| Prior authorization for neither reference biologic nor biosimilars | 10 | 2 |

Socal MP et al. *Am J Health Syst Pharm*. 2021;78:216.

## Coverage for infliximab and its biosimilars in 3761 Medicare Part D prescription drug plans, as of September 2018

| | Coverage (n, %) |
|---|---|
| Reference biologic and biosimilar | 1060 (28.2) |
| Reference biologic only | 2528 (67.2) |
| Reference biosimilar only | "Very few" (~1) |

Socal MP et al. *Am J Health Syst Pharm*. 2021;78:216.

## Utilization of TNF inhibitors prescribed in quarter 1 of 2019 in the United States, including infliximab biosimilars.

| | % of TNF inhibitor prescriptions |
|---|---|
| Infliximab reference biologic | 49.4 |
| Adalimumab | 19.6 |
| Certolizumab | 19.5 |
| Golimumab | 4.6 |
| Etanercept | 6.0 |
| Infliximab biosimilar | 0.9 |

Kim SC et al. *Arthritis Rheumatol*. 2020;72:1036.