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# Switching From Reference to Biosimilar Adalimumab for Patients With Various Inflammatory Conditions

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## Key Messages

- Ten randomized controlled trials and 4 non-randomized studies were identified regarding the clinical effectiveness of switching from reference to biosimilar adalimumab in adult or pediatric patients with rheumatoid arthritis, Crohn disease, ulcerative colitis, hidradenitis suppurativa, plaque psoriasis, or psoriatic arthritis.
- No evidence was identified regarding the clinical effectiveness of switching from reference to biosimilar adalimumab in adult or pediatric patients with uveitis or ankylosing spondylitis and in pediatric patients with polyarticular juvenile idiopathic arthritis.

## Research Questions

1. What is the clinical effectiveness of switching from reference to biosimilar adalimumab in adult or pediatric patients with rheumatoid arthritis, ankylosing spondylitis, Crohn disease, ulcerative colitis, hidradenitis suppurativa, plaque psoriasis, psoriatic arthritis, or uveitis?
2. What is the clinical effectiveness of switching from reference to biosimilar adalimumab in pediatric patients with polyarticular juvenile idiopathic arthritis?

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were adalimumab; rheumatoid arthritis, ankylosing spondylitis, Crohn disease, ulcerative colitis, hidradenitis suppurativa, plaque psoriasis, psoriatic arthritis, uveitis, and polyarticular juvenile idiopathic arthritis; and biosimilars. When possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2016, and January 28, 2021. Internet links were provided, where available.

### Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications.

## Table 1: Selection Criteria

| Criteria | Description |
|---|---|
| **Population** | Q1: Patients (any age) with rheumatoid arthritis, ankylosing spondylitis, Crohn disease, ulcerative colitis, hidradenitis suppurativa, plaque psoriasis, psoriatic arthritis, or uveitis<br>Q2: Pediatric patients with polyarticular juvenile idiopathic arthritis |
| **Intervention** | Q1 and Q2: Switching from reference adalimumab (i.e., Humira) to biosimilar adalimumab (i.e., Hulio, Hyrimoz, Amgevita, Idacio, Hadlima, Abrilada) |
| **Comparator** | Q1 and Q2: Continuous use of reference adalimumab; pre-post switch comparisons |
| **Outcomes** | Q1 and Q2: Effectiveness (e.g., change in disease severity or clinical response, disease activity, clinical remission, health-related quality of life) and safety (e.g., adverse events, withdrawal due to adverse event) |
| **Study designs** | Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies |

# Results

Ten randomized controlled trials[1-10] and 4 non-randomized studies[11-14] were identified regarding the clinical effectiveness of switching from reference to biosimilar adalimumab in adult or pediatric patients with rheumatoid arthritis, Crohn disease, ulcerative colitis, hidradenitis suppurativa, plaque psoriasis, or psoriatic arthritis. No health technology assessments or systematic reviews were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

# Overall Summary of Findings

Ten randomized controlled trials[1-10] and 4 non-randomized studies[11-14] were identified. Seven randomized controlled trials[1,2,4-6,8,9] and 1 non-randomized study[11] looked at outcomes related to switching from reference adalimumab to various adalimumab biosimilar drugs for patients with rheumatoid arthritis. These studies found that drug efficacy, safety issues, and clinical response in terms of drug immunogenicity were not impacted for patients with rheumatoid arthritis who had switched from reference adalimumab to any of the identified biosimilar drugs.[1,2,4-6,8,9,11] Three randomized controlled trials[3,7,10] looked at outcomes related to switching from reference to various biosimilar adalimumab drugs in patients with plaque psoriasis. Authors of these studies found that switching to the biosimilar adalimumab had no impact on drug efficacy, patient safety, or drug immunogenicity.[3,7,10] One non-randomized study[11] looked at outcomes related to switching from reference to a common biosimilar adalimumab in patients with psoriatic arthritis. The authors found that switching to the biosimilar adalimumab was safe and had no impact on drug efficacy.[11] Two non-randomized studies[12,13] found that switching from reference to biosimilar adalimumab was safe and had no impact on effectiveness for patients with inflammatory bowel disease, specifically Crohn disease and ulcerative colitis. One non-randomized study[14] found that switching from reference to biosimilar adalimumab was well-tolerated and had no impact on treatment effectiveness for patients with hidradenitis suppurativa. No evidence was identified regarding patients

with uveitis or ankylosing spondylitis. A detailed summary of the identified studies can be found in Table 2.

No relevant literature was found regarding the clinical effectiveness of switching from reference to biosimilar adalimumab specifically in pediatric patients with polyarticular juvenile idiopathic arthritis; therefore, no summary can be provided.

## Table 2: Summary of Included Studies

| First author, year | Study characteristics and population | Intervention and comparator(s) of interest | Relevant outcome(s) | Authors' conclusions |
|---|---|---|---|---|
| **Randomized controlled trials** | | | | |
| Alten, 2020[1] | **Study design:** RCT<br>**Population:** Patients with RA<br>**N** = NR | **Intervention:** Switch from ADL product to adalimumab biosimilar (FKB327)<br>**Comparator(s):** ADL | Immunogenicity (clinical response) | Development of immunogenic response was similar with FKB327 and ADL, and was not impacted by switching and double-switching between treatments |
| Genovese, 2020[2] | **Study design:** RCT<br>**Population:** Patients with moderate-to-severe active RA<br>**N** = 645 | **Intervention:** Switch from ADL to FKB327<br>**Comparator(s):** ADL | Long-term safety, efficacy, immunogenicity | Safety, efficacy, and immunogenicity were similar among FKB327 and ADL for up to 2 years and were not impacted by single- or double-switching between treatments |
| Hercogova, 2020[3] | **Study design:** RCT<br>**Population:** Patients with moderate-to-severe plaque psoriasis<br>**N** = 443 | **Intervention:** Switch from ADL to adalimumab biosimilar (MSB11022)<br>**Comparator(s):** ADL | Efficacy, safety, immunogenicity | Efficacy, safety, and immunogenicity were not impacted after a switch from ADL to MSB11022 |
| Wiland, 2020[4] | **Study design:** RCT<br>**Population:** Patients with moderate-to-severe RA<br>**N** = 353 | **Intervention:** Switch from ADL to adalimumab biosimilar (Sandoz adalimumab [SDZ-ADL])<br>**Comparator(s):** ADL | Efficacy, safety, immunogenicity | SDZ-ADL demonstrated similar efficacy, safety, and immunogenicity to ADL, and efficacy was sustained after switching from ADL to SDZ-ADL with no impact on safety |
| Cohen, 2019[5] | **Study design:** RCT<br>**Population:** Patients with RA<br>**N** = 467 | **Intervention:** Switch from ADL to adalimumab biosimilar (ABP 501)<br>**Comparator(s):** ADL | Long-term safety, immunogenicity, efficacy | ABP 501 was found to be similar to ADL for long-term safety, immunogenicity, and efficacy, and the switch from ADL to ABP 501 did not impact immunogenicity |
| Genovese, 2019[6] | **Study design:** RCT<br>**Population:** Patients with moderate-to-severe active RA<br>**N** = 645 | **Intervention:** Switch from ADL to FKB327<br>**Comparator(s):** ADL | Efficacy, immunogenicity, safety | Switching had no effect between FKB327 and ADL |

| First author, year | Study characteristics and population | Intervention and comparator(s) of interest | Relevant outcome(s) | Authors' conclusions |
|---|---|---|---|---|
| Blauvelt, 2018[7] | **Study design:** RCT<br>**Population:** Patients with active moderate-to-severe plaque psoriasis<br>**N** = 465 | **Intervention:** Switch from ADL to adalimumab biosimilar (GP2017)<br>**Comparator(s):** ADL | Efficacy, safety, immunogenicity | Switching between GP2017 and ADL had no impact on efficacy, safety, or immunogenicity |
| Cohen, 2018[8] | **Study design:** RCT<br>**Population:** Patients with active RA<br>**N** = 645 | **Intervention:** Switch from ADL to adalimumab biosimilar (BI 695501)<br>**Comparator(s):** ADL | Efficacy, safety, immunogenicity | Switching from ADL to BI 695501 had no impact on efficacy, safety, and immunogenicity |
| Weinblatt, 2018[9] | **Study design:** RCT<br>**Population:** Patients with moderate-to-severe RA<br>**N** = 542 | **Intervention:** Switch from ADL to adalimumab biosimilar (SB5)<br>**Comparator(s):** ADL | Efficacy, safety, immunogenicity | Switching from ADL to SB5 had no treatment issues related to safety, immunogenicity, or efficacy |
| Papp, 2017[10] | **Study design:** RCT<br>**Population:** Patients with moderate-to-severe plaque psoriasis<br>**N** = 308 | **Intervention:** Switch from ADL to ABP 501<br>**Comparator(s):** ADL | Efficacy, safety, immunogenicity | ABP 501 was found to have similar efficacy, safety, and immunogenicity to ADL, including after switching from ADL to ABP 501 |
| **Non-randomized studies** | | | | |
| Bruni, 2021[11] | **Study design:** Prospective cohort study<br>**Population:** Patients with adult RA, axial spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis<br>**N** = 82 | **Intervention:** Switch from ADL to SB5<br>**Comparator(s):** ADL | Efficacy and safety | Switching from ADL to SB5 was shown to be safe in patients with RA and was supported in patients with psoriatic arthritis.<br>Type of juvenile idiopathic arthritis and associated outcomes NR in abstract |
| Lukas, 2020[12] | **Study design:** Prospective cohort study<br>**Population:** Patients with inflammatory bowel disease (measured by Crohn disease and ulcerative colitis indexes)<br>**N** = 186 | **Intervention:** Switch from ADL to SB5<br>**Comparator(s):** ADL | Efficacy and safety | Switching from ADL to SB5 had no effect on treatment efficacy and no new safety signals were detected |

| First author, year | Study characteristics and population | Intervention and comparator(s) of interest | Relevant outcome(s) | Authors' conclusions |
|---|---|---|---|---|
| Ribaldone, 2020[13] | **Study design:** Prospective cohort study<br>**Population:** Patients with Crohn disease<br>**N** = 87 | **Intervention:** Switch from ADL to ABP 501<br>**Comparator(s):** ADL | Effectiveness and safety | Switching from ADL to ABP 501 was shown to be effective and well-tolerated for the treatment of Crohn disease |
| Ricceri, 2020[14] | **Study design:** Retrospective observational study<br>**Population:** Patients with hidradenitis suppurativa<br>**N** = 11 | **Intervention:** Switch from ADL to SB5<br>**Comparator(s):** ADL | Efficacy and safety | Switching from ADL to SB5 was supported in terms of effectiveness and was well-tolerated for the treatment of hidradenitis suppurativa |

ADL = reference adalimumab; NR = not reported; RA = rheumatoid arthritis; RCT = randomized controlled trial.

# References

## Health Technology Assessments

No literature identified.

## Systematic Reviews and Meta-analyses

No literature identified.

## Randomized Controlled Trials


1. Alten R, Markland C, Boyce M, Kawakami K, Muniz R, Genovese MC. Immunogenicity of an adalimumab biosimilar, FKB327, and its reference product in patients with rheumatoid arthritis. *Int J Rheum Dis*. 2020 Nov;23(11):1514-1525. Medline
2. Genovese MC, Kellner H, Arai Y, Muniz R, Alten R. Long-term safety, immunogenicity and efficacy comparing FKB327 with the adalimumab reference product in patients with active rheumatoid arthritis: data from randomised double-blind and open-label extension studies. *RMD Open*. 2020 04;6(1):04. Medline
3. Hercogova J, Papp KA, Chyrok V, Ullmann M, Vlachos P, Edwards CJ. AURIEL-PsO: a randomized, double-blind phase III equivalence trial to demonstrate the clinical similarity of the proposed biosimilar MSB11022 to reference adalimumab in patients with moderate-to-severe chronic plaque-type psoriasis. *Br J Dermatol*. 2020 02;182(2):316-326. Medline
4. Wiland P, Jeka S, Dokoupilova E, et al. Switching to biosimilar SDZ-ADL in patients with moderate-to-severe active rheumatoid arthritis: 48-week efficacy, safety and immunogenicity results from the phase III, randomized, double-blind ADMYRA study. *Biodrugs*. 2020 Dec;34(6):809-823. Medline
5. Cohen S, Pablos JL, Pavelka K, et al. An open-label extension study to demonstrate long-term safety and efficacy of ABP 501 in patients with rheumatoid arthritis. *Arthritis Res Ther*. 2019 03 29;21(1):84. Medline
6. Genovese MC, Glover J, Greenwald M, et al. FKB327, an adalimumab biosimilar, versus the reference product: results of a randomized, phase III, double-blind study, and its open-label extension. *Arthritis Res Ther*. 2019 12 12;21(1):281. Medline
7. Blauvelt A, Lacour JP, Fowler JF, Jr., et al. Phase III randomized study of the proposed adalimumab biosimilar GP2017 in psoriasis: impact of multiple switches. *Br J Dermatol*. 2018 09;179(3):623-631. Medline

8. Cohen SB, Alonso-Ruiz A, Klimiuk PA, et al. Similar efficacy, safety and immunogenicity of adalimumab biosimilar BI 695501 and Humira reference product in patients with moderately to severely active rheumatoid arthritis: results from the phase III randomised VOLTAIRE-RA equivalence study. *Ann Rheum Dis*. 2018 06;77(6):914-921. Medline

9. Weinblatt ME, Baranauskaite A, Dokoupilova E, et al. Switching from reference adalimumab to SB5 (adalimumab biosimilar) in patients with rheumatoid arthritis: fifty-two-week phase III randomized study results. *Arthritis Rheumatol*. 2018 06;70(6):832-840. Medline

10. Papp K, Bachelez H, Costanzo A, et al. Clinical similarity of the biosimilar ABP 501 compared with adalimumab after single transition: long-term results from a randomized controlled, double-blind, 52-week, phase III trial in patients with moderate-to-severe plaque psoriasis. *Br J Dermatol*. 2017 12;177(6):1562-1574. Medline

## Non-Randomized Studies

11. Bruni C, Bitti R, Nacci F, et al. Efficacy and safety of switching from reference adalimumab to SB5 in a real-life cohort of inflammatory rheumatic joint diseases. *Clin Rheumatol*. 2021 Jan;40(1):85-91. Medline

12. Lukas M, Malickova K, Kolar M, et al. Switching from originator adalimumab to the biosimilar SB5 in patients with inflammatory bowel disease: short-term experience from a single tertiary clinical centre. *J Crohns Colitis*. 2020 Jul 30;14(7):915-919. Medline

13. Ribaldone DG, Caviglia GP, Pellicano R, et al. Effectiveness and safety of adalimumab biosimilar ABP 501 in Crohn's disease: an observational study. *Rev Esp Enferm Dig*. 2020 Mar;112(3):195-200. Medline

14. Ricceri F, Rosi E, Di Cesare A, Pescitelli L, Fastame MT, Prignano F. Clinical experience with adalimumab biosimilar imraldi in hidradenitis suppurativa. *Dermatol Ther*. 2020 Nov;33(6):e14387. Medline

# Appendix 1: References of Potential Interest

## Systematic Reviews

### *Methodology Not Specified*

15. Huizinga TWJ, Torii Y, Muniz R. Adalimumab biosimilars in the treatment of rheumatoid arthritis: a systematic review of the evidence for biosimilarity. *Rheumatol*. 2020 Dec 01;01:01. Medline

## Non-Randomized Study

### *Alternative Outcome – Pharmacokinetic Evaluation*

16. Kang J, Eudy-Byrne RJ, Mondick J, Knebel W, Jayadeva G, Liesenfeld KH. Population pharmacokinetics of adalimumab biosimilar adalimumab-adbm and reference product in healthy subjects and patients with rheumatoid arthritis to assess pharmacokinetic similarity. *Br J Clin Pharmacol*. 2020 Nov;86(11):2274-2285. Medline

## Review Articles

17. Lee A, Shirley M. PF-06410293: an adalimumab biosimilar. *Biodrugs*. 2020 Oct;34(5):695-698. Medline

18. Viscido A, Latella G. Effectiveness and safety of switching to adalimumab biosimilar ABP 501 in Crohn's disease. *Rev Esp Enferm Dig*. 2020 Nov 19;19:19. Medline

19. Al-Salama ZT. FKB327: an adalimumab biosimilar. *Biodrugs*. 2019 Feb;33(1):113-116. Medline

20. Frampton JE. SB5: an adalimumab Biosimilar. *Biodrugs*. 2018 Oct;32(5):507-510. Medline

21. Heo YA. GP2017: an adalimumab biosimilar. *Biodrugs*. 2018 Dec;32(6):635-638. Medline

## Additional Information

### *Product Assessment Report*

22. Committee for Medicinal Products for Human Use. Assessment report: Imraldi (adalimumab). (*European public assessment report*). Amsterdam (NL): European Medicines Agency; 2017 Jun 22: https://www.ema.europa.eu/en/documents/assessment-report/imraldi-epar-public-assessment-report_en.pdf. Accessed 2021 Feb 3.
*Note: Refer to Section 2.5.3. Discussion on Clinical Efficacy: Design and Conduct of Clinical Studies (p. 63).*