

CADTH Reference List

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

Authors: Shannon Hill, Charlene Argáez

Disclaimer: The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to requests@cadth.ca

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 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 trials¹⁻¹⁰ and 4 non-randomized studies¹¹⁻¹⁴ 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 trials¹⁻¹⁰ and 4 non-randomized studies¹¹⁻¹⁴ were identified. Seven randomized controlled trials^{1,2,4-6,8,9} and 1 non-randomized study¹¹ 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 study¹¹ 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 study¹⁴ 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 Population: Patients with RA N = NR	Intervention: Switch from ADL product to adalimumab biosimilar (FKB327) 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 Population: Patients with moderate-to-severe active RA N = 645	Intervention: Switch from ADL to FKB327 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 Population: Patients with moderate-to-severe plaque psoriasis N = 443	Intervention: Switch from ADL to adalimumab biosimilar (MSB11022) 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 Population: Patients with moderate-to-severe RA N = 353	Intervention: Switch from ADL to adalimumab biosimilar (Sandoz adalimumab [SDZ-ADL]) 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 Population: Patients with RA N = 467	Intervention: Switch from ADL to adalimumab biosimilar (ABP 501) 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 Population: Patients with moderate-to-severe active RA N = 645	Intervention: Switch from ADL to FKB327 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 Population: Patients with active moderate-to-severe plaque psoriasis N = 465	Intervention: Switch from ADL to adalimumab biosimilar (GP2017) 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 Population: Patients with active RA N = 645	Intervention: Switch from ADL to adalimumab biosimilar (BI 695501) 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 Population: Patients with moderate-to-severe RA N = 542	Intervention: Switch from ADL to adalimumab biosimilar (SB5) 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 Population: Patients with moderate-to-severe plaque psoriasis N = 308	Intervention: Switch from ADL to ABP 501 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 Population: Patients with adult RA, axial spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis N = 82	Intervention: Switch from ADL to SB5 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. Type of juvenile idiopathic arthritis and associated outcomes NR in abstract
Lukas, 2020 ¹²	Study design: Prospective cohort study Population: Patients with inflammatory bowel disease (measured by Crohn disease and ulcerative colitis indexes) N = 186	Intervention: Switch from ADL to SB5 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 Population: Patients with Crohn disease N = 87	Intervention: Switch from ADL to ABP 501 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 Population: Patients with hidradenitis suppurativa N = 11	Intervention: Switch from ADL to SB5 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).