Humira and Biosimilars

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Objectives

- To provide information surrounding Adalimumab on:
  - Biosimilars and its equivalence
  - New emerging therapies
  - New and rare complications
  - Upcoming combination therapies
  - New formulations
- To Explain the difference between biosimilars and interchangeable biosimilars.

Humira (Adalimumab)

- Biologic
- Tumor necrosis factor (TNF) blocking agent
- Used to treat various inflammatory and autoimmune disorders.
- Approved by the FDA in 2002.

FDA Approved Indications

Rheumatoid Arthritis (RA)	Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA
Juvenile Idiopathic Arthritis (JIA)	Reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older.
Psoriatic Arthritis (PsA)	Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
Ankylosing Spondylitis (AS)	Reducing signs and symptoms in adult patients with active AS.
Crohn's Disease (CD)	Treatment of moderately to severely active Crohn's disease in adults and pediatric patients 6 years of age and older.
Ulcerative Colitis (UC)	Treatment of moderately to severely active ulcerative colitis in adults and pediatric patients 5 years of age and older. Limitations of Use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF blockers
Plaque Psoriasis (Ps)	Treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
Hidradenitis Suppurativa (HS)	Treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older.
Uveitis (UV)	Treatment of non-infectious intermediate, posterior, and panuveitis in adults and pediatric patients 2 years of age and older.

AbbVie Inc. Humira (Adalimumab). [Package Insert] U.S. Food and Drug Administration website. Revised February 2021. Accessed December 16, 2023.

Humira (Adalimumab)

- Administration
  - Injectable subcutaneous syringe, prefilled pen or solution
  - Must conduct a TB test prior to use
- Side effects
  - Injection site reactions
  - Antibody development
- Black box warning
  - Malignancy
  - Serious infections

AbbVie Inc. Humira (Adalimumab). [Package Insert] U.S. Food and Drug Administration website. Revised February 2021. Accessed December 16, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125057s410lbl.pdf

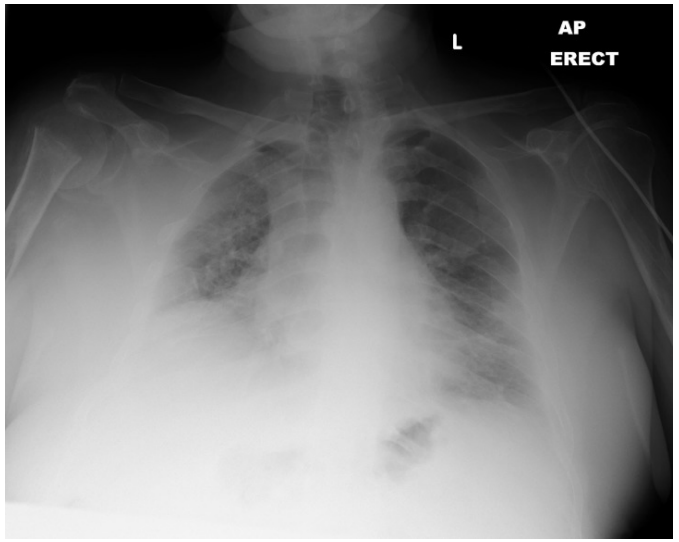
New and Rare Complications

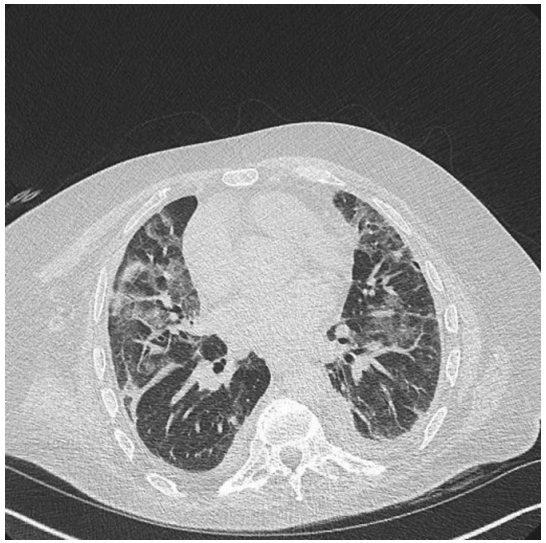
- Interstitial lung diseases
  - Low incidence rate of ILD
  - Incidence with is higher when combined with DMARDs
  - Lowest incidence of ILD when compared to other anti-TNF alfa therapy
  - Pathway is still unknown for pathogenesis of ILD

Interstitial Lung Diseases induced by adalimumab

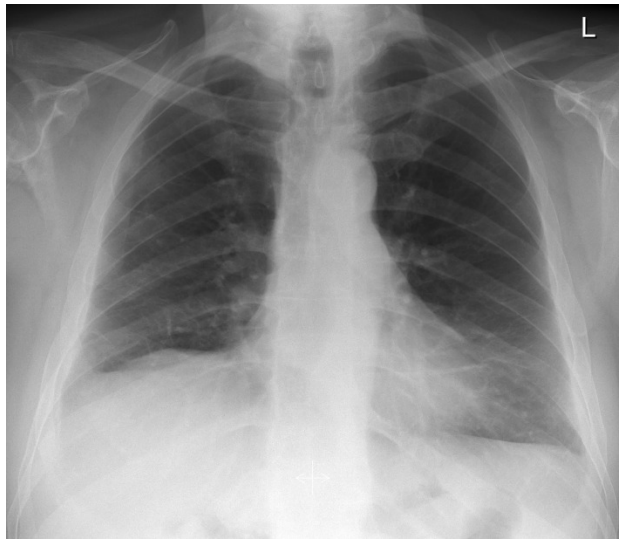
- There are multiple reports of anti-tumor necrosis factor (TNF)-induced lung disease, especially in patients with rheumatologic diseases. Adalimumab is an anti-TNF drug used to induce and maintain remission in patients with immune-mediated diseases
  - Case of drug-induced interstitial lung disease secondary to adalimumab
  - Adalimumab-induced interstitial pneumonia with an improvement of pre-existing rheumatoid arthritis-associated lung involvement

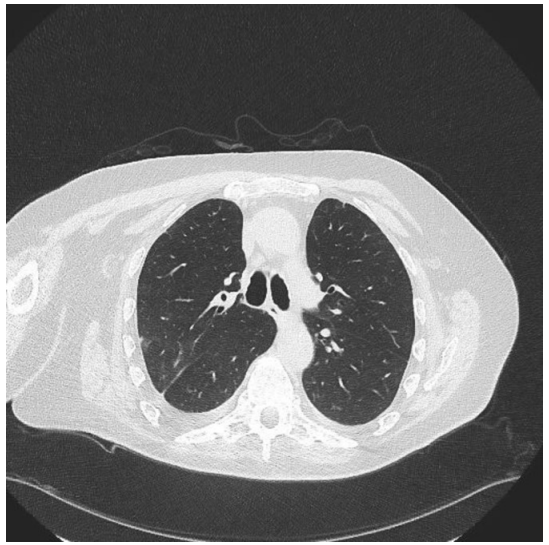
With concurrent use of adalimumab





After 2 months discontinuation of adalimumab





Alaee S, Jones Q. Case of drug-induced interstitial lung disease secondary to adalimumab. BMJ Case Rep. 2018 May 15;2018:bcr2018224375. doi: 10.1136/bcr-2018-224375. PMID: 29764848; PMCID: PMC5965751.

Hot Topic

- For the first time, biosimilars of Humira have became available in the U.S.
- Up to a dozen biosimilars became available in 2023
- Patent on Humira expired in 2016
- Patent thickening prevented other manufacturers from making biosimilars

What are Biosimilars?

- Biologic drugs that are highly similar to the FDA-approved reference biologic product notwithstanding minor differences in clinically inactive components.
- Approved through an abbreviated pathway that relies on existing safety and efficacy data of the reference product.
- No clinically meaningful differences from the reference product in terms of safety, efficacy, purity, and potency.
- Biosimilars can have fewer indications and route of administration than the reference product.
- Cannot be substituted for the reference biologic product.

What Makes a Biosimilar Interchangeable?

- Interchangeable biosimilar product is expected to produce the same clinical result as the reference product in any given patient
- Have to demonstrate similar safety and efficacy outcomes in clinical studies
- Can be substituted for the reference biologic product
- Interchangeable biosimilars Can lead to lowering drug prices & Yield savings to the U.S. healthcare system
- The purple book

Humira Biosimilars

Product	Company	Launch Date	Concentration	Interchangeability Designation Approved	Citrate free
Abrilada™	Pfizer	November 2023	Low (50MG)	No[2]	Yes
Amjevita™	Amgen	Jan 31, 2023	Low (50MG)	No[3]	Yes
Cyltezo®	Boehringer Ingelheim	July 1, 2023	Low (50MG)	Yes[4]	Yes
Adalimumab-adbm	Boeheringer Ingelheim	October 2, 2023	Low (50MG)	Yes	Yes
Hadlima™	Organon/Samsung Bioepis	July 1, 2023	Low (50MG)	No[5]	No
Hadlima™	Organon/Samsung Bioepis	July 31, 2023	High (100MG)	No[6]	Yes
Hulio®	Mylan/Viatris/Biocon/Fujifilm Koywa Kirin	July 31, 2023	Low (50MG)	No	Yes
Adalimumab-fkjp	Biocon	July 1, 2023	Low (50MG)	No	Yes
Hyrimoz®	Sandoz/Novartis	July 1, 2023	Low (50MG)	No[8]	No
Adalimumab-adaz	Sandoz	July 1, 2023	Low (50MG)	No	No
Hyrimoz®	Sandoz/Novartis	July 1, 2023	High (100MG)	No[8]	Yes
Adalimumab-adaz	Sandoz	July 1, 2023	High (100MG)	No	Yes
Idacio®	Fresenius Kabi	July 2023	Low (50MG)	No[7]	Yes
Yuflyma®	Celltrion	July 1, 2023	High (100MG)	No	Yes
Yusimry™	Coherus BioSciences	July 1, 2023	Low (50MG)	No	Yes

"Humira Biosimilar Landscape Overview." Cardinal Health, June 2023. Accessed November 28, 2023.

FDA NEWS RELEASE

FDA Approves Cyltezo, the First Interchangeable Biosimilar to Humira

Second Interchangeable Biosimilar Product Approved by Agency

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For Immediate Release: October 18, 2021

The U.S. Food and Drug Administration approved the first interchangeable biosimilar product to treat certain inflammatory diseases. Cyltezo (adalimumab-adbm), originally approved in August 2017, is both biosimilar to, and interchangeable with (may be substituted for), its reference product Humira (adalimumab) for Cyltezo's approved uses. Cyltezo is the second interchangeable biosimilar product approved by the agency and the first interchangeable monoclonal antibody. Once on the market, approved biosimilar and interchangeable biosimilar products can play a role in facilitating access to treatments for many serious health conditions.

"The biosimilar and interchangeable approval pathway was created to help increase access to treatment options for patients with serious medical conditions," said Acting FDA Commissioner Janet Woodcock, M.D. "We continue to be steadfast in our commitment to provide patients with alternative high-quality, affordable medications that are proven to be safe and effective."

"FDA Approves Cyltezo, the first Interchangeable Biosimilar to Humira." U.S. Food and Drug Administration, FDA. October 18, 2021. Accessed December 8th, 2023

Cyltezo

- Brand for Adalimumab-adbm
- Both biosimilar to and interchangeable with Humira
- Approved for same indications as Humira
- Administration: a single-dose, pre-filled glass syringe (40 mg/0.8 mL, 20 mg/0.4 mL), is administered subcutaneously.
- Most serious Side effects: infections and malignancies.
- Most common expected ADRs: upper respiratory and sinus infections, injection site reactions, headache and rash.
- Boxed warning:
  - Serious infections that may lead to hospitalization or death.
  - lymphoma and other malignancies

"FDA Approves Cyltezo, the first Interchangeable Biosimilar to Humira." U.S. Food and Drug Administration, FDA. October 18, 2021. Accessed December 8th, 2023

References

AbbVie Inc. Humira (Adalimumab). [Package Insert] U.S. Food and Drug Administration website. Revised February 2021. Accessed December 16, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125057s410lbl.pdf

"FDA Approves Cyltezo, the first Interchangeable Biosimilar to Humira." U.S. Food and Drug Administration, FDA. October 18, 2021. Accessed December 8th, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-cyltezo-first-interchangeable-biosimilar-humira

"Humira Biosimilar Landscape Overview." Cardinal Health, June 2023. Accessed Nov 28, 2023. https://www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/humira-biosimilar-landscape-overview.html

"Prepare for up to a Dozen Humira Biosimilars." Pharmacist's Letter, Nov 2022. Accessed Nov 28, 2023. https://pharmacist.therapeuticresearch.com/Content/Articles/PL/2022/Nov/Prepare-for-up-to-a-Dozen-Humira-Biosimilars

Jukka Lehtonen, Valtteri Uusitalo, Pauli Pöyhönen, Mikko I Mäyränpää, Markku Kupari, Cardiac sarcoidosis: phenotypes, diagnosis, treatment, and prognosis, European Heart Journal, Volume 44, Issue 17, 1 May 2023, Pages 1495–1510, https://doi.org/10.1093/eurheartj/ehad067

Baker MC, Liu Y, Lu R, Lin J, Melehani J, Robinson WH. Incidence of Interstitial Lung Disease in Patients With Rheumatoid Arthritis Treated With Biologic and Targeted Synthetic Disease-Modifying Antirheumatic Drugs. JAMA Netw Open. 2023 Mar 1;6(3):e233640. doi: 10.1001/jamanetworkopen.2023.3640. PMID: 36939701; PMCID: PMC10028485.

References Continued

Yalcin M, Akarsu M, Celik A, Sagol O, Tunali S, Ertener O, Bengi G, Akpinar H. A comparison of the effects of infliximab, adalimumab, and pentoxifylline on rats with non-alcoholic steatohepatitis. Turk J Gastroenterol. 2014 Dec;25 Suppl 1:167-75. doi: 10.5152/tjg.2014.5121. PMID: 25910299.

Nonalcoholic steatohepatitis treatment. American Liver Foundation. (2023, November 1). https://liverfoundation.org/liver-diseases/fatty-liver-disease/nonalcoholic-steatohepatitis-nash/nash-treatment/

Stievenart, J., Le Guenno, G., Ruivard, M., Rieu, V., André, M., & Grobost, V. (2021). Case Report: TNFα Antagonists Are an Effective Therapy in Cardiac Sarcoidosis. Frontiers in cardiovascular medicine, 8, 676407. https://doi.org/10.3389/fcvm.2021.676407

Sweis, J. J. G., Sweis, N. W. G., Ascoli, C., Levin, B., Avitall, B., Rubinstein, I., Kondos, G., Culver, D. A., Judson, M., Baughman, R., Darbar, D., Drake, W., Shahrara, S., Cooper, L. T., Jr, & Sweiss, N. J. (2022). Adalimumab in the treatment of cardiac sarcoidosis: Single center case series and narrative literature review. *Respiratory medicine case reports*, *40*, 101766. https://doi.org/10.1016/j.rmcr.2022.101766

Jukka Lehtonen, Valtteri Uusitalo, Pauli Pöyhönen, Mikko I Mäyränpää, Markku Kupari, Cardiac sarcoidosis: phenotypes, diagnosis, treatment, and prognosis, *European Heart Journal*, Volume 44, Issue 17, 1 May 2023, Pages 1495–1510, https://doi.org/10.1093/eurheartj/ehad067

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