Hadlima™ (adalimumab-bwwd) – New biosimilar approval

- On July 24, 2019, Samsung Bioepis announced the FDA approval of Hadlima (adalimumab-bwwd), a biosimilar to AbbVie's Humira® (adalimumab).
    - Hadlima is the fourth FDA-approved biosimilar to Humira.
    - Amgen's Amjevita™ (adalimumab-atto) was the first biosimilar to Humira and was approved on September 23, 2016. The second biosimilar to Humira was Boehringer Ingelheim's Cyltezo™ (adalimumab-adbm), approved on August 25, 2017. Sandoz's Hyrimoz™ (adalimumab-adaz) was approved on October 31, 2018.
    - Licensing agreements have been signed with AbbVie allowing launch of Amjevita on January 31, 2023, Cyltezo on July 1, 2023, and Hyrimoz on September 30, 2023.

- Hadlima, Amjevita, Cyltezo, Hyrimoz and Humira share the following 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 4 years of age and older. In contrast, Humira is approved for JIA in patients ≥ 2 years of age.
    - **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.
    - **Adult Crohn's Disease (CD)**: Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's Disease who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab products.
    - **Ulcerative Colitis (UC)**: Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine. The effectiveness of adalimumab products has not been established in patients who have lost response to or were intolerant to TNF blockers.
    - **Plaque Psoriasis (PsO)**: The 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.

- In addition, Humira is also approved for pediatric CD, hidradenitis suppurativa, and uveitis.

- A biosimilar product is a biological agent that is considered highly similar to an already-approved biological drug, known as the reference product. Biological products are generally derived from a living organism and can come from many sources, including humans, animals, microorganisms or yeast.
    - A biosimilar product must show no clinically meaningful differences in terms of safety and effectiveness from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products.
    - In addition, a biosimilar product may only be approved for the indication(s) and condition(s) that have been FDA approved for the reference product, and must have the same mechanism(s) of action, route(s) of administration, dosage form(s) and strength(s) as the reference product.

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- Hadlima has been approved as a biosimilar, ***not*** as an interchangeable product.
- The approval of Hadlima is based on a review of analytical, non-clinical, pharmacokinetic and clinical data confirming that Hadlima is highly similar to Humira.
- Similar to Amjevita, Cyltezo, Hyrimoz and Humira, Hadlima carries a boxed warning for serious infections and malignancy.
- Warnings and precautions of Hadlima include hypersensitivity reactions, hepatitis B virus reactivation, neurologic reactions, hematological reactions, use with Kineret® (anakinra), heart failure, autoimmunity, immunizations, and use with Orencia® (abatacept).
- The most common adverse reactions (> 10%) with Hadlima use were infections (eg, upper respiratory, sinusitis), injection site reactions, headache and rash.
- The recommended dose of Hadlima administered by subcutaneous (SC) injection is as follows:

Indication	Recommended Dose
Adult RA*, PsA, AS	40 mg every other week
JIA† (weight ≥ 30 kg)	40 mg every other week
Adult CD and UC	Day 1: 160 mg Day 15: 80 mg Day 29 and maintenance: 40 mg every other week§
Adult PsO	Day 1: 80 mg Day 8 and maintenance: 40 mg every other week

*Some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week.
†Amjevita and Humira are also approved for 15 kg and < 30 kg: 20 mg every other week. Humira is approved for 10 kg to < 15 kg: 10 mg every other week.
§Hadlima should only be continued in UC if patients have shown clinical remission by 8 weeks (day 57).

- Hadlima is intended for use under the guidance and supervision of a physician. A patient may self-inject Hadlima or a caregiver may inject Hadlima if a physician determines that it is appropriate, and with medical follow-up, as necessary, after proper training in SC injection technique.
- Consult the Humira drug label for dosing recommendations for additional indications.
- Per a licensing agreement signed with AbbVie, Merck will launch Samsung Bioepis' Hadlima after June 30, 2023. Hadlima will be available as a 40 mg/0.8 mL prefilled syringe and autoinjector.