Cyltezo™ (adalimumab-adbm) – New biosimilar approval

- On August 25, 2017, the FDA approved Cyltezo (adalimumab-adbm), Boehringer Ingelheim's (BI) biosimilar to AbbVie's Humira® (adalimumab).
    - This is the second FDA-approved biosimilar to Humira. The first was Amgen's Amjevita™ (adalimumab-atto).
    - Cyltezo and Amjevita share 7 of the 10 indications approved for Humira.

- Cyltezo, Amjevita and Humira are approved for:
    - **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. In contrast, Humira is approved for JIA in patients ≥ 2 years old.
    - **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 CD 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 Remicade® (infliximab).
    - **Ulcerative colitis (UC)**: inducing and sustaining clinical remission in adult patients with moderately to severely active UC who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine.
    - **Plaque psoriasis (PsO)**: treatment of adult patients with moderate to severe chronic PsO 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.

- Cyltezo is approved as a biosimilar to Humira, ***not*** as an interchangeable product.
    - BI announced it is conducting an interchangeability study of Cyltezo vs. Humira in patients with plaque psoriasis. This is the first interchangeability study being conducted in the U.S. Results are expected in the second half of 2019.

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- The approval of Cyltezo is based on a review of analytical, non-clinical, pharmacokinetic and clinical data confirming that Cyltezo is highly similar to Humira. An efficacy and safety similarity study conducted in patients with RA demonstrated comparable clinical efficacy between Cyltezo and Humira.

- Similar to Humira and Amjevita, Cyltezo carries a boxed warning for serious infections and malignancies.

- Other warnings and precautions of Cyltezo include hypersensitivity reactions, hepatitis B virus reactivation, neurologic reactions, hematological reactions, use with Kineret® (anakinra) or Orencia® (abatacept), heart failure, autoimmunity, and immunizations.

- The most common adverse reactions (> 10%) with Cyltezo use were infections (eg, upper respiratory, sinusitis), injection site reactions, headache and rash.

- The recommended dose of Cyltezo administered by subcutaneous injection is as follows:

Indication	Recommended Dose
Adult RA, AS, and PsA	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 & Maintenance Dose: 40 mg every other week
Adult PsO	Day 1: 80 mg Day 8 & Maintenance Dose: 40 mg every other week

* Amjevita and Humira are also approved for 15 kg to < 30 kg: 20 mg every other week. Humira is approved for 10 kg to < 15 kg: 10 mg every other week.

- Dosing of Humira for additional indications can be found in its drug label.

- The launch plans for Cyltezo are pending due to ongoing patent litigation. Upon launch, Cyltezo will be available as a 40 mg/0.8 mL single-dose prefilled syringe.

    — Launch plans for Amjevita are also pending due to ongoing patent litigation.