Zymfentra™ (infliximab-dyyb) – New drug approval

- On October 23, 2023, Celltrion announced the FDA approval of Zymfentra (infliximab-dyyb), in adults for maintenance treatment of:
    - Moderately to severely active ulcerative colitis (UC) following treatment with an infliximab product administered intravenously (IV)
    - Moderately to severely active Crohn's disease (CD) following treatment with an infliximab product administered IV.
- Zymfentra is the first subcutaneous (SC) formulation of infliximab. Infliximab was previously only available as an IV infusion under the brand name Remicade® and its biosimilars.
    - In addition to treatment of adult UC and CD, Remicade is also approved for pediatric UC, pediatric CD, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis.
- The efficacy of Zymfentra was established in a randomized, double-blind, placebo-controlled study in adult patients with moderately to severely active UC. All patients received three IV induction doses at weeks 0, 2 and 6. In order to be randomized to treatment in the study, patients had to be in clinical response at week 10. A total of 438 patients were randomized at week 10 to Zymfentra or placebo every 2 weeks. The primary endpoint was the proportion of patients in clinical remission at week 54.
    - Clinical remission was achieved in 43% and 21% of patients treated with Zymfentra and placebo, respectively (treatment difference 21, 95% CI: 12, 29; $p < 0.0001$).
- The efficacy of Zymfentra was also established in a randomized, double-blind, placebo-controlled study in adult subjects with moderately to severely active CD. The study design was similar to the UC trial. A total of 323 patients were randomized at week 10 to Zymfentra or placebo every 2 weeks. The co-primary endpoints were clinical remission (based on Crohn's Disease Activity Index [CDAI]) and endoscopic response at week 54.
    - Clinical remission was achieved in 63% and 30% of patients treated with Zymfentra and placebo, respectively (treatment difference 35, 95% CI: 24, 45; $p < 0.0001$).
    - Endoscopic response was achieved in 50% and 18% of patients treated with Zymfentra and placebo, respectively (treatment difference 34, 95% CI: 23, 43; $p < 0.0001$).
- Zymfentra carries a boxed warning for serious infections and malignancy.
- Additional warnings and precautions for Zymfentra include hepatitis B virus reactivation; hepatotoxicity; congestive heart failure; hematologic reactions; hypersensitivity and other administration reactions; neurologic reactions; risk of infection with concurrent administration of other biological products; risk of additive immunosuppressive effects from prior biological products; autoimmunity; vaccinations and use of live vaccines/therapeutic infectious agents.
- The most common adverse reactions (≥ 3%) with Zymfentra use were:
    - UC: COVID-19, anemia, arthralgia, injection site reaction, increased alanine aminotransferase, and abdominal pain.

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    - CD: COVID-19, headache, upper respiratory tract infection, injection site reaction, diarrhea, increased blood creatine phosphokinase, arthralgia, increased alanine aminotransferase, hypertension, urinary tract infection, neutropenia, dizziness, and leukopenia.

- Zymfentra is indicated as maintenance treatment only, starting at week 10 and thereafter. All patients must complete an IV induction regimen with an infliximab product before starting Zymfentra. The recommended maintenance dose of Zymfentra starting at week 10 and thereafter is 120 mg SC once every two weeks.

    - To switch patients who are responding to maintenance therapy with an infliximab product administered IV, the first SC dose of Zymfentra should be administered in place of the next scheduled IV infusion and every two weeks thereafter.
    - Zymfentra is intended for use under the guidance and supervision of a healthcare professional. If a healthcare professional determines that it is appropriate, patients may self-inject Zymfentra, or caregivers may inject Zymfentra after proper training in SC injection technique.

- Celltrion's launch plans for Zymfentra are pending. Zymfentra will be available as a 120 mg/mL single-dose prefilled syringe, single-dose pre-filled syringe with needle shield, and single-dose pre-filled pen.