Use, Safety and Efficacy of Zrc 3197, a Biosimilar Candidate for Reference Adalimumab (Humira) from a Tertiary Pediatric Rheumatology Centre in India

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Background/Purpose & Methods

• This is the first study to analyse the use, safety and efficacy of ZRC 3197 in pediatric rheumatology patients.

• Records of 29 children, who have been given ZRC3197 from Dec ‘14 till 15 June ’16 were analysed to assess
  i. Use, safety and efficacy in children with JIA
  ii. Use, safety and efficacy in children with Uveitis. A predesigned proforma captured the demographic details, medications, 74 joint count and SUN classification for uveitis.
Result

29 children (16 males) have received ZRC 3197 to date.

- **Indications:** JIA: (n=15) ERA 12, IBD and Psoriatic arthritis 1 each, PJIA 1.
  - Median age at commencing ZRC3197: 8.66yrs.(5.16-20.16) All patients were on methotrexate/ and/or oral steroids/topical steroid eye drops. Median duration of therapy with ZRC3197: 6 months (0.5-17 months).
Safety:

- **Prebiologic screen:** Tuberculosis screening positive in 4: 2 drug anti tubercular therapy (ATT) for latent TB given to 3; 1 treated for TB disease.

- **Post biologic:** 1 child had multi dermatomal herpes zoster after 1 dose and drug was discontinued.

Efficacy:

- In 13 children with JIA, (2 patient's follow up <3 mo) ZRC3197 was effective in all domains noted at 3mo and 6mo of use as determined by the Wilcoxon Signed Ranks test. Median duration to achieve inactive disease in 12 children was 3 weeks (2-32 weeks), 3 were still active at last follow up, none flared till last follow-up.

- In children with uveitis, ZRC 3197 was effective, median duration to achieve inactivity per SUN in 10 children was 4 weeks (2-24 weeks).
Conclusion

• ZRC 3197 is a safe and rapidly effective agent for children with JIA and uveitis resistant to methotrexate. This is the first report of the use of ZRC3197 in children.
Adalimumab (Adalimumab) 40 mg /0.8 mL single use prefilled syringe and 20 mg /0.4 mL single use prefilled syringe

**DESCRIPTION:** EXEMPTIATM (Adalimumab) is a recombinant human IgG1 monoclonal antibody specific for human tumor necrosis factor (TNF-α). EXEMPTIATM is supplied as a sterile, preservative-free solution of Adalimumab for subcutaneous administration. The solution of EXEMPTIATM is clear and colorless.

**MECHANISM OF ACTION:** Adalimumab binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF-α receptors. Adalimumab also lyses surface TNF expressing cells in vitro in the presence of complement. Elevated levels of TNF-α is found in the synovial fluid of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis patients and play an important role in both the pathologic inflammation and the joint destruction that are hallmarks of these diseases.

**INDICATIONS & DOSAGE:** Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis: The recommended dose of EXEMPTIATM for adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or ankylosing spondylitis (AS) is 40 mg subcutaneously administered every other week. Methotrexate (MTX), other non-biologic DMARDs, glucocorticoids, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or analgesics may be continued during treatment with EXEMPTIATM. Juvenile Idiopathic Arthritis: Exemptia™ dosing in JIA is based on weight: for 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg s.c. every other week. For 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg s.c. every other week and for ≥ 30 kg (66 lbs): 40 mg s.c. every other week. Plaque Psoriasis or Non-Infectious Uveitis: Initial dose of 80 mg, followed by 40 mg every other week starting from week one after initial dose. Hidradenitis Suppurativa: 160 mg (Day 1) (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days), followed by 80 mg two weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg every week. Adult Crohn’s Disease and Ulcerative Colitis: Initial dose (Day 1): 160 mg s.c. (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days). Second dose two weeks later (Day 15): 80 mg. Two weeks later (Day 29): Begin a maintenance dose of 40 mg s.c. every other week. Pediatric Crohn’s Disease: For weight 17 kg (37 lbs) to < 40 kg (88 lbs): Initial dose (Day 1): 80 mg s.c. (two 40 mg injections in one day). Second dose two weeks later (Day 15): 40 mg s.c.. Two weeks later (Day 29): Begin a maintenance dose of 20 mg s.c. every other week. For ≥ 40 kg (88 lbs): Initial dose (Day 1): 160 mg s.c. (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days). Second dose two weeks later (Day 15): 80 mg s.c. (two 40 mg injections in one day). Two weeks later (Day 29): Begin a maintenance dose of 40 mg s.c. every other week.

**CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients, Moderate to severe heart failure, Active tuberculosis or other severe infections such as sepsis and opportunistic infections. Special Warnings and Precautions: Serious and fungal infections: Do not start EXEMPTIATM during an active infection. If an infection develops, monitor carefully, and stop EXEMPTIATM if infection becomes serious.

**SIDE EFFECTS:** The most serious adverse reactions include the following: Serious Infections- Tuberculosis and Opportunistic Infections, Malignancies. The Clinical experience has reported Upper Respiratory Tract Infection (URT), Increased creatine phosphokinase, Headache, Rash, Sinusitis, Nausea, Urinary Tract Infection (UTI), Abdominal pain, Flulike syndrome, Hyperlipidemia, Back pain, Hypercholesterolemia, Hematuria, Hypertension, Increased alkaline phosphatase as common side effects. STORAGE CONDITION: Store between + 2 °C and + 8 °C, in the carton to protect from light. Do not freeze Exemptia™. Do not use Exemptia™ if frozen, even if it has been thawed. Keep out of reach of children. PRESENTATION: a) Injection: 40 mg/0.8 mL in a single-use prefilled syringe b) Injection: 20 mg/0.4 mL in a single-use prefilled syringe.
Please consult full Prescribing Information before prescribing.

Zydus Cadila does not recommend the use of any product in any different manner than as described in the prescribing information.

Further information is available on request from:

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Thank you