

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

Manjari Agarwal¹ , Abhay Shivpuri² , Sumidha Mittal³ , Amit Khosla⁴ and Sujata Sawhney⁵

1. Institute of Child Health, Attending Consultant, New Delhi, India,

2,3. Division of Pediatric Rheumatology, Institute of Child Health, Post Doctoral Fellow, New Delhi, India

4. Department of Ophthalmology, Sir Ganga Ram Hospital, New Delhi, India

5. Pediatric rheumatology, New Delhi, India

Published in: ACR-ARHP/Arthritis & Rheumatology November/2016/68(10)

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 ZRC 3197: 14.66yrs.(10.08-23.66) Uveitis (n=14); idiopathic:4, PJIA:4, OJIA:4, ERA:1, Behcets with uveitis: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 (2-32weeks), 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(2-24weeks).

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.

Abridged Prescribing Information

COMPOSITION: Exemptia™ (Adalimumab) 40 mg /0.8 mL single use pre filled syringe and 20mg /0.4 mL single use pre filled 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- α 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 \geq 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. For patients with Ulcerative Colitis only: Only continue EXEMPTIATM in patients who have shown evidence of clinical remission by eight weeks (Day 57) of therapy. 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 \geq 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 • Anaphylaxis or serious allergic reactions may occur • Hepatitis B virus reactivation: Monitor HBV carriers during and several months after therapy. If reactivation occurs, stop EXEMPTIATM and begin antiviral therapy • Demyelinating disease: Exacerbation or new onset, may occur • Heart failure: Worsening or new onset, may occur • Lupus-like syndrome: Stop EXEMPTIATM if syndrome develops **USE IN PREGNANCY AND LACTATION:** Pregnancy Category B: Adequate and well controlled studies with EXEMPTIATM have not been conducted in pregnant women. Adalimumab is an IgG1 monoclonal antibody and IgG1 is actively transferred across the placenta during the third trimester of pregnancy. Lactation: No data is available on the absorption of adalimumab from breast milk in newborn or preterm infants. Caution should be exercised when EXEMPTIATM is administered to a nursing woman. **DRUG INTERACTION** Biological Products- Concomitant administration of EXEMPTIATM with other biologic DMARDs (e.g., Anakinra and Abatacept) or other TNF blockers is not recommended • Live Vaccines- Avoid the use of live vaccines with EXEMPTIATM. • Cytochrome P450 Substrates- The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNF α , IL-6) during chronic inflammation. Upon initiation or discontinuation of EXEMPTIATM in patients being treated with CYP450 substrates with a narrow therapeutic index, monitoring of the effect (e.g., Warfarin) or drug concentration (e.g., Cyclosporine or Theophylline) is recommended and the individual dose of the drug product may be adjusted as needed. **UNDESIRE 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 (URTI), 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.

Zydu Biovation – Copyright ©

Please refer to the full Prescribing Information before starting EXEMPTIATM.

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:

Cadila Healthcare Limited

Zydus Corporate Park

Nr. Vaishno Devi Circle,

SG Highway,

Ahmedabad – 382 481

Gujarat, India.

PHONE: +91-79-71800000

Thank you

