Reduced Injection Site Pain with Succinate Buffer-Based Adalimumab Biosimilar (ZRC-3197) Injection (SUFFER Study): An Observational Study

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Pain due to subcutaneous (s.c.) injections is often more severe and the most common reason for patient noncompliance, other than erythema, edema, hematoma, and pruritus. Since citrate buffer based formulations have been associated with pain and discomfort at injection site, hence we wanted to evaluate the pain associated with adalimumab biosimilar (Exemptia), which was formulated using succinate buffer.

We carried out an observational study, where a prospective questionnaire-based study in patients (N=494) treated with adalimumab injection for different rheumatological conditions was carried out.

Patients aged ≥12 years of either sex, who had received at least three doses of injection, were included.

Primary objective is pain at the site within 24 hour of injection. Pain was assessed using the verbal pain intensity scale (National Initiative on Pain Control).
### Result

Table 1: Comparison of pain intensity using succinate and citrate buffer of adalimumab

<table>
<thead>
<tr>
<th>VAS category (pain intensity)</th>
<th>Patient (%)</th>
<th>ZRC-3197 (succinate buffer)</th>
<th>Humira (citrate buffer)[4]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>38.8</td>
<td>42.6</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>58.9</td>
<td>43.4</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>13.9</td>
<td></td>
</tr>
<tr>
<td>Total number of patients</td>
<td>494</td>
<td>122</td>
<td></td>
</tr>
</tbody>
</table>

VAS: Visual analog scale
Result

• Our results showed, on numeric pain scale, that 192/494 patients (38.8%) reported no pain and 291/494 (58.9%) patients reported mild pain.

• On verbal description pain scale, 182 (36.4%) patients reported “No Pain” and 230 (46%) patients reported “Slight Pain.” Majority of patients of both gender described their pain as absent or mild and very few had moderate or severe injection site pain.

• This study demonstrated that 94.6% of the patients had “No Pain” or “Mild Pain” on numeric pain rating scale and 82.4% of the patients had “No Pain” or “Slight Pain” on verbal description pain scale after adalimumab injection which contains succinate buffer.
Conclusion

• Incidence and severity of pain associated with injection of succinate buffer formulation is less compared to citrate buffer formulation.
**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-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•Anaphylaxis or serious allergic reactions may occur• Hepatitis B virus reactivation: Monitor HBV carriers during and several months after therapy. **INTERACTION:** Adalimumab is an IgG1 monoclonal antibody and IgG1 is actively transferred across the placenta during the third trimester of pregnancy. Increased creatine phosphokinase, Headache, Rash, Sinusitis, Nausea, Urinary Tract Infection (UTI), Abdominal pain, Flu-like 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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