Exemptia™ Adalimumab
EMPOWERING YOU

Low-dose adalimumab biosimilar (ZRC-3197) in the treatment of hidradenitis suppurativa

Sharmila Patil

Department of Dermatology, Dr. DY Patil Hospital, Navi Mumbai, Maharashtra, India

Published in: Indian J Dermatol Venereol Leprol, 2018

Background

- Hidradenitis suppurativa is a chronic inflammatory disease mostly affecting the axillary, inguinal, and perineal areas. It clinically presents as painful, deep-seated, inflamed nodules.

- Adalimumab (Humira®), a recombinant, fully human monoclonal antibody, is the only approved TNF-α inhibitor for treatment of hidradenitis suppurativa. A biosimilar adalimumab (ZRC-3197, Exemptia™; Cadila Healthcare Ltd., India), was indigenously developed as a 'fingerprint match' of Humira®, and currently approved for use in India.

Case 1:

Exemptia Adalimumab

- A 30-year-old overweight male (BMI 25.1 kg/m2) presented with complaints of painful discharging swellings around the buttocks, chest, beard and underarms [Figure 1a].

- He had a history of pea-sized painful swelling in the buttock that had gradually softened at the centre leading to a yellowish sticky foul smelling discharge. Multiple such lesions had appeared at different parts of his body. This restricted his shoulder mobility, indicating compromised daily activities.

- He was previously treated with rifampicin and doxycycline for 6 weeks, without any satisfactory outcome.

- Laboratory investigations, pus culture and blood pressure were normal. A diagnosis of severe hidradenitis suppurativa with Hurley's stage III disease was made. Pre-screening for infectious diseases like tuberculosis and hepatitis was negative.

Case 1:

- Treatment with biosimilar adalimumab was initiated at a low dose of 40 mg administered subcutaneously (SC) weekly for initial 3 weeks, and every other week for 3 months thereafter. Pus reduction and suppression of new lesion formation were observed after 3 months of biosimilar adalimumab therapy [Figure 1b]. Existing lesions regressed with significant pain reduction, indicating an improved transition from Hurley stage III to I.

- Therapy was tolerated well, and monthly maintenance dose for 6 months was continued with concomitant methotrexate to prolong the immunosuppressant activity to control inflammation and to prevent auto-antibodies against adalimumab.

Case 1:

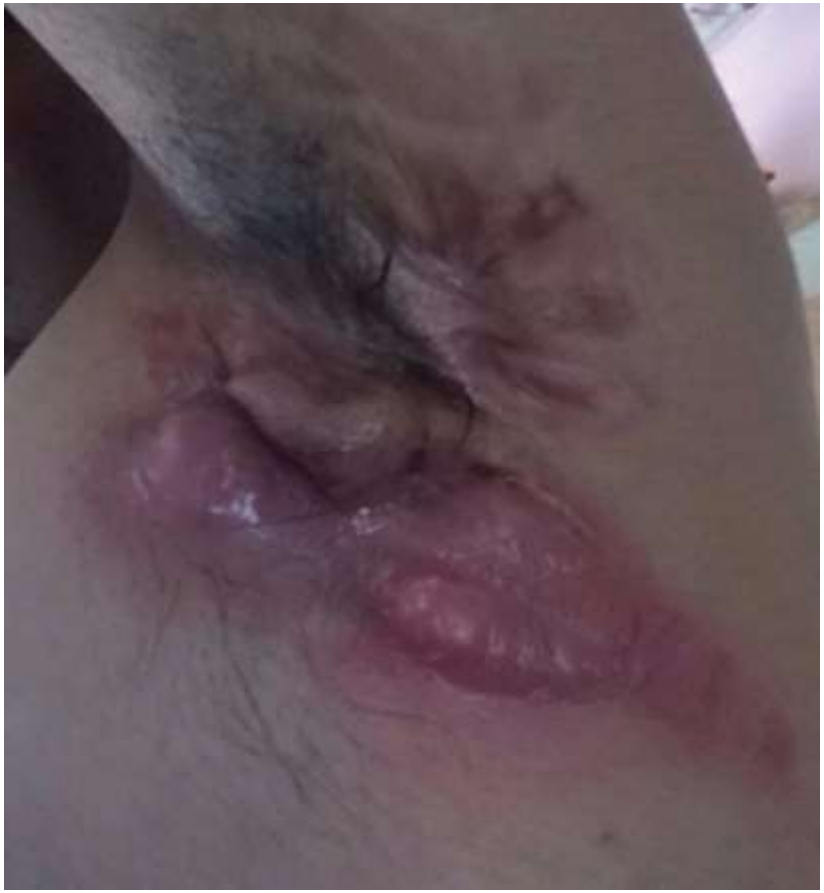

Figure 1a: Case 1 - Lesions in axilla before biosimilar adalimumab therapy

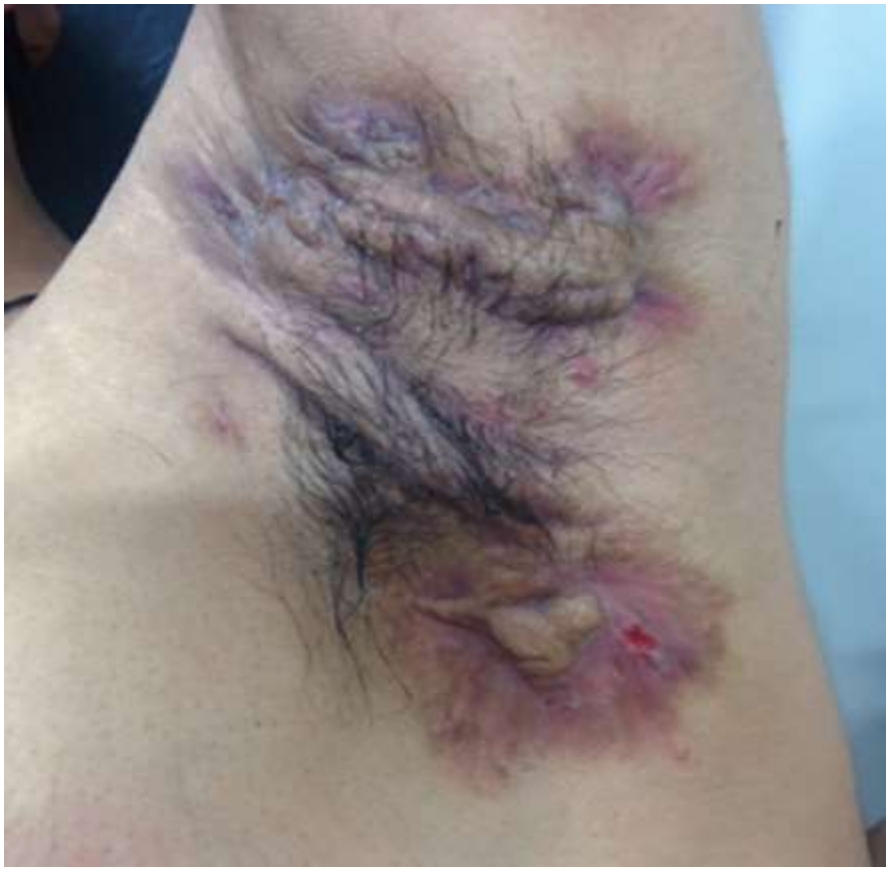

Figure 1b: Case1 – Lesions in axilla after 12 weeks of biosimilar adalimumab therapy with decreased erythema, discharge and number of inflammatory nodules

Case 2:

- Second case was a 31-year-old male (BMI 23.7 kg/m2) with a history of multiple raised painful reddish pea-sized swellings in the groins.

- Previous treatments included rifampicin and levofloxacin for 6 weeks, and dapsone with retinoids. However, his disease progressed to form multiple nodules, abscesses, and discharging sinuses over the past 2 years [Figure 2a].

- Laboratory investigations, pus culture and blood pressure were normal. On examination, severe hidradenitis suppurativa with Hurley's stage III disease was diagnosed.

- For clinically managing the recalcitrant form of hidradenitis suppurativa, a low dose of biosimilar adalimumab 40 mg SC was started weekly for 3 weeks, and thereafter every other week for 3 months. Baseline lesion count of 9 nodules and 4 sinuses reduced to 0 nodules and 2 partially healed sinuses [Figure 2b] post biosimilar adalimumab therapy, indicating an improved transition from Hurley stage III to I.

Case 2:

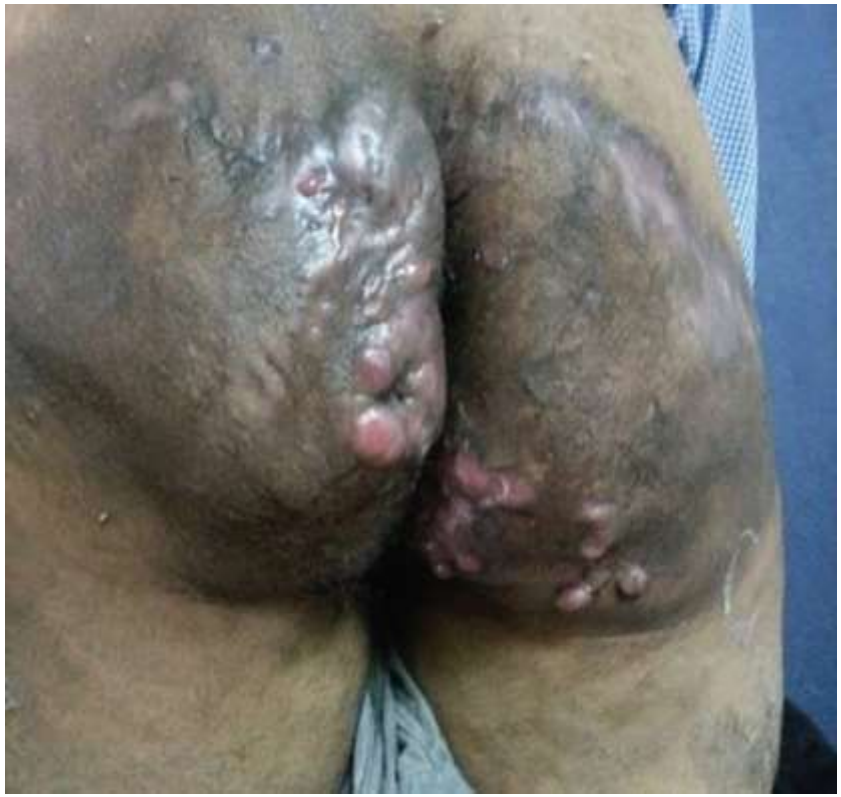

Figure 2a: Case 2 – Lesions in buttocks before biosimilar adalimumab therapy

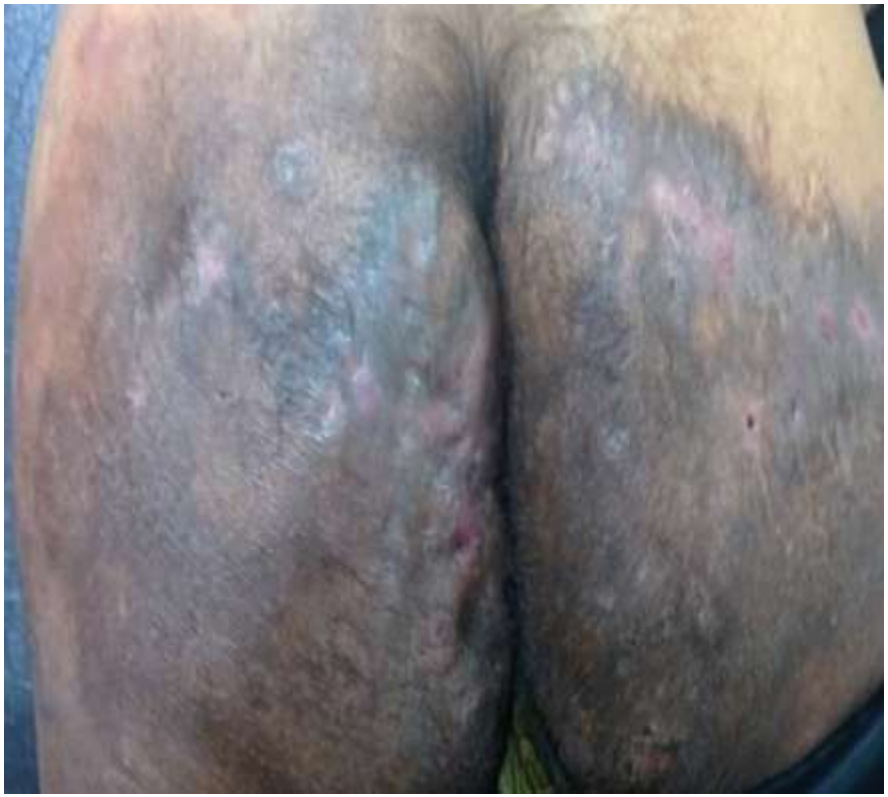

Figure 2b: Case 2 - Lesions in buttocks after 12 weeks of biosimilar adalimumab therapy with decreased erythema and number of inflammatory
nodules

Case 2:

- Additionally, hidradenitis suppurativa clinical response of 75% (AN75) was achieved and the patient's quality of life also improved significantly. As maintenance therapy, biosimilar adalimumab was continued monthly for 6 months with concomitant doxycycline. Additional immunosuppressants were avoided as an improvement of AN75 was obtained.

- In our cases, significant clearance of abscess and nodules prompted the dosage reduction in a tapering fashion so as to allow the disease to stay in control even with reduced dosage.

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 spondylitispatients 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 EXEMPTIA™. 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. For patients with Ulcerative Colitis only: Only continue EXEMPTIA™ 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 ≥ 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 EXEMPTIA™ 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 EXEMPTIA™ and begin antiviral therapy• Demyelinating disease: Exacerbation or new onset, may occur• Heart failure: Worsening or new onset, may occur• Lupus-like syndrome: Stop EXEMPTIA™ 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 EXEMPTIA™ 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 EXEMPTIA™. •Cytochrome P450 Substrates- The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNFα, IL-6) during chronic inflammation. Upon initiation or discontinuation of EXEMPTIA™ 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. **UNDESIRED 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.

Please refer to the full Prescribing Information before starting EXEMPTIA™.

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

Exemptia™ Adalimumab