TRITONIB ER

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for **TRITONIB ER**

(Tofacitinib Extended Release Tablets 11 mg) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action:

Tofacitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Tofacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. JAK enzymes transmit cytokine signaling through pairing of JAKs (e.g., JAK1/JAK3, JAK1/JAK2, JAK1/TyK2, JAK2/JAK2). Tofacitinib inhibited the in vitro activities of JAK1/JAK2, JAK1/JAK3, and JAK2/JAK2 combinations with IC50 of 406, 56, and 1377 nM respectively. However, the relevance of specific JAK combinations to therapeutic effectiveness is not known.

INDICATIONS: Rheumatoid Arthritis: Indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more TNF blockers.

Psoriatic Arthritis: Indicated for the treatment of adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.

Ulcerative Colitis: Indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have an inadequate response or intolerance to one or more TNF blockers

DOSAGE AND ADMINISTRATION: As directed by the Physician.

CONTRAINDICATION: Hypersensitivity to the active substance.

WARNINGS & PRECAUTIONS:

Serious Infections: Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving Tofacitinib. The most common serious infections reported with Tofacitinib included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. *Tuberculosis:* Patients should be evaluated and tested for latent or active infection prior to and per applicable guidelines during administration of tofacitinib. *Viral Reactivation:* Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were observed in clinical studies with Tofacitinib. The impact of Tofacitinib on chronic viral hepatitis reactivation is unknown. *Malignancy and Lymphoproliferative Disorders:* Consider the risks and benefits of Tofacitinib treatment prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing Tofacitinib in patients who develop a malignancy. *Non-Melanoma Skin Cancer*: Non-melanoma skin cancers (NMSCs) have been reported in patients treated with Tofacitinib. Periodic skin examination is recommended for patients who are at increased risk for skin cancer. *Gastrointestinal Perforations:* Events of gastrointestinal perforation have been reported in clinical studies with Tofacitinib, although

the role of JAK inhibition in these events is not known. In these studies, many patients with rheumatoid arthritis were receiving background therapy with Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). *Laboratory Abnormalities:* Lymphocyte Abnormalities Treatment with Tofacitinib was associated with initial lymphocytosis at one month of exposure followed by a gradual decrease in mean absolute lymphocyte counts. *Neutropenia*: Treatment with Tofacitinib was associated with an increased incidence of neutropenia (less than 2000 cells/mm3) compared to placebo. *Anemia:* Avoid initiation of Tofacitinib treatment in patients with a low hemoglobin level (i.e., less than 9 g/dL). *Vaccinations:* Avoid use of live vaccines concurrently with Tofacitinib. *Hypersensitivity Reactions:* such as angioedema and urticaria that may reflect drug hypersensitivity have been observed in patients receiving Tofacitinib some events were serious.

DRUG INTERACTIONS: *Strong CP3A4 Inhibitors:* Increased exposure to tofacitinib**,** *Moderate CYP3A4 Inhibitors Coadministered with Strong CYP2C19 Inhibitors (e.g., fluconazole):* Increased exposure to tofacitinib, *Strong CYP3A4 Inducers (e.g., rifampin):* Decreased exposure to tofacitinib and may result in loss of or reduced clinical response, *Immunosuppressive Drugs (e.g., azathioprine, tacrolimus, cyclosporine):* isk of added immunosuppression; coadministration with biologic DMARDs or potent immunosuppressants has not been studied in patients with rheumatoid arthritis, psoriatic arthritis, or UC.

ADVERSE REACTIONS: *Rheumatoid arthritis:* The most common serious adverse reactions were serious infections. In the long-term safety all exposure population, the most common serious infections reported with tofacitinib were pneumonia (1.7%), herpes zoster (0.6%), urinary tract infection (0.4%), cellulitis (0.4%), diverticulitis (0.3%), and appendicitis (0.2%). *Psoriatic arthritis*: Overall, the safety profile observed in patients with active PsA treated with tofacitinib was consistent with the safety profile observed in patients with RAtreated with tofacitinib. *Infections and infestations:* Pneumonia, Influenza, Herpes zoster ,Urinary tract infection, *Neoplasms benign, malignant and unspecified (incl cysts and polyps):* Lung cancer ,Nonmelanoma ,skin cancers. *Blood and lymphatic system disorders:* Leukopenia ,Lymphopenia ,Neutropenia, Anaemia.

MARKETED BY:

torrent PHARMA

TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

IN/TRITONIB ER/Apr-23/01/ABPI

(Additional information is available on request)