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

TRITONIB ER

1. **Generic Name:**

   Tofacitinib Extended-Release Tablets 11 mg

2. **Qualitative and quantitative composition:**

   Each film coated extended-release tablet contains:

   Tofacitinib Citrate I.P.

   Eq. to Tofacitinib……..11 mg

   Excipients: …….. q.s.

   Colours: Red Oxide of Iron, Black Oxide of Iron & Titanium Dioxide I.P.

   The Excipients used are Microcrystalline cellulose, Lactose Sprey Dried Monohydrate, Methocel, Low Substituted Hydroxy Propyl Cellulose, Magnesium Stearate, Talcum, Croscarmellose Sodium, Opadry Pink, Isopropyl Alcohol, Methylene Dichloride.

3. **Dosage form and strength:**

   Dosage form: Extended-Release Tablets

   Strength: 11 mg

4. **Clinical particulars:**

4.1 Therapeutic indication:

- **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.

4.2 Posology and method of administration:

Once a day or as directed by physician

To be taken orally

4.3 Contraindications:

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use:

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. Among opportunistic infections, tuberculosis and other mycobacterial infections, cryptococcosis, histoplasmosis, esophageal candidiasis, pneumocystosis, multidermatomal herpes zoster, cytomegalovirus infections, BK virus infection, and listeriosis were reported with Tofacitinib. Some patients

have presented with disseminated rather than localized disease and were often taking concomitant immune modulating agents such as methotrexate or corticosteroids.

In the UC population, Tofacitinib treatment with 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Additionally, opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with Tofacitinib 10 mg twice daily.

Other serious infections that were not reported in clinical studies may also occur (e.g., coccidioidomycosis).

Avoid use of Tofacitinib in patients with an active, serious infection, including localized infections. The risks and benefits of treatment should be considered prior to initiating Tofacitinib in patients:

- with chronic or recurrent infection
- who have been exposed to tuberculosis
- with a history of a serious or an opportunistic infection
- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or
- with underlying conditions that may predispose them to infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Tofacitinib should be interrupted if a patient develops a serious infection, an opportunistic infection, or sepsis. A patient who develops a new infection during treatment with Tofacitinib should undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient; appropriate antimicrobial therapy should be initiated, and the patient should be closely monitored.

Caution is also recommended in patients with a history of chronic lung disease, or in those who develop interstitial lung disease, as they may be more prone to infections.

Risk of infection may be higher with increasing degrees of lymphopenia and consideration should be given to lymphocyte counts when assessing individual patient risk of infection. Discontinuation and monitoring criteria for lymphopenia are recommended.

Tuberculosis

Patients should be evaluated and tested for latent or active infection prior to and per applicable guidelines during administration of tofacitinib.

Anti-tuberculosis therapy should also be considered prior to administration of Tofacitinib in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but who have risk factors for tuberculosis infection. Consultation with a physician with expertise in the treatment of tuberculosis is recommended to aid in the decision about whether initiating anti-tuberculosis therapy is appropriate for an individual patient.

Patients should be closely monitored for the development of signs and symptoms of tuberculosis, including patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Patients with latent tuberculosis should be treated with standard antimycobacterial therapy before administering 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. Patients who screened positive for hepatitis B or C were excluded from clinical trials. Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with Tofacitinib. The risk of herpes zoster is increased in patients treated with Tofacitinib and appears to be higher in patients treated with Tofacitinib in Japan and Korea.

Mortality

Consider the benefits risk for the individual patient prior to initiating or continuing therapy with Tofacitinib.

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. Malignancies were observed in clinical studies of Tofacitinib.

Other malignancies were observed in clinical studies and the post-marketing setting, including, but not limited to, lung cancer, breast cancer, melanoma, prostate cancer, and pancreatic cancer.

Major Adverse Cardiovascular Events

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Tofacitinib particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur.

Discontinue tofacitinib in patients that have experienced a myocardial infarction or stroke.

Thrombosis

Thrombosis, including pulmonary embolism (PE), deep venous thrombosis (DVT), and arterial thrombosis, have occurred in patients treated with Tofacitinib and other Janus kinase (JAK) inhibitors used to treat inflammatory conditions.

Promptly evaluate patients with symptoms of thrombosis and discontinue. Tofacitinib in patients with symptoms of thrombosis.

Avoid Tofacitinib in patients that may be at increased risk of thrombosis.

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).

There was no discernable difference in frequency of gastrointestinal perforation between the placebo and the Tofacitinib arms in clinical trials of patients with UC, and many of them were receiving background corticosteroids.

Tofacitinib should be used with caution in patients who may be at increased risk for gastrointestinal perforation (e.g., patients with a history of diverticulitis or taking NSAIDs).

Patients presenting with new onset abdominal symptoms should be evaluated promptly for early identification of gastrointestinal perforation.

Hypersensitivity

Reactions such as angioedema and urticaria that may reflect drug hypersensitivity have been observed in patients receiving Tofacitinib some events were serious. If a serious hypersensitivity reaction occurs, promptly discontinue tofacitinib while evaluating the potential cause or causes of the reaction

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 below the baseline of approximately 10% during 12 months of therapy. Lymphocyte counts less than 500 cells/mm3 were associated with an increased incidence of treated and serious infections.

Avoid initiation of Tofacitinib treatment in patients with a low lymphocyte count (i.e., less than 500 cells/mm3). In patients who develop a confirmed absolute lymphocyte count less than 500 cells/mm3, treatment with Tofacitinib is not recommended.

Monitor lymphocyte counts at baseline and every 3 months thereafter. For recommended modifications based on lymphocyte counts.

Neutropenia

Treatment with Tofacitinib was associated with an increased incidence of neutropenia (less than 2000 cells/mm3) compared to placebo.

Avoid initiation of Tofacitinib treatment in patients with a low neutrophil count (i.e., ANC less than 1000 cells/mm3). For patients who develop a persistent ANC of 500 to 1000 cells/mm3, interrupt Tofacitinib dosing until ANC is greater than or equal to 1000 cells/mm3. In patients who develop an ANC less than 500 cells/mm3, treatment with Tofacitinib is not recommended.

Monitor neutrophil counts at baseline and after 4-8 weeks of treatment and every 3 months thereafter. For recommended modifications based on ANC results.

Anemia

Avoid initiation of Tofacitinib treatment in patients with a low hemoglobin level (i.e., less than 9 g/dL). Treatment with Tofacitinib should be interrupted in patients who develop hemoglobin levels less than 8 g/dL or whose hemoglobin level drops greater than 2 g/dL on treatment.

Monitor hemoglobin at baseline and after 4-8 weeks of treatment and every 3 months thereafter. For recommended modifications based on hemoglobin results.

Liver Enzyme Elevations

Treatment with Tofacitinib was associated with an increased incidence of liver enzyme elevation compared to placebo. Most of these abnormalities occurred in studies with background DMARD (primarily methotrexate) therapy.

Routine monitoring of liver tests and prompt investigation of the causes of liver enzyme elevations is recommended to identify potential cases of drug-induced liver injury. If drug-induced liver injury is suspected, the administration of Tofacitinib should be interrupted until this diagnosis has been excluded.

Lipid Elevations

Treatment with Tofacitinib was associated with dose-dependent increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Maximum effects were generally observed within 6 weeks. There were no clinically relevant changes in LDL/HDL cholesterol ratios. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined.

Assessment of lipid parameters should be performed approximately 4-8 weeks following initiation of Tofacitinib therapy.

Manage patients according to clinical guidelines [e.g., National Cholesterol Educational Program (NCEP)] for the management of hyperlipidemia.

Vaccinations

Avoid use of live vaccines concurrently with Tofacitinib. The interval between live vaccinations and initiation of tofacitinib therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents.

A patient experienced dissemination of the vaccine strain of varicella zoster virus, 16 days after vaccination with live attenuated (Zostavax) virus vaccine and 2 days after treatment start with tofacitinib 5 mg twice daily. The patient was varicella virus naïve, as evidenced by no previous history of varicella infection and no anti-varicella antibodies at baseline. Tofacitinib was discontinued and the patient recovered after treatment with standard doses of antiviral medication.

Update immunizations in agreement with current immunization guidelines prior to initiating Tofacitinib therapy.

Risk of Gastrointestinal Obstruction with a Non-Deformable Extended-Release Formulation such as Tofacitinib

As with any other non-deformable material, caution should be used when administering Tofacitinib to patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic). There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of other drugs utilizing a non-deformable extended-release formulation.

4.5 Drug Interaction:

Clinically Relevant Interactions Affecting Tofacitinib ER When Co-administered with Other Drugs:

Strong CP3A4 Inhibitors (e.g., ketoconazole)	
Clinical Impact	Increased exposure to tofacitinib
Intervention	Dosage adjustment of Tofacitinib XR is recommended
Moderate CYP3A4 Inhibitors Coadministered with Strong CYP2C19 Inhibitors (e.g., fluconazole)	
Clinical Impact	Increased exposure to tofacitinib
Intervention	Dosage adjustment of Tofacitinib XR is recommended
Strong CYP3A4 Inducers (e.g., rifampin)	
Clinical Impact	Decreased exposure to tofacitinib and may result in loss of or reduced clinical response
Intervention	Coadministration with Tofacitinib XR is not recommended

Immunosuppressive Drugs (e.g., azathioprine, tacrolimus, cyclosporine)	
Clinical Impact	Risk of added immunosuppression; coadministration with biologic DMARDs or potent immunosuppressants has not been studied in patients with rheumatoid arthritis, psoriatic arthritis, or UC.
Intervention	Coadministration with Tofacitinib XR is not recommended

4.6 Use in special populations (such as pregnant women, lactating women, Paediatric patients, geriatric patients etc.)

Pregnancy

Pregnancy Exposure Registry There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Tofacitinib during pregnancy. Patients should be encouraged to enroll in the Tofacitinib pregnancy registry if they become pregnant.

Risk Summary Available data with Tofacitinib use in pregnant women are insufficient to establish a drug associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There are risks to the mother and the fetus associated with rheumatoid arthritis and UC in pregnancy. In animal reproduction studies, fetocidal and teratogenic effects were noted when pregnant rats and rabbits received Tofacitinib during the period of organogenesis at exposures multiples of 73-times and 6.3-times the maximum recommended dose of 10 mg twice daily, respectively. Further, in a peri and post-natal study in rats, tofacitinib resulted in reductions in live litter size, postnatal survival, and pup body weights at exposure multiples of approximately 73-times the recommended dose of 5 mg twice daily and approximately 36 times the maximum recommended dose of 10 mg twice daily, respectively.

Lactation

Risk Summary

There are no data on the presence of tofacitinib in human milk, the effects on a breastfed infant, or the effects on milk production. Tofacitinib is present in the milk of lactating rats (see Data). When a drug is present in animal milk, it is likely that the drug will be present in human milk. Given the serious adverse reactions seen in adults treated with Tofacitinib, such as increased risk of serious infections, advise patients that breastfeeding is not recommended during treatment and for at least 18 hours after the last dose of Tofacitinib or 36 hours after the last dose of Tofacitinib (approximately 6 elimination half-lives).

Females and Males of Reproductive Potential

Contraception

Females

In an animal reproduction study, tofacitinib at AUC multiples of 13 times the recommended dose of 5 mg twice daily and 6.3 times the maximum recommended dose of 10 mg twice daily demonstrated adverse embryo-fetal findings [see Use in Specific Populations (8.1)]. However, there is uncertainty as to how these animal findings relate to females of reproductive potential treated with the recommended clinical dose. Consider pregnancy planning and prevention for females of reproductive potential.

Infertility

Females

Based on findings in rats, treatment with Tofacitinib may result in reduced fertility in females of reproductive potential. It is not known if this effect is reversible.

4.7 Effects on ability to drive and use machines:

Tofacitinib has no or negligible influence on the ability to drive and use machine.

4.8 Undesirable effects:

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%). Among opportunistic infections, TB and other mycobacterial infections, cryptococcus, histoplasmosis, oesophageal candidiasis, multidermatomal herpes zoster, cytomegalovirus, BK virus infections and listeriosis were reported with tofacitinib. Some patients have presented with disseminated rather than localised disease. Other serious infections that were not reported in clinical studies may also occur (e.g., coccidioidomycosis). The most commonly reported adverse reactions during the first 3 months of the double-blind, placebo or MTX controlled clinical studies were headache (3.9%), upper respiratory tract infections (3.8%), viral upper respiratory tract infection (3.3%), diarrhoea (2.9%), nausea (2.7%), and hypertension (2.2%). The proportion of patients who discontinued treatment due to adverse reactions during first 3 months of the double-blind, placebo or MTX controlled studies was 3.8% for patients taking tofacitinib. The most common infections resulting in discontinuation of therapy during the first 3 months in controlled clinical studies were herpes zoster (0.19%) and pneumonia (0.15%).

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 RA treated with tofacitinib.

Tabulated list of adverse reactions

The adverse reactions listed in the table below are from clinical studies in patients with RA, PsA, and UC and are presented by System Organ Class (SOC) and frequency categories, defined using the following convention: very common 1/10), common 1/100 to < 1/10), uncommon 1/1,000 to < 1/100), rare 1/10,000 to < 1/1,000), very rare (< 1/10,000), or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table: Adverse reactions

System organ class	Common 21/100 to <1/10		Uncommon k111,000 to <1/100	Rare 21/10,000 to <1/1,000	Very rare <1/10,000	Not known (cannot be estimated from the available data)
Infections and infestations		Pneumonia Influenza Herpes zoster Urinary tract infection Sinusitis Bronchitis Nasopharyngitis Pharyngitis	Tuberculosis Diverticulitis Pyelonephritis Cellulitis Herpes simplex Gastroenteritis viral Viral infection	Sepsis Urosepsis Disseminated TB Necrotizing fasciitis Bacteraemia Staphylococcal bacteraemia Pneumocystis jirovecii pneumonia Pneumonia pneumococcal Pneumonia bacterial Encephalitis Atypical mycobacterial infection Cytomegalovirus infection Arthritis bacterial	Tuberculosis of central nervous system Meningitis cryptococcal Mycobacterium avium complex infection	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			Lung cancer Nonmelanoma skin cancers	Lymphoma		
Blood and lymphatic system disorders		Anaemia	Leukopenia Lymphopenia Neutropena			
Immune system disorders						Hypersensitivity Angioedema Urticaria
Metabolism and nutrition disorders			Dyslipidaemia Hyperlipidaemia			

System organ class	Common 21/100 to <1/10		Uncommon k111,000 to <1/100	Rare 21/10,000 to <1/1,000	Very rare <1/10,000	Not known (cannot be estimated from the available data)
Psychiatric disorders			Insomnia			
Nervous system disorders		Headache	Paraesthesia			
Cardiac disorders			Myocardial infarction			
Vascular disorders		Hypertension	Venous thromboembolism			
Respiratory, thoracic and mediastinal disorders		Cough	Dyspnoea Sinus congestion			
Gastrointestinal disorders		Abdominal pain Vomiting Diarrhoea Nausea Gastritis Dyspepsia				
Hepatobil-iary disorders			Hepatic steatosis Hepatic enzyme increased			
		Liver function test abnormal Gamma glutamyl-transferase increased				
Skin and subcutaneous tissue disorders	Rash	Erythema Pruritus	Skin and subcutaneous tissue disorders	Rash	Erythema Pruritus	Skin and subcutaneous tissue disorders

System organ class	Common 21/100 to <1/10		Uncommon k111,000 to <1/100	Rare 21/10,000 to <1/1,000	Very rare <1/10,000	Not known (cannot be estimated from the available data)
Musculoskeletal and connective tissue disorders	Arthralgia	Musculoskeletal pain Joint swelling	Musculoskeletal and connective tissue disorders	Arthralgia	Musculoskeletal pain Joint swelling	Musculoskeletal and connective tissue disorders
Tendonitis			Tendonitis			Tendonitis
General disorders and administration site conditions	Pyrexia Oedema peripheral Fatigue		General disorders and administration site conditions	Pyrexia Oedema peripheral Fatigue		General disorders and administration site conditions
Investigations	Blood		Investigations	Blood		Investigations
Injury, poisoning and procedural complications		Ligament sprain Muscle strain				

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com .

4.9 Overdose:

There is no specific antidote for overdose with Tofacitinib. In case of an overdose, it is recommended that the patient be monitored for signs and symptoms of adverse reactions.

5. Pharmacodynamic properties

5.1 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.

5.2 Pharmacokinetic properties:

Tofacitinib Following oral administration of Tofacitinib, peak plasma concentrations are reached within 0.5-1-hour, elimination half-life is about 3 hours and a dose-proportional increase in systemic exposure was observed in the therapeutic dose range. Steady state concentrations are achieved in 24-48 hours with negligible accumulation after twice daily administration.

Absorption

The absolute oral bioavailability of Tofacitinib is 74%. Coadministration of Tofacitinib with a high-fat meal resulted in no changes in AUC while Cmax was reduced by 32%. In clinical trials, Tofacitinib was administered without regard to meals.

Distribution

After intravenous administration, the volume of distribution is 87 L. The protein binding of tofacitinib is approximately 40%. Tofacitinib binds predominantly to albumin and does not appear to bind to α1-acid glycoprotein. Tofacitinib distributes equally between red blood cells and plasma.

Metabolism and Excretion

Clearance mechanisms for tofacitinib are approximately 70% hepatic metabolism and 30% renal excretion of the parent drug. The metabolism of tofacitinib is primarily mediated by CYP3A4 with minor contribution from CYP2C19. In a human radiolabeled study, more than 65% of the total circulating radioactivity was accounted for by unchanged tofacitinib, with the remaining 35% attributed to 8 metabolites, each accounting for less than 8% of total radioactivity. The pharmacologic activity of tofacitinib is attributed to the parent molecule.

Pharmacokinetic and Statistical Evaluation:

Table: Descriptive Statistics of Pharmacokinetic Parameters of Test Product (T) and Reference Product (R) for Tofacitinib (N = 24)

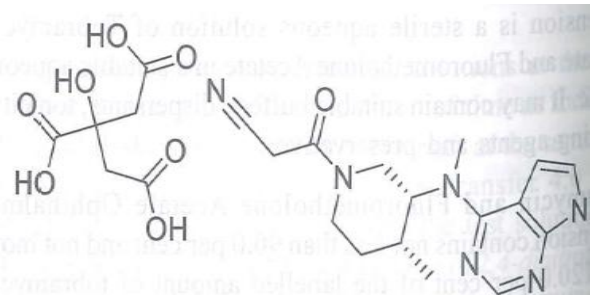
Form	Variable	Mean	SD	Minimum	Median	Maximum	CV%
R	C_{max} (ng/mL)	53.8905	10.2708	30.9780	53.3110	71.2260	19.0587
	T_{max} (hr)	3.9271	1.0199	1.6700	3.5150	5.0000	25.9704
	AUC_{0-t} (ng.hr/mL)	268.7833	75.0944	119.3510	261.5785	465.0390	27.9378
	$AUC_{0-\infty}$ (ng.hr/mL)	287.2363	83.1200	127.1950	284.4180	516.7900	28.9378
	K_{el} (hr^{-1})	0.1285	0.0832	0.0570	0.1100	0.4310	64.7760
	$t_{1/2}$ (hr)	6.7546	2.6931	1.6100	6.3000	12.0700	39.8707
	$AUC_{\_\%Extrap\_obs}$	6.1683	3.2858	1.6100	5.6800	13.8400	53.2689
T	C_{max} (ng/mL)	52.8842	12.4135	31.8100	52.6145	76.0160	23.4730
	T_{max} (hr)	4.0504	1.1333	1.6700	4.2500	6.0000	27.9790
	AUC_{0-t} (ng.hr/mL)	273.6348	85.8366	134.3780	262.6800	453.6380	31.3691
	$AUC_{0-\infty}$ (ng.hr/mL)	286.2189	88.4227	148.2000	269.5930	476.6550	30.8951
	K_{el} (hr^{-1})	0.1428	0.0617	0.0550	0.1210	0.2900	43.1668
	$t_{1/2}$ (hr)	5.7675	2.4588	2.3900	5.7250	12.6200	42.6314
	$AUC_{\_\%Extrap\_obs}$	4.5488	3.4318	0.9800	3.7950	16.7800	75.4441

6. Nonclinical properties

Not available

7. Description:

Tofacitinib Citrate is 3-{(3R, 4R)-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl) amino]piperidin-1-yl)-3-oxo Propanenitrile 2-hydroxypropane-1,2,3-tricarboxylic acid. Its empirical formula is $C_{22}H_{28}N_6O_8$ and molecular weight is 504.5 g/mol. The chemical structure is:



TRITONIB ER

Tofacitinib Extended Release Tablets are pink to light pink coloured, oval shaped, biconvex, film coated tablet plain on both sides. The excipients used are Microcrystalline cellulose, Lactose Sprey Dried Monohydrate, Methocel, Low Substituted Hydroxy Propyl Cellulose, Magnesium Stearate, Talcum, Croscarmellose Sodium, Opadry Pink, Isopropyl Alcohol, Methylene Dichloride

8. Pharmaceutical particulars:

8.1 Incompatibilities:

None stated.

8.2 Shelf-life:

Do not use later than date of expiry.

8.3 Packaging information:

TRITONIB ER is available in pack of 10 Tablets.

8.4 Storage and handing instructions:

Store below 30°C & Protect from light and moisture.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies.
- Have kidney or liver problems.
- Are pregnant or plan to become pregnant.
- Are breastfeeding or plan to breastfeed.
- Have any serious illness.
- Are taking any medicines (prescription, over the counter, vitamins, or herbal products)

10. Details of manufacturer

Synokem Pharmaceuticals Ltd

Plot No.: 56-57, Sector-6A,

I.I.E (SIDCUL), Ranipur (BHEL),

Haridwar-249403 (Uttarakhand)

11. Details of permission or licence number with date

Mfg. Licence No.: 27/UA/2018 issued on 18.11.2022.

12. Date of revision -

DEC 25

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/TRITONIB ER 11 mg/DEC-25/02/PI