To be sold by retail on the prescription of Neurologist only

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Teriflunomide Tablets 7mg and 14mg
Teru-MS 7 & 14

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COMPOSITION
Each Film coated tablet contains:
Teriflunomide 7mg
Each Film coated tablet contains:
Teriflunomide 14mg

WARNING: HEPATOTOXICITY and RISK OF TERATOGENICITY

Hepatotoxicity
Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Concomitant use of Teriflunomide with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of Teriflunomide therapy. Monitor ALT levels at least monthly for six months after starting Teriflunomide. If drug induced liver injury is suspected, discontinue Teriflunomide and start an accelerated elimination procedure with cholestyramine or charcol. Teriflunomide is contraindicated in patients with severe hepatic impairment. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking Teriflunomide.

Risk of Teratogenicity
Teriflunomide is contraindicated for use in pregnant women and in women of reproductive potential who are not using effective contraception because of the potential for fetal harm. Teratogenicity and embryolethality occurred in animals at plasma teriflunomide exposures lower than that in humans. Exclude pregnancy before the start of treatment with Teriflunomide in females of reproductive potential. Advise females of reproductive potential to use effective contraception during Teriflunomide treatment and during an accelerated drug elimination procedure after Teriflunomide treatment. Stop Teriflunomide and use an accelerated drug elimination procedure if the patient becomes pregnant

DRUG DESCRIPTION
Teriflunomide is an oral de novo pyrimidine synthesis inhibitor of the DHO-DH enzyme, with the chemical name (Z)-2-Cyano-3-hydroxy-but-2-enoic acid-(4 trifluoromethylphenyl)-amide. Its molecular weight is 270.21, and the empirical formula is $C_{12}H_9F_3N_2O_2$ with the following chemical structure:

Teriflunomide is a white to almost white powder that is sparingly soluble in acetone, slightly soluble in polyethylene glycol and ethanol, very slightly soluble in isopropanol and practically insoluble in water. Teriflunomide is formulated as film-coated tablets for oral administration.

DOSAGE FORM AND STRENGTHS
Teriflunomide is available as a 7 mg and 14 mg tablets for once daily oral administration.

INDICATIONS
Teriflunomide is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

DOSE AND METHOD OF ADMINISTRATION
The recommended dose of Teriflunomide is 7mg or 14mg orally once daily.

Monitoring to assess safety
- Obtain transaminase and bilirubin levels within 6months before initiation of Teriflunomide therapy. Monitor ALT levels at least monthly for 6 months after starting Teriflunomide.
- Obtain a complete blood cell count (CBC) within 6 months before initiation of treatment with Teriflunomide. Further monitoring should be based on signs and symptoms of infection.
- Prior to initiating Teriflunomide, screen patients for latent tuberculosis infection with a tuberculin skin test or blood test for tuberculosis infection.
- Exclude pregnancy prior to initiation of treatment with Teriflunomide in females of reproductive potential.
- Check blood pressure before start of Teriflunomide treatment and periodically thereafter.

Administration
The tablets are for oral use. The tablets should be swallowed whole with some water. Teriflunomide can be taken with or without food.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary:
Teriflunomide is contraindicated for use in pregnant women and females of reproductive potential not using effective contraception because of the potential for fetal harm based on animal data. Human data are not available at this time to inform the presence or absence of drug-associated risk with the use of Teriflunomide during pregnancy. In animal reproduction studies in rat and rabbits, oral administration of teriflunomide during organogenesis caused teratogenicity and embryolethality at plasma exposures (AUC) lower than that at the maximum human recommended dose (MHRD) of 14 mg/day. The background risk of major birth defects and miscarriage in the indicated population is unknown.Clinical Considerations:
Women who wish to become pregnant should discontinue use of Teriflunomide and undergo an accelerated elimination procedure to decrease the plasma concentration of teriflunomide to less than 0.02 mg/L (0.02 mcg/mL). Effective contraception should be used until is it verified that plasma concentrations of teriflunomide are less than 0.02 mg/L (0.02 mcg/mL). Human plasma concentrations of teriflunomide less than 0.02 mg/L (0.02 mcg/mL) are expected to have minimal embryofetal risk.
If the patient becomes pregnant while taking this drug, stop treatment with Teriflunomide, inform the patient of the potential risk to the fetus, and perform the accelerated drug elimination procedure to achieve plasma concentrations of less than 0.02 mg/L (0.02 mcg/mL). Refer the patient to an obstetrician/gynecologist, preferably experienced in reproductive toxicity, for further evaluation and counseling.

Data
Animal Data When teriflunomide (oral doses of 1, 3, or 10 mg/kg/day) was administered to pregnant rats throughout the period of organogenesis, high incidences of fetal malformation (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death were observed at doses not associated with maternal toxicity. Adverse effects on embryofetal development were observed following dosing at various stages throughout organogenesis. Maternal plasma exposure at the no-effect level (1.0 mg/kg/day) for embryofetal developmental toxicity in rats was less than that in humans at the maximum recommended human dose (MRHD, 14 mg/day).
Administration of teriflunomide (oral doses of 1, 3.5, or 12 mg/kg/day) to pregnant rabbits throughout organogenesis resulted in high incidences of fetal malformation (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death at doses associated with minimal maternal toxicity. Maternal plasma exposure at the no-effect dose (1.0 mg/kg/day) for embryofetal developmental toxicity in rabbits was less than that in humans at the MRHD.
In studies in which teriflunomide (oral doses of 0.05, 0.1, 0.3, 0.6, or 1.0 mg/kg/day) was administered to rats during gestation and lactation, decreased growth, eye and skin abnormalities, and high incidences of malformation (limb defects) and postnatal death were observed in the offspring at doses not associated with maternal toxicity. Maternal plasma exposure at the no-effect dose for pre-and postnatal developmental toxicity in rats (0.10 mg/kg/day) was less than that in humans at the MRHD.
In animal reproduction studies of leflunomide, embryolethality and teratogenic effects were observed in pregnant rat and rabbit at or below clinically relevant plasma teriflunomide exposures (AUC). In published reproduction studies in pregnant mice, leflunomide was embryolethal and increased the incidence of malformations (craniofacial, axial skeletal, heart and great vessel). Supplementation with exogenous uridine reduced the teratogenic effects in pregnant mice, suggesting that the mode of action (inhibition of mitochondrial enzyme dihydroorotate dehydrogenase) is the same for therapeutic efficacy and developmental toxicity.
At recommended doses in humans, teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide.

Lactation
Risk Summary:
It is not known whether this drug is excreted in human milk. Teriflunomide was detected in rat milk following a single oral dose.
The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for teriflunomide and any potential adverse effects on the breastfed infant from teriflunomide or from the underlying maternal condition.

Females and Males of Reproductive Potential

Pregnancy Testing
Exclude pregnancy prior to initiation of treatment with teriflunomide in females of reproductive potential. Advise females to notify their healthcare provider immediately if pregnancy occurs or is suspected during treatment.

Contraception
Females
Females of reproductive potential should use effective contraception while taking teriflunomide. If teriflunomide is discontinued, use of contraception should be continued until is it verified that plasma concentrations of teriflunomide are less than 0.02 mg/L (0.02 mcg/mL).
Females of reproductive potential who wish to become pregnant should undergo an accelerated elimination procedure. Effective contraception should be used until it is verified that plasma concentrations of teriflunomide are less than 0.02 mg/L (0.02 mcg/mL).

Males
Teriflunomide is detected in human semen. Animal studies to specifically evaluate the risk of male-mediated fetal toxicity have not been conducted. To minimize any possible risk, men not wishing to father a child and their female partners should use effective contraception. Men wishing to father a child should discontinue use of teriflunomide and either undergo an accelerated elimination procedure or wait until verification that the plasma teriflunomide concentration is less than 0.02 mg/L (0.02 mcg/mL).

Infertility
Administration of teriflunomide to male rats resulted in no adverse effects on fertility. However, reduced epididymal sperm count was observed. Effects of teriflunomide on fertility in humans have not been evaluated.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use Teriflunomide should be used with caution in patients aged 65 years and over due to insufficient data on safety and efficacy.

Hepatic Impairment
No dosage adjustment is necessary for patients with mild and moderate hepatic impairment. The pharmacokinetics of teriflunomide in severe hepatic impairment has not been evaluated. Teriflunomide is contraindicated in patients with severe hepatic impairment.

Renal Impairment
No dosage adjustment is necessary for patients with mild, moderate, and severe renal impairment.

CONTRAINDICATIONS

Teriflunomide is contraindicated in/with:
- Patients with a history of a hypersensitivity reaction to teriflunomide, leflunomide, or to any of the inactive ingredients. Reactions have included anaphylaxis, angioedema, and serious skin reactions
- Patients with severe hepatic impairment (Child-Pugh class C).
- Pregnant women, or women of childbearing potential who are not using reliable contraception during treatment with teriflunomide and thereafter as long as its plasma levels are above 0.02 mg/l. Pregnancy must be excluded before start of treatment.
- Breast-feeding women.
- Patients with severe immunodeficiency states, e.g. AIDS.
- Patients with significantly impaired bone marrow function or significant anaemia, leucopenia, neutropenia or thrombocytopenia.
- Patients with severe active infection until resolution.
- Patients with severe renal impairment undergoing dialysis, because insufficient clinical experience is available in this patient group.
- Patients with severe hypoproteinaemia, e.g. in nephrotic syndrome.
- Coadministration with leflunomide.

WARNINGS AND PRECAUTIONS

Accelerated elimination procedure
Teriflunomide is eliminated slowly from the plasma. Without an accelerated elimination procedure, it takes an average of 8 months to reach plasma concentrations less than 0.02 mg/l, although due to individual variation in substance clearance it may take up to 2 years. An accelerated elimination procedure can be used at any time after discontinuation of teriflunomide.
An accelerated elimination procedure could be used at any time after discontinuation of Teriflunomide. Elimination can be accelerated by either of the following procedures:
- Administration of cholestyramine 8 g every 8 hours for 11 days. If cholestyramine 8 g three times a day is not well tolerated, cholestyramine 4 g three times a day can be used.
- Administration of 50 g oral activated charcoal powder every 12 hours for 11 days.

Hepatotoxicity
Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking Teriflunomide. Patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (ALT) greater than two times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with Teriflunomide. Teriflunomide is contraindicated in patients with severe hepatic impairment.
Obtain serum transaminase and bilirubin levels within 6 months before initiation of Teriflunomide therapy. Monitor ALT levels at least monthly for six months after starting Teriflunomide. Consider additional monitoring when Teriflunomide is given with other potentially hepatotoxic drugs. Consider discontinuing Teriflunomide if serum transaminase increase (greater than three times the ULN) is confirmed. Monitor serum transaminase and bilirubin on Teriflunomide therapy, particularly in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. If liver injury is suspected to be Teriflunomide -induced, discontinue Teriflunomide and start an accelerated elimination procedure and monitor liver tests weekly until normalized. If Teriflunomide -induced liver injury is unlikely because some other probable cause has been found, resumption of Teriflunomide therapy may be considered.
- Since teriflunomide is highly protein bound and as the binding is dependent upon the concentrations of albumin, unbound plasma teriflunomide concentrations are expected to be increased in patients with hypoproteinaemia, e.g. in nephrotic syndrome. Teriflunomide should not be used in patients with conditions of severe hypoproteinaemia.
- The medicinal product should be used with caution in patients who consume substantial quantities of alcohol.

Teratogenicity
Teriflunomide is contraindicated for use in pregnant women and females of reproductive potential not using effective contraception.

Bone Marrow Effects/Immunosuppression Potential/Infections

Bone Marrow Effects
In patients with pre-existing anaemia, leucopenia, and /or thrombocytopenia as well as in patients with impaired bone marrow function or those at risk of bone marrow suppression, the risk of haematological disorders is increased. If such effects occur, the accelerated elimination procedure to reduce plasma levels of teriflunomide should be considered.
In cases of severe haematological reactions, including pancytopenia, Teriflunomide and any concomitant myelosuppressive treatment must be discontinued and a teriflunomide accelerated elimination procedure should be considered.

Risk of Infection/Tuberculosis Screening
Patients with active acute or chronic infections should not start treatment until the infection(s) is resolved. If a patient develops a serious infection consider suspending treatment with v and using an accelerated elimination procedure. Reassess the benefits and risks prior to resumption of therapy. Instruct patients receiving Teriflunomide to report symptoms of infections to a physician. Teriflunomide is not recommended for patients with severe immunodeficiency, bone marrow disease, or severe, uncontrolled infections. Medications like Teriflunomide that have immunosuppression potential may cause patients to be more susceptible to infections, including opportunistic infections.

Vaccination
No clinical data are available on the efficacy and safety of live vaccinations in patients taking Teriflunomide. Vaccination with live vaccines is not recommended. The long half-life of Teriflunomide should be considered when contemplating administration of a live vaccine after stopping Teriflunomide.

Malignancy
The risk of malignancy, particularly lymphoproliferative disorders, is increased with the use of some immunosuppressive medications. There is a potential for immunosuppression with Teriflunomide.

Hypersensitivity and Serious Skin Reactions
Teriflunomide can cause anaphylaxis and severe allergic reactions. Signs and symptoms have included dyspnoea, urticaria, and angioedema including lips, eyes, throat, and tongue. Inform patients of the signs and symptoms of anaphylaxis and angioedema and signs and symptoms that may signal a serious skin reaction. Inform patients that a fever associated with signs of other organ system involvement (e.g., rash, lymphadenopathy, or hepatic dysfunction) may be drug-related. Instruct patients to discontinue Teriflunomide and seek immediate medical care should these signs and symptoms occur. Discontinue Teriflunomide unless the reactions are clearly not drug-related, and begin an accelerated elimination procedure immediately. In such cases, patients should not be re-exposed to teriflunomide.

Peripheral Neuropathy
Age older than 60 years, concomitant neurotoxic medications, and diabetes may increase the risk for peripheral neuropathy. If a patient taking v develops symptoms consistent with peripheral neuropathy, such as bilateral numbness or tingling of hands or feet, consider discontinuing v therapy and performing an accelerated elimination procedure.

Increased Blood Pressure
Elevation of blood pressure may occur during treatment with teriflunomide. Blood pressure must be checked before the start of teriflunomide treatment and periodically thereafter. Blood pressure elevation should be appropriately managed before and during treatment with teriflunomide.

Respiratory Effects
Interstitial lung disease (ILD) may occur acutely at any time during therapy with a variable clinical presentation.
ILD may be fatal. New onset or worsening pulmonary symptoms, such as persistent cough and dyspnoea, may be a reason for discontinuation of the therapy and for further investigation, as appropriate. If discontinuation of the drug is necessary, consider initiation of an accelerated elimination procedure.

Concomitant Use with Immunosuppressive or Immunomodulating Therapies
Coadministration with antineoplastic or immunosuppressive therapies used for treatment of multiple sclerosis has not been evaluated. Safety studies in which Teriflunomide was concomitantly administered with other immune modulating therapies for up to one year (interferon beta, glatiramer acetate) did not reveal any specific safety concerns. The long term safety of these combinations in the treatment of multiple sclerosis has not been established. In any situation in which the decision is made to switch from Teriflunomide to another agent with a known potential for hematologic suppression, it would be prudent to monitor for hematologic toxicity, because there will be overlap of systemic exposure to both compounds. Use of an accelerated elimination procedure may decrease this risk, but may also potentially result in return of disease activity if the patient had been responding to Teriflunomide treatment.

DRUG INTERACTIONS

Pharmacokinetic interactions of other substances on teriflunomide
The primary biotransformation pathway for teriflunomide is hydrolysis, with oxidation being a minor pathway.
Potent cytochrome P450 (CYP) and transporter inducers: Co-administration of repeated doses (600 mg once daily for 22 days) of rifampicin (a CYP2B6, 2C8, 2C9, 2C19, 3A inducer), as well as an inducer of the efflux transporters P-glycoprotein [P-gp] and breast cancer resistant protein [BCRP] with teriflunomide (70 mg single dose) resulted in an approximately 40% decrease in teriflunomide exposure. Rifampicin and other known potent CYP and transporter inducers such as carbamazepine, phenobarbital, phenytoin and St John's Wort should be used with caution during the treatment with teriflunomide.

Cholestyramine or activated charcoal
It is recommended that patients receiving teriflunomide are not treated with Cholestyramine or activated charcoal because this leads to a rapid and significant decrease in plasma concentration unless an accelerated elimination is desired.

Effect of Teriflunomide on CYP2C8 substrates
Teriflunomide is an inhibitor of CYP2C8 *in vivo*. In patients taking Teriflunomide, exposure of drugs metabolized by CYP2C8 (e.g., paclitaxel, pioglitazone, repaglinide, rosiglitazone) may be increased. Monitor these patients and adjust the dose of the concomitant drug(s) metabolized by CYP2C8 as required.

Effect of Teriflunomide on warfarin
Coadministration of Teriflunomide with warfarin requires close monitoring of the international normalized ratio (INR) because Teriflunomide may decrease peak INR by approximately 25%.

Effect of Teriflunomide on oral contraceptives
Teriflunomide may increase the systemic exposures of ethinylestradiol and levonorgestrel. Consideration should be given to the type or dose of contraceptives used in combination with Teriflunomide.

Effect of Teriflunomide on CYP1A2 substrates
Teriflunomide may be a weak inducer of CYP1A2 *in vivo*. In patients taking Teriflunomide, exposure of drugs metabolized by CYP1A2 (e.g., alosetron, duloxetine, theophylline, tizanidine) may be reduced. Monitor these patients and adjust the dose of the concomitant drug(s) metabolized by CYP1A2 as required.

Effect of Teriflunomide on organic anion transporter 3 (OAT3) substrates
Teriflunomide inhibits the activity of OAT3 *in vivo*. In patients taking Teriflunomide, exposure of drugs which are OAT3 substrates (e.g., cefaclor, cimetidine, ciprofloxacin, penicillin G, ketoprofen, furosemide, methotrexate, zidovudine) may be increased. Monitor these patients and adjust the dose of the concomitant drug(s) which are OAT3 substrates as required.

Effect of Teriflunomide on BCRP and organic anion transporting polypeptide B1 and B3 (OATP1B1/1B3) substrates
Teriflunomide inhibits the activity of BCRP and OATP1B1/1B3 *in vivo*. For a patient taking Teriflunomide, the dose of rosuvastatin should not exceed 10 mg once daily. For other substrates of BCRP (e.g., mitoxantrone) and drugs in the OATP family (e.g., methotrexate, rifampin), especially HMG-Co reductase inhibitors (e.g., atorvastatin, nateglinide, pravastatin, repaglinide, and simvastatin), consider reducing the dose of these drugs and monitor patients closely for signs and symptoms of increased exposures to the drugs while patients are taking Teriflunomide.

UNDESIRABLE EFFECTS

Tabulated list of adverse reactions
Adverse reactions are ranked below 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); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System organ class	Very common	Common	Uncommon	Rare	Very rare	Not known
Infections and infestations		Influenza, Upper respiratory tract infection, Urinary tract infection, Bronchitis, Sinusitis, Pharyngitis, Cystitis, Gastroenteritis viral, Oral herpes, Tooth infection, Laryngitis, Tinea pedis				Severe infections including sepsis
Blood and lymphatic system disorders		Neutropenia, Anaemia	Mild thrombocytopenia (platelets <100G/l)			
Immune system disorders		Mild allergic reactions				Hyper-sensitivity reactions (immediate or delayed) including anaphylaxis and angioedema
Psychiatric disorders		Anxiety				
Nervous system disorders	Headache	Paraesthesia, Sciatica, Carpal tunnel syndrome	Hyperaesthesia, Neuralgia, Peripheral neuropathy			
Cardiac disorders		Palpitations				
Vascular disorders		Hypertension				
Respiratory, thoracic and mediastinal disorders						Interstitial lung disease
Gastrointestinal disorders	Diarrhoea, Nausea	Abdominal pain upper, Vomiting, Toothache				Pancreatitis, Stomatitis
Hepatobiliary disorders	Alanine aminotransferase (ALT) increase	Gamma-glutamyltransferase (GGT) increase, Aspartate aminotransferase increase				Acute hepatitis
Skin and subcutaneous tissue disorders	Alopecia	Rash, Acne				Severe skin reactions including toxic epidermal necrolysis and Stevens-Johnson syndrome Nail disorders
Musculoskeletal and connective tissue disorders		Musculoskeletal pain, Myalgia, Arthralgia				
Renal and urinary disorders		Pollakiuria				
Reproductive system and breast disorders		Menorrhagia				
General disorders and administration site conditions		Pain				Asthenia
Investigations		Weight decrease, Neutrophil count decrease, White blood cell count decrease, Blood creatine phosphokinase increased				
Injury, poisoning and procedural complications			Post-traumatic pain			

Reporting of suspected 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. To report SUSPECTED ADVERSE REACTIONS, contact MSN Laboratories Private Limited at pharmacovigilance@msnlabs.com or through company website: www.msnlabs.com->Contact us->Medical Enquiry/To report a side effect.

OVERDOSE
There is no experience regarding teriflunomide overdose or intoxication in humans. Teriflunomide 70 mg daily up to 14 days was well tolerated by healthy subjects. In the event of clinically significant overdose or toxicity, cholestyramine or activated charcoal is recommended to accelerate elimination.

PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: Selective immunosuppressants, ATC Code: L04AA31

Mechanism of action
Teriflunomide, an immunomodulatory agent with anti-inflammatory properties, inhibits dihydroorotate dehydrogenase, a mitochondrial enzyme involved in de novo pyrimidine synthesis. The exact mechanism by which teriflunomide exerts its therapeutic effect in multiple sclerosis is unknown but may involve a reduction in the number of activated lymphocytes in CNS.

Pharmacodynamic effects
Immune system
Effects on immune cell numbers in the blood: In the placebo-controlled studies, teriflunomide 14 mg once a day led to a mild mean reduction in lymphocyte count, of less than 0.3 x 10^9/l, which occurred over the first 3 months of treatment and levels were maintained until the end of the treatment.

Potential to prolong the QT interval
In a placebo-controlled thorough QT study performed in healthy subjects, teriflunomide at mean steady-state concentrations did not show any potential for prolonging the QTcF interval compared with placebo: the largest time matched mean difference between teriflunomide and placebo was 3.45 ms with the upper bound of the 90% CI being 6.45 ms.

Effect on renal tubular functions
In the placebo-controlled studies, mean decreases in serum uric acid at a range of 20 to 30% were observed in patients treated with teriflunomide compared to placebo. Mean decrease in serum phosphorus was around 10% in the teriflunomide group compared to placebo. These effects are considered to be related to increase in renal tubular excretion and not related to changes in glomerular functions.

PHARMACOKINETIC PROPERTIES
Teriflunomide is the principal active metabolite of leflunomide and is responsible for leflunomide's activity *in vivo*. At recommended doses, teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide.

Absorption
Median time to reach maximum plasma concentrations is between 1 to 4 hours post dose following oral administration of teriflunomide. Food does not have a clinically relevant effect on teriflunomide pharmacokinetics.

Distribution
Teriflunomide is extensively bound to plasma protein (>99%) and is mainly distributed in plasma. The volume of distribution is 11 L after a single intravenous (IV) administration.

Metabolism
Teriflunomide is the major circulating moiety detected in plasma. The primary biotransformation pathway to minor metabolites of teriflunomide is hydrolysis, with oxidation being a minor pathway. Secondary pathways involve oxidation, N-acetylation and sulfate conjugation.

Elimination
Teriflunomide is eliminated mainly through direct biliary excretion of unchanged drug as well as renal excretion of metabolites. Over 21 days, 60.1% of the administered dose is excreted via feces (37.5%) and urine (22.6%). After an accelerated elimination procedure with cholestyramine, an additional 23.1% was recovered (mostly in feces). After a single IV administration, the total body clearance of teriflunomide is 30.5 mL/h.

Incompatibilities
Not applicable.

Packing information
10's Alu-Alu Blister.

Storage and handling information
Do not store above 30°C.

Keep away from infants and small children

Manufactured by:
MSN Laboratories Private Limited,
Formulation Division,
Unit-II, Sy.No. 1277, 1319 to 1324,
Nandigama (Village & Mandal),
Rangareddy (District),
Telangana - 509 228, India.

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