For the use of a Registered Neurologist only

Abridged Prescribing Information

Alemtuzumab Concentrate for solution for infusion **12mg/1.2 ml (10 mg/ml)**

Lemtrada®

COMPOSITION: Each vial contains Alemtuzumab 12 mg in 1.2 ml

THERAPEUTIC INDICATION: Treatment of patients with an aggressive form of Relapsing Remitting Multiple Sclerosis (RRMS) in whom there has been a failure of one first line disease modifying therapy

DOSAGE & ADMINISTRATION: Recommended dose is 12 mg/day administered by IV infusion for 2 or more treatment courses. Initial treatment of 2 courses: First treatment course: 12 mg/day on 5 consecutive days (60 mg total dose). Second treatment course: 12 mg/day on 3 consecutive days (36 mg total dose) administered 12 months after the first treatment course.

SAFETY RELATED INFORMATION

Contraindications: LEMTRADA is contraindicated:

- in patients with known Type 1 hypersensitivity or anaphylactic reactions to the active substance or any of the excipients
- in patients who are infected with Human Immunodeficiency Virus (HIV)
- in patients with severe active infection
- in patients with uncontrolled hypertension
- in patients with a history of arterial dissection of the cervicocephalic arteries
- in patients with a history of stroke
- in patients with a history of angina pectoris or myocardial infarction
- in patients with known coagulopathy or on concomitant anti-coagulant therapy

Pregnancy: Should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women of child bearing potential should use effective contraceptive measures when receiving treatment with Lemtrada and for 4 months following treatment.

Lactation: Caution should be exercised when Lemtrada is administered to a nursing woman. Breast feeding should be discontinued during each course of treatment with Lemtrada and for 4 months following the last infusion of each treatment course.

Warnings and Precautions for use: During postmarketing use, AOSD (Adult Onset Still's Disease_)has been reported in patients treated with LEMTRADA . Patients with AOSD may have a combination of the following signs and symptoms: fever, arthritis, rash and leukocytosis in the absence of infections, malignancies and other rheumatic conditions. Before treatment, patients must receive educational information and be informed about the risks and benefits, and the need to commit to follow up from treatment initiation until 48 months after the last infusion of the second Lemtrada treatment course. ***Autoimmunity***: Treatment with Lemtrada may result in the formation of autoantibodies and increase the risk of autoimmune mediated conditions including immune thrombocytopenic purpura (ITP), thyroid disorders or, rarely, nephropathies (e.g., anti-glomerular basement membrane disease) and autoimmune hepatitis (AIH) and thrombotic thrombocytopenic purpura (TTP) and autoimmune encephalitis. ***Autoimmune Hepatitis (AIH)***: Autoimmune hepatitis causing clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with LEMTRADA in the postmarketing setting ***Immune Thrombocytopenic Purpura:*** Serious events of ITP have been observed in controlled MS clinical trials. ***Nephropathies:*** Nephropathies, including anti-glomerular basement membrane (anti-GBM) disease have been observed. Serum creatinine levels and urinalysis with cell counts should be obtained prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion. **Autoimmune Encephalitis:**Cases of autoimmune encephalitis during postmarketing use have been reported in patients treated with LEMTRADA. Autoimmune encephalitis is confirmed by the presence of neural autoantibodies as well as a variety of clinical manifestations like subacute onset of memory impairment, altered mental status, psychiatric symptoms, neurological findings and seizures.

Thyroid Disorders: Observed autoimmune thyroid disorders included hyperthyroidism or hypothyroidism. Thyroid disease pose special risks in women who are pregnant. ***Cytopenias:*** Suspected autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in patients. CBC results should be used to monitor for cytopenias. ***Infusion Associated Reactions***: In clinical trials, infusion associated reactions (IARs) were defined as any adverse event occurring during or within 24 hours of Lemtrada infusion. The majority of these may be due to cytokine release during infusion. Most patients treated with Lemtrada in clinical trials in MS experienced mild to moderate IARs during and/or up to 24 hours after Lemtrada 12 mg administration.

Other serious reactions temporally associated with Lemtrada infusion-

During post-marketing use, rare, serious, sometimes fatal and unpredictable adverse events from various organ systems have been reported. In the majority of cases, time to onset was within 1-3 days of the Lemtrada infusion. ***Infections:*** Infections were predominantly mild to moderate in severity. Infections included nasopharyngitis, urinary tract infection, upper respiratory tract infection, sinusitis, oral herpes, influenza, and bronchitis. Serious infections occurred in 2.7% of Lemtrada patients.

TPP:During postmarketing use, TTP, which can be fatal, has been reported in patients treated with LEMTRADA. TTP is a serious condition that requires urgent evaluation and treatment. TTP may be characterized by thrombocytopenia, microangiopathic hemolytic anemia, neurological sequelae, fever and renal impairment. It is associated with high morbidity and mortality rates if not recognized and treated early.

Hemorrhagic stroke:

Several of the patients reported were below 50 years of age and had no history of hypertension, bleeding disorders or concomitant anticoagulants or platelet inhibitors. In some patients there was increased blood pressure from baseline before the hemorrhage.

Myocardial ischemia and myocardial infarction:

Several of the patients reported were below 40 years of age and had no risk factors for ischemic heart disease. It was noted that in some of the patients, blood pressure and /or heart rate was temporarily abnormal during the infusion.

Pneumonitis: Most cases occurred within first month after treatment. Patients should be advised to report symptoms of pneumonitis. ***Acute Acalculous Cholecystitis:*** May increase the risk of acute acalculous cholecystitis. ***Contraception:*** See Pregnancy ***Vaccines:*** It is recommended that patients have completed local immunization requirements at least 6 weeks prior to treatment with Lemtrada. Live vaccines should not be administered to patients who have been recently treated.

ADVERSE REACTIONS:

Post- Marketing Experience with Lemtrada: Nervous System Disorders: Stroke, including hemorrhagic and ischemic stroke, cervicocephalic arterial dissection and autoimmune encephalitis. Gastrointestinal System Disorders: Cases of cholecystitis have been reported. Infection and Infestations: Cytomegalovirus infections have been reported with concomitant corticosteroid use; Epstein- Barr virus (EBV) infection, Respiratory Thoracic and Mediastinal Disorders: Pulmonary alveolar hemorrhage. Blood and lymphatic system disorders,thrombotic thrombocytopenic purpura (TTP),Haemophagocytic lymphohistiocytosis, Sarcoidosis. Cardiac disorders: Transient myocardial ischemia as an infusion associated reaction, Hepatobiliary Disorders: Autoimmune hepatitis, Hepatitis (associated with EBV infection), Musculoskeletal and connective tissue disorder: Adult Onset Still's Disease (AOSD) ,Skin disorders: Vitiligo

For full prescribing information please contact: Sanofi Healthcare India Private Ltd, Sanofi House, CTS No. 117-B, L&T Business Park, Saki Vihar Road, Powai 400072

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