Alemtuzumab: Drug information

Brand Names: US

Lemtrada

Brand Names: Canada

Lemtrada; MabCampath

Pharmacologic Category

Antineoplastic Agent, Anti-CD52; Antineoplastic Agent, Monoclonal Antibody;

Monoclonal Antibody

Mechanism of Action

Alemtuzumab binds to CD52, a nonmodulating antigen present on the surface of B and T lymphocytes, a majority of monocytes, macrophages, NK cells, and a subpopulation of granulocytes. After binding to $CD52^{+}$ cells, an antibody-dependent lysis of malignant cells occurs. In multiple sclerosis, alemtuzumab immunomodulatory effects may include alteration in the number, proportions, and properties of some lymphocyte subsets following treatment.

Generic Equivalent Available (US): No

Dosage Forms

- Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
- Solution, Intravenous [preservative free]:
- Campath: 30 mg/mL (1 mL) [contains edetate disodium dihydrate, mouse (murine) and/or hamster protein, polysorbate 80]
- Lemtrada: 12 mg/1.2 mL (1.2 mL) [contains edetate disodium dihydrate, mouse (murine) and/or hamster protein, polysorbate 80]

Dosage Forms: Canada

Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

Injection, solution [preservative free]:

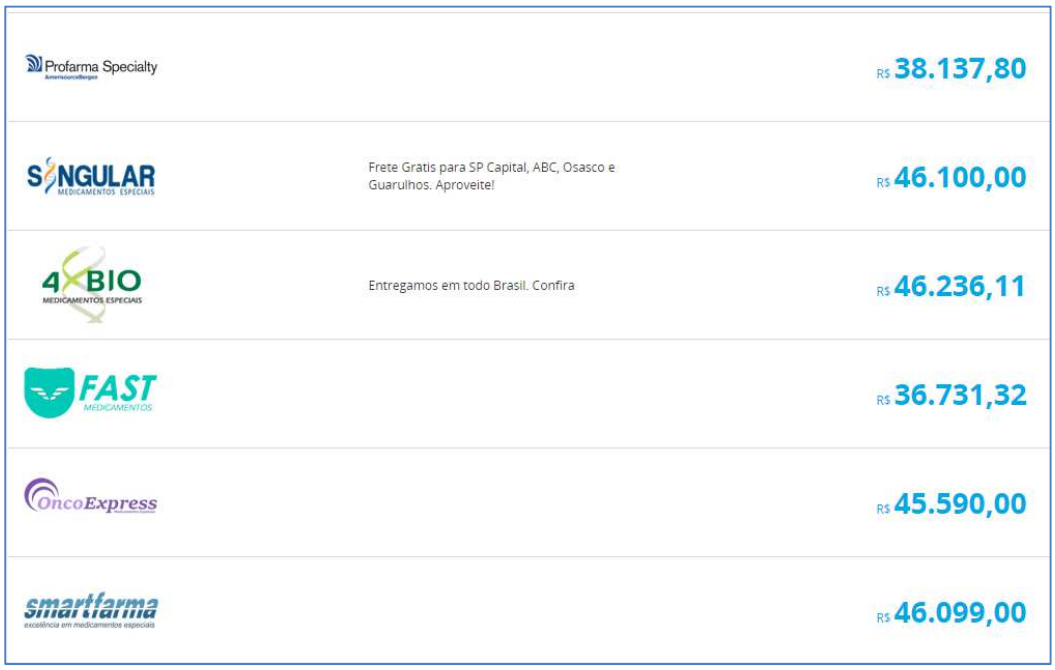
MabCampath: 30 mg/mL (1 mL) [contains edetate disodium, polysorbate 80]

Injection, solution [preservative free]:

Lemtrada: 10 mg/mL (1.2 mL) [contains edetate disodium, polysorbate 80]

Pricing: US

- **Solution** (Campath Intravenous): 30 mg/mL (per mL): $0.00
- **Solution** (Lemtrada Intravenous): 12 mg/1.2 mL (per mL): $22,345.33



Fonte: www.consultaremedios.com.br

Use

- **B-cell chronic lymphocytic leukemia:** Campath or MabCampath [Canadian product]: Treatment (as a single agent) of B-cell chronic lymphocytic leukemia (B-CLL)
- **Multiple sclerosis, relapsing:** Lemtrada: Treatment of patients with relapsing forms of multiple sclerosis (MS), generally reserved for patients who have had an inadequate response to 2 or more medications indicated for the treatment of MS.

Use: Off-Label

- Acute graft-versus-host disease (steroid refractory) (treatment); Aplastic anemia, refractory; Autoimmune hemolytic anemia, chronic lymphocytic leukemia (CLL)-induced; B-cell chronic lymphocytic leukemia (B-CLL) (subcutaneous [off-label route]); Hemophagocytic lymphohistiocytosis, refractory; Mycosis fungoides/Sézary syndrome (advanced); Solid organ transplantation: Heart transplant (induction); Solid organ transplantation: Lung transplant (induction); Solid organ transplantation: Renal transplant (induction); Solid organ transplantation: Renal transplant (steroid-resistant cellular rejection); Stem cell transplant (allogeneic) conditioning regimen and/or graft-versus-host disease prophylaxis; T-cell large granular lymphocytic leukemia (TLGLL); T-cell prolymphocytic leukemia (T-PLL)

Dosing: Adult

Note: Alemtuzumab is associated with a moderate emetic potential in the oncology setting; antiemetics may be recommended to prevent nausea and vomiting.

B-cell chronic lymphocytic leukemia (B-CLL): Campath, MabCampath [Canadian product]: IV: Gradually escalate to a maintenance of 30 mg per dose 3 times weekly on alternate days for a total duration of therapy of up to 12 weeks (Hillmen 2007; Keating 2002)

B-CLL (off-label route): Campath: SubQ: Initial: 3 mg on day 1; if tolerated 10 mg on day 3; if tolerated increase to 30 mg on day 5; maintenance: 30 mg per dose 3 times weekly on alternate days for a maximum of 18 weeks (Lundin 2002) **or** 3 mg on day 1; if tolerated 10 mg on day 2; if tolerated 30 mg on day 3, followed by 30 mg per dose 3 times weekly on alternate days for 4 to 12 weeks (Stilgenbauer 2009)

Multiple sclerosis, relapsing: Lemtrada: IV: 12 mg daily for 5 consecutive days (total 60 mg), followed 12 months later by 12 mg daily for 3 consecutive days (total 36 mg); total duration of therapy: 24 months.

Note: Premedicate with corticosteroids (methylprednisolone 1,000 mg or equivalent) immediately prior to alemtuzumab for the first 3 days of each treatment course. Antihistamines and/or antipyretics may also be considered. Administer antiviral prophylaxis (for herpetic viral infections) beginning on the first day of treatment and continue for at least 2 months after completion of alemtuzumab or until $CD4^+$ lymphocyte count is ≥200/mm^3 (whichever occurs later). In some clinical trials patients received an additional alemtuzumab 12 mg daily for 3 consecutive days 12 months later (total duration of 36 months) (CAMMS223 2008; Coles 2012).

Aplastic anemia, refractory (off-label use): Campath:

IV: 10 mg daily for 10 days (as monotherapy); patients received a 1 mg test dose initially (Scheinberg 2012) **or**

SubQ: 3 mg day 1, 10 mg day 2, then 30 mg/day days 3, 4, and 5 (total dose: 103 mg over 5 consecutive days; in combination with cyclosporine) (Risitano 2009)

Autoimmune cytopenias, CLL-induced, refractory (off-label use): Campath: IV, SubQ: Gradually escalate to a maintenance of 10 to 30 mg per dose 3 times weekly for 4 to 12 weeks (Karlsson 2007; Osterborg 2009)

Graft versus host disease (GVHD), acute, steroid refractory, treatment (off-label use): Campath: IV: 10 mg daily for 5 consecutive days, then 10 mg weekly on days 8, 15, and 22 if CR not achieved (Martinez 2009) **or** 10 mg weekly until symptom resolution (Schnitzler 2009)

Hemophagocytic lymphohistiocytosis, refractory (off-label use): Campath: IV, SubQ: **Note:** The optimal dose and duration of therapy is not known. Median dose: 1 mg/kg (range 0.1 to 8.9 mg/kg; maximum initial dose: 3 mg) **divided** over a median of 4 days (range 2 to 10 days); refer to article for further information (Marsh 2013)

Mycosis fungoides/Sézary syndrome, advanced (off-label use): Campath: IV: Initial: 3 mg, increase to 10 mg and then to 30 mg as soon as infusion-related reactions were tolerated; Maintenance: 30 mg 3 times weekly for up to 12 weeks, or until complete remission is achieved or disease progression is noted; for dosing interruptions >7 days due to toxicity, reinitiate at 3 or 10 mg (Lundin 2003).

Solid organ transplantation: Campath:

Heart transplant, induction (off-label use): IV: 30 mg once intra-operatively at the time of transplant followed by minimized maintenance immunosuppression (Teuteberg 2010). Additional data may be necessary to further define the role of alemtuzumab in this condition.

Lung transplant, induction (off-label use): IV, SubQ: 30 mg once either immediately before allograft reperfusion or immediately following transplant; followed by minimized maintenance immunosuppression (Jaksch 2014; Shyu 2011; Whited 2015). Additional data may be necessary to further define the role of alemtuzumab in this condition.

Renal transplant, induction (off-label use): IV: 30 mg as a single dose at the time of transplant (immediately following reperfusion) followed by a second 30 mg dose 24 hours later (the second dose was omitted in patients >60 years of age); followed by minimized maintenance immunosuppression (Haynes 2014).

Renal transplant, steroid resistant cellular rejection (off-label use): IV, SubQ: 15 to 30 mg/dose SubQ on 2 subsequent days (van den Hoogen 2013) **or** 30 mg/dose IV over 2 to 4 hours for 1 to 2 doses (Basu 2005). Additional data may be necessary to further define the role of alemtuzumab in this condition.

Stem cell transplant (allogeneic) conditioning regimen (off-label use): Campath: IV: 20 mg daily for 5 days (in combination with fludarabine and melphalan) beginning 8 days prior to transplant (Mead 2010) **or** beginning 7 days prior to transplant (Van Besien 2009)

T-cell large granular lymphocytic leukemia (off-label use): Campath: IV: 10 mg daily for 10 days; patients received a 1 mg test dose initially (Dumitriu 2016)

T-cell prolymphocytic leukemia (T-PLL; off-label use): Campath: IV: Initial test dose 3 mg or 10 mg, followed by dose escalation to 30 mg per dose 3 times weekly as tolerated until maximum response (Dearden 2001) **or**Initial dose: 3 mg day 1, if tolerated increase to 10 mg day 2, if tolerated increase to 30 mg on day 3 (days 1, 2, and 3 are consecutive days), followed by 30 mg per dose every Monday, Wednesday, Friday for a total of 4 to 12 weeks (Keating 2002)

Dosing: Renal Impairment: Adult

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment: Adult

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Pediatric

Aplastic anemia, refractory (off-label use): Campath:

Children ≥2 years of age and Adolescents (<50 kg): IV: 0.2 mg/kg/dose (maximum: 10 mg/dose) for 10 days (as monotherapy); patients received a 1 mg test dose initially (Scheinberg 2012)

Children ≥2 years of age and Adolescents (≥50 kg): IV: 10 mg daily for 10 days (as monotherapy); patients received a 1 mg test dose initially (Scheinberg 2012)

Hemophagocytic lymphohistiocytosis, refractory (off-label use): Infants, Children, and Adolescents: Campath: IV, SubQ: **Note:** The optimal dose and duration of therapy is not known. Median dose: 1 mg/kg (range 0.1 to 8.9 mg/kg; maximum initial dose: 3 mg) **divided** over a median of 4 days (range 2 to 10 days); refer to article for further information (Marsh 2013)

Dosage adjustment for nonhematologic toxicity:

Treatment of B-CLL: Campath, MabCampath [Canadian product]:

Note: If treatment is withheld ≥7 days, reinitiate at 3 mg with re-escalation to 10 mg and then 30 mg.

Grade 3 or 4 infusion reaction: Withhold infusion

Serious infection or other serious adverse reaction: Withhold alemtuzumab until resolution

Autoimmune anemia or autoimmune thrombocytopenia: Discontinue alemtuzumab

Treatment of MS: Lemtrada: Serious infusion reaction: Consider immediate discontinuation

Administration

IV: Campath or MabCampath [Canadian product]: Administer by IV infusion over 2 hours. Premedicate with diphenhydramine 50 mg and acetaminophen 500 to 1000 mg 30 minutes before each infusion. IV glucocorticoids have been effective in decreasing severe infusion-related events. Start anti-infective prophylaxis. Other drugs should not be added to or simultaneously infused through the same IV line. Do not give IV push or bolus. Compatible in polyvinylchloride (PVC) or polyethylene lined administration sets or low protein binding filters. May be given through peripheral IV.

Infusion times may have varied in studies for off-label uses; refer to specific reference citations.

Lemtrada: Administer by IV infusion over 4 hours (beginning within 8 hours after dilution); do not administer by IV push or IV bolus. May extend the infusion duration if clinically indicated. Do not infuse other medications through the same IV line. Premedicate with corticosteroids (methylprednisolone 1,000 mg or equivalent) for first 3 days of each treatment course. Administer in a setting with personnel and equipment appropriate to manage infusion reactions. Monitor vital signs prior to and periodically during the infusion. Infusion reactions should be managed symptomatically; consider discontinuing immediately for severe infusion reaction. Observe for at least 2 hours after each infusion, longer if clinically indicated.

SubQ: Campath: SubQ (off-label route): SubQ administration has been studied (Lundin 2002; Stilgenbauer 2009); an increased rate of injection site reactions has been observed, with only rare incidences of chills or infusion-like reactions typically observed with IV infusion. A longer dose escalation time (1 to 2 weeks) may be needed due to injection site reactions (Lundin 2002). Premedicate with diphenhydramine 50 mg and acetaminophen 500 to 1000 mg 30

minutes before dose. The subQ route should **NOT** be used for the treatment of T-PLL (Deardon 2011).

Alemtuzumab is associated with a moderate emetic potential in adults in the oncology setting; antiemetics may be recommended to prevent nausea and vomiting (Hesketh 2017; Roila 2016).

Medication Safety Issues

Duplicate therapy issues: Campath and MabCampath contain alemtuzumab, which is the same ingredient contained in Lemtrada; patients receiving Lemtrada should not be treated with Campath or MabCampath.

Adverse Reactions

Multiple sclerosis:

>10%:

Central nervous system: Headache (52%), fatigue (18%), insomnia (16%), paresthesia (10%)

Dermatologic: Skin rash (53%), urticaria (16%), pruritus (14%)

Endocrine & metabolic: Thyroid disease (13% to 34%; including Graves disease, hyperthyroidism, hypothyroidism)

Gastrointestinal: Nausea (21%), diarrhea (12%)

Genitourinary: Urinary tract infection (19%)

Hematologic & oncologic: Lymphocytopenia (100%)

Immunologic: Antibody development (neutralizing: 5% to 94%; anti-alemtuzumab: 2% to 83%; no effect on drug efficacy)

Infection: Infection (71%), herpes virus infection (16%), fungal infection (12% to 13%; including oral candidiasis, vulvovaginal candidiasis)

Local: Infusion-related reaction (92%)

Neuromuscular & skeletal: Arthralgia (12%), back pain (12%), limb pain (12%)

Respiratory: Nasopharyngitis (25%), upper respiratory tract infection (16%), oropharyngeal pain (11%), sinusitis (11%)

Miscellaneous: Fever (29%)

1% to 10%:

Cardiovascular: Flushing (10%), tachycardia (8%), chest discomfort (7%), peripheral edema (5%), atrial fibrillation (≤3%), bradycardia (≤3%), chest pain (≤3%), hypertension (≤3%), hypotension (≤3%)

Central nervous system: Dizziness (10%), chills (9%), anxiety (7%), neurological signs and symptoms (≤3%; transient)

Dermatologic: Dermatitis (8%), erythema (5%)

Gastrointestinal: Abdominal pain (10%), vomiting (10%), oral herpes (9%), dysgeusia (8%), dyspepsia (8%), appendicitis (≤3%), gastroenteritis (≤3%), tooth infection (≤3%)

Genitourinary: Occult blood in urine (8%), uterine hemorrhage (5%), herpes genitalis (1%)

Hematologic & oncologic: Decreased CD-4 cell count (6%), decreased CD-8 cell counts (6%), decreased T cell lymphocytes (5%), immune thrombocytopenia (2%), hematoma (1%), petechia (1%)

Hypersensitivity: Angioedema (≤3%)

Infection: Influenza (8%), herpes zoster (4%), herpes simplex infection (2%), human papilloma virus infection (2%)

Neuromuscular & skeletal: Myasthenia (7%), muscle spasm (6%), myalgia (6%), neck pain (5%), weakness (5%)

Ophthalmic: Graves ophthalmopathy (1%)

Respiratory: Cough (9%), dyspnea (8%), bronchitis (7%), epistaxis (5%), bronchospasm (≤3%), pneumonia (≤3%)

B-cell chronic lymphocytic leukemia:

>10%:

Cardiovascular: Hypotension (16%), cardiac arrhythmia (14%), hypertension (14%)

Central nervous system: Chills (53%), headache (14%)

Dermatologic: Urticaria (16%), skin rash (13%)

Hematologic & oncologic: Lymphocytopenia (97%; grades 3/4: 97%), neutropenia (77%; grades 3/4: 42% to 64%), anemia (76%; grades 3/4: 12% to 38%), thrombocytopenia (71%; grades 3/4: 13% to 52%)

Infection: Infection (50% to 74%), CMV viremia (55%), cytomegalovirus disease (6% to 16%)

Respiratory: Dyspnea (14%)

Miscellaneous: Fever (69%)

1% to 10%:

Cardiovascular: Tachycardia (10%)

Central nervous system: Insomnia (10%), anxiety (8%), dysesthesia (>5%), fatigue (>5%)

Dermatologic: Erythema (4%)

Gastrointestinal: Diarrhea (10%), anorexia (>5%), mucositis (>5%), nausea (>5%), vomiting (>5%)

Hematologic & oncologic: Febrile neutropenia (≥ grade 3: 5% to 10%), autoimmune thrombocytopenia (2%)

Immunologic: Antibody development (2% to 8%; neutralizing: 2%)

Infection: Sepsis (≥ grade 3: 3% to 10%)

Neuromuscular & skeletal: Musculoskeletal pain (>5%), tremor (3%)

Respiratory: Bronchospasm (>5%)

Contraindications

US labeling: Lemtrada is contraindicated in patients infected with HIV (due to prolonged reduction in CD4+ lymphocytes). There are no contraindications listed in the manufacturer's Campath labeling.

Canadian labeling:

Lemtrada: Hypersensitivity to alemtuzumab or any component of the formulation; HIV infection; active or latent tuberculosis; severe active infections; active malignancies; concurrent antineoplastic or immunosuppressive therapy; history of progressive multifocal leukoencephalopathy (PML)

MabCampath: Known type 1 hypersensitivity or anaphylactic reactions to alemtuzumab or any component of the formulation; active infections; underlying immunodeficiency (eg, seropositive for HIV); active secondary malignancies; current or history of progressive multifocal leukoencephalopathy (PML)

Special populations:

- HBV or HCV infected patients: Alemtuzumab has not been studied in MS patients infected with HBV or HCV; consider screening patients at increased risk of infection prior to initiating treatment. Use with caution in HBV or HCV carriers; patients may be at risk for viral reactivation.

Other warnings/precautions:

- Appropriate use: Alemtuzumab is not recommended for use in MS patients with inactive disease or who are stable on other treatment. Patients should commit to at least 48 months of follow-up after the last infusion.

- Duplicate therapy: If considering Lemtrada treatment for use in a patient who has previously received Campath/MabCampath, consider the additive and long-lasting immune system effects.

- Immunizations: Patients should not be immunized with live, viral vaccines during or recently after treatment. The ability to respond to any vaccine following therapy is unknown. Testing for antibodies to varicella zoster virus (VZV) is recommended prior to initiation of Lemtrada if history of chickenpox or VZV vaccination status is unknown. When using for the treatment of MS, complete necessary immunizations at least 6 weeks prior to initiating alemtuzumab. Determine if patient has a history varicella or vaccination for VZV; if not, test for VZV antibodies and consider vaccinations for antibody-negative patients; postpone alemtuzumab treatment for 6 weeks following VZV vaccination.

- REMS Program: **[US Boxed Warning (Lemtrada)]: Due to the risk of autoimmunity, infusion reactions, and malignancies, alemtuzumab is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) Program when used for the treatment of MS. Contact 1-855-676-6326 to enroll in the Lemtrada REMS program.** Prescribers and pharmacies must be certified with the REMS program, and patients and healthcare facilities must be enrolled and comply with ongoing monitoring.

Monitoring Parameters

Campath: CBC with differential and platelets (weekly, more frequent if worsening); signs and symptoms of infection; $CD4^+$ lymphocyte counts (after treatment until recovery); CMV antigen (routinely during and for 2 months after treatment); consider TSH at baseline and then every 2 to 3 months during alemtuzumab treatment (Hamnvik 2011). Monitor closely for infusion reactions (including hypotension, rigors, fever, shortness of breath, bronchospasm, chills, and/or rash); vital signs (prior to and during infusion); carefully monitor BP especially in patients with ischemic heart disease or on antihypertensive medications.

Lemtrada: CBC with differential prior to initiation then monthly until 48 months after last infusion; serum creatinine prior to initiation then monthly until 48 months after last infusion or at any time during therapy if clinically indicated; urinalysis with urine cell counts (prior to initiation then monthly); signs/symptoms of infection; TSH at baseline and every 3 months until 48 months after last infusion or longer or at any time during therapy if clinically indicated; observe for at least 2 hours after each infusion, longer if clinically indicated; ECG prior to each treatment course; annual HPV screening; tuberculosis screening; signs/symptoms of PML; baseline and annual skin exams (for melanoma).