Cladribine (Mavenclad®)

Mavenclad tablets are indicated for the treatment of relapsing forms of multiple sclerosis (MS), and are generally reserved for second line use given safety profile.

Pre-Treatment Labs: B-HCG, QuantiFERON Gold, Hepatitis panel, RPR, HIV, Varicella IgG, CBC, CMP

Pre-Treatment vaccines: Varicella if antibody negative

Pre-Treatment Cancer Screens: Age-appropriate testing only

Standing labs: Blood counts (CBC) every-3-months x12 months post each treatment course

Anti-viral prophylaxis: Valacyclovir 1gm daily if patients with ALC less than 200

Efficacy Based on CLAIRTY trial: Annualized Relapse Rate of cladribine (RR 0.14) vs placebo (RR 0.33), 57% relative risk reduction.

New Gad lesions vs placebo: 86% relative risk reduction. New/ Enlarged T2 lesions vs placebo: 73% relative risk reduction.

CONTRAINDICATIONS for taking Mavneclad:

1. Patients with current malignancy
2. Pregnant women
3. Women intending to breastfeed while taking Mavenclad tablets and for 10 days after the last dose.
4. Patients of reproductive potential not using effective contraception x 6 months after last dose in each treatment course
5. Patients with human immunodeficiency virus (HIV) or active chronic infections (e.g., hepatitis or tuberculosis)
6. Patients with a history of hypersensitivity to cladribine.
7. Use in patients with moderate to severe renal or hepatic impairment (not recommended)

WARNINGS AND PRECAUTIONS:

1. Adverse Reactions: Most common adverse reactions (>20%) are upper respiratory tract infection, headache, and lymphopenia

2. Malignancies: May increase the risk of malignancy. After the completion of 2 treatment courses, do not administer additional Mavenclad treatment during the next 2 years (year 3 and 4). Follow standard cancer screening guidelines in patients treated with Mavenclad.

3. Risk of Teratogenicity: May cause fetal harm when administered to pregnant women. In females of reproductive potential, exclude pregnancy before initiation of each treatment course of Mavenclad. Patients must use effective contraception during Mavenclad dosing and for at least 6 months after the last dose of each treatment course. Women who become pregnant during treatment with Mavenclad should discontinue treatment.

4. Lymphopenia: Mavenclad causes a dose-dependent reduction in lymphocyte count (87% of Mavenclad treated patients in clinical studies). The lowest absolute lymphocyte counts occurred ~ 2-3 months after the start of each treatment course and were lower with each additional treatment course. Concomitant use of hematotoxin drugs may increase the risk. Monitor lymphocyte counts before and during treatment, periodically thereafter, and when clinically indicated.

5. Infections: May reduce the body's immune defense and increase the risk of infections. In clinical trials, infections occurred in 49% of Mavenclad -treated patients vs. 44% of placebo-treated patients. The most frequent serious infections included herpes zoster and pyelonephritis. Single fatal cases of tuberculosis and fulminant hepatitis B were reported in the clinical program. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. Monitor for infections.

6. PML: In patients treated with parenteral cladribine for oncologic indications, cases of progressive multifocal leukoencephalopathy (PML) have been reported. No case of PML has been reported in clinical studies of cladribine in patients with MS.

7. Vaccines: Administer live attenuated or live vaccines at least 4 to 6 weeks prior to starting Mavenclad. Screen patients for latent infections and consider delaying treatment until infection is fully controlled. Vaccinate patients who are antibody-negative to varicella zoster virus prior to treatment.

8. Hematologic Toxicity: In addition to lymphopenia, mild to moderate decreases in neutrophil counts, hemoglobin levels, and platelet counts have been reported with Mavenclad in clinical studies. Severe decreases in neutrophil counts were observed in 3.6% of Mavenclad -treated patients vs 2.8% of placebo patients. Obtain complete blood count (CBC) with differential including lymphocyte count before and during treatment, periodically thereafter, and when clinically indicated.

9. Risk of Graft-versus-Host Disease with Blood Transfusions: Transfusion-associated graft-versus-host disease has been observed rarely after transfusion of nonirradiated blood in patients treated with cladribine for non-MS treatment indications.

10. Liver Injury: In clinical studies, 0.3% of Mavenclad -treated patients had liver injury (serious or causing treatment discontinuation) compared to 0% placebo patients. We will obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels prior to treatment. Discontinue if clinically significant injury is suspected.

11. Hypersensitivity: In clinical studies, 11% of Mavenclad -treated patients had hypersensitivity reactions, compared to 7% of placebo patients. Hypersensitivity reactions that were serious and/or led to discontinuation of Mavenclad, occurred in 0.5% of Mavenclad -treated patients, compared to 0.1% of placebo patients. If a hypersensitivity reaction is suspected, discontinue Mavenclad therapy. Do not use Mavenclad in patients with a history of hypersensitivity to cladribine.

12. Drug Interactions/Concomitant Medication: Concomitant use of immunosuppressive or myelosuppressive drugs and some immunomodulatory drugs (e.g., interferon beta) is not recommended. Avoid concomitant use of certain antiviral and antiretroviral drugs, BCRP or ENT/CNT. Acute short-term therapy with corticosteroids can be administered.