PRESCRIBING INFORMATION – UNITED KINGDOM

MAVENCLAD® cladribine (Please refer to the full Summary of Product Characteristics before prescribing)
PRESENTATION: Cartons of 1, 4 or 6 tablets. Each tablet contains 10 mg of cladribine.
INDICATIONS: Treatment of adults with relapsing forms of multiple sclerosis (RMS) with active disease as defined by clinical or imaging features.
DOSAGE AND ADMINISTRATION: Must be initiated and supervised by a physician experienced in MS treatment. Recommended cumulative dose: 3.5 mg/kg body weight over 2 years, administered as one treatment course of 1.75 mg/kg per year. Each course comprises 2 treatment weeks, one at the start of the first month and one at the start of the second month of each year. If medically necessary (e.g. for recovery of lymphocytes), the treatment course in year 2 can be delayed for up to 6 months. Each treatment week comprises 4 or 5 days on which the patient receives 10 mg or 20 mg as a single daily dose, depending on body weight. For details, see dosage tables in the SPC. No further cladribine treatment is required in years 3 and 4.
CONTRAINDICATIONS: Hypersensitivity to cladribine or to the excipients; HIV infection; active chronic infection (tuberculosis or hepatitis); initiation in immunocompromised patients including those receiving immunosuppressive or myelosuppressive therapy; active malignancy; moderate or severe renal impairment (creatinine clearance <60 mL/min); pregnancy and breast-feeding.
PRECAUTIONS: Not recommended in moderate or severe hepatic impairment. Exercise caution in elderly patients. Determine lymphocyte counts before initiation in years 1 and 2, 2 and 6 months after treatment start in each treatment year. Count should be normal pre-treatment in year 1. If count below 500 cells/mm^3 at 2 or 6 months, actively monitor until values increase. If count below 800 cells/mm^3 pretreatment in year 2, delay treatment. Stop treatment if recovery takes more than 6 months. Screen for latent infections prior to initiation in years 1 and 2. Delay initiation in latent or acute infection until treated. Varicella zoster vaccination is recommended in antibody-negative patients prior to treatment initiation. Delay initiation for 4-6 weeks following vaccination. Consider anti-herpes prophylaxis during grade 4 lymphopenia. If lymphocyte count falls below 500 cells/mm^3, actively monitor for symptoms suggestive of infection and initiate anti-infective treatment accordingly. Interrupt or delay MAVENCLAD until infection has resolved. Serious, severe, and opportunistic infections - including events with fatal outcome- have been observed with MAVENCLAD treatment. Perform baseline MRI before initiating MAVENCLAD (usually within 3 months). Evaluate benefit-risk prior to initiation in patients with previous malignancy. Advise patients to follow standard cancer screening guidelines. Take a comprehensive patient history prior to initiation regarding previous episodes of liver injury with other drugs or underlying liver disorders. Assess serum aminotransferase, alkaline phosphatase and total bilirubin levels prior to initiation in year 1 and year 2. Monitor liver enzyme and bilirubin during treatment, based on clinical signs and symptoms. If a patient develops clinical signs, unexplained liver enzyme elevations or symptoms suggestive of hepatic dysfunction, promptly measure serum transaminases and total bilirubin and interrupt or discontinue treatment as appropriate. Exclude pregnancy before initiation in years 1 and 2. Before initiation in year 1 and 2, counsel male and female patients on potential for risk to the foetus and need for effective contraception. Contraception should be used by both male and female patients during treatment and for at least 6 months after the last dose. In patients previously treated with immunomodulatory or immunosuppressive products, consider their mode of action and duration of effect before initiation of MAVENCLAD. Consider an additive effect on the immune system when such products are used after treatment with MAVENCLAD. When

switching from another MS agent, perform a baseline MRI. In patients requiring blood transfusion, irradiation of cellular blood components is recommended prior to administration. Take into account the additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose).
Separate administration of any other oral medicinal product by at least three hours from MAVENCLAD administration. Concomitant treatment with other disease-modifying treatments for MS not recommended. Monitor haematological parameters when taken with other substances that affect the haematological profile. Do not initiate treatment within 4-6 weeks of live or attenuated live vaccines. Avoid vaccines during and after treatment while white blood cells not within normal limits. Avoid co-administration of ENT1, CNT3 or BCRP inhibitors during the 4-5 day treatment period. Consider possible decrease in cladribine exposure if potent BCRP or P-gp transporter inducers are co-administered.
SIDE EFFECTS: Very common: Lymphopenia **Common**: Oral herpes, dermatomal herpes zoster, decreased neutrophils, hypersensitivity (including pruritus, urticaria, rash and rare cases of angio-oedema), rash, alopecia **Other side effects**: Liver injury, tuberculosis. In clinical studies and long-term follow-up, malignancies were observed more frequently in cladribine-treated patients compared to placebo.
Prescribers should consult the Summary of Product Characteristics in relation to other side effects.
LEGAL CATEGORY: POM.
PRICE:
Pack of 1 tablet: £2,047.24
Pack of 4 tablets: £8,188.97
Pack of 6 tablets: £12,283.46
Marketing Authorisation Holder and Number:
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PLGB 11648/0272
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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Merck Serono Limited - Tel: +44(0)20 8818 7373 or by email to: medinfo.uk@merckgroup.com.