INFORMATION ON MAVENCLAD® (CLADRIBINE 10 MG TABLETS) FOR PRIMARY CARE AND COMMUNITY CARE COLLEAGUES

Dear Doctor

Your patient _____ (NHS Number: _____)
has been prescribed MAVENCLAD® 10 mg tablets. MAVENCLAD® received marketing authorisation in August 2017 and this medicine may be new to you. This leaflet is designed to provide you with some key information. If you have any questions or require additional information please contact your local neurology team.

MAVENCLAD® is indicated for the treatment of adult patients with highly active relapsing multiple sclerosis. The mode of action of MAVENCLAD® is closely linked to a reduction in lymphocyte count.

MAVENCLAD® has a unique dosing schedule in MS, only requiring 2 weeks of oral treatment in years 1 and 2, and no additional treatment required in years 3-4. Each treatment course consists of 2 treatment weeks of 4-5 days, scheduled in the first week of months 1 and 2. It is important that your patient commits to these treatment periods.

The dose of MAVENCLAD® is weight dependent and the recommended cumulative dose of MAVENCLAD® is 3.5 mg/kg body weight over 2 years, administered as 1 treatment course of 1.75 mg/kg per year.

Your prescribing neurologist can advise you on what assessments and screening have been conducted for your patient. Further monitoring of lymphocyte counts should be carried out:

- Before initiating the second course of MAVENCLAD® treatment in year 2
- 2 and 6 months after start of treatment in each treatment year
- If the lymphocyte count is below 500 cells/mm^3, it should be actively monitored until values increase again

MAVENCLAD® is supported by a Patient Support Programme called adveva™ through Lloyds Pharmacy Clinical Homecare. The programme is designed to support your patient with the administration and monitoring of MAVENCLAD® treatment.

Should your patient be considering pregnancy the advice is as follows:

- Women of childbearing potential must prevent pregnancy by use of effective contraception during MAVENCLAD® treatment and for at least 6 months after the last dose
- Male patients should also take precautions to prevent pregnancy of their female partner during MAVENCLAD® treatment and for at least 6 months after the last dose
- It is currently unknown whether MAVENCLAD® may reduce the effectiveness of systemically acting hormonal contraceptives. Therefore, women using systemically acting hormonal contraceptives should add a barrier method during MAVENCLAD® treatment and for at least 4 weeks after the last dose in each treatment year

Please always refer to the MAVENCLAD® Summary of Product Characteristics for further information.

THIS COMMUNICATION HAS BEEN PREPARED BY MERCK

MAVENCLAD® cladribine tablets | INNOVATIVELY SIMPLE†

PRESCRIBING INFORMATION – UK AND IRELAND

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 highly active relapsing multiple sclerosis (MS) 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. 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. 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. 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. Women using systemically acting hormonal contraception should add barrier method during treatment and for at least 4 weeks after last dose in each treatment year. 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. Not to be taken by patients with hereditary fructose intolerance. 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, rash, alopecia **Other side effects:** 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. For prices in Ireland, consult distributor Allphar Services Ltd.

Marketing Authorisation Holder and Numbers:
Merck Europe B.V., Gustav Mahlerplein 102,1082 MA Amsterdam, The Netherlands; EU/1/17/1212/001, 002 & 004

For further information contact:

UK: Merck Serono Ltd, Bedfont Cross, Stanwell Road, Feltham, Middlesex, TW14 8NX. Tel: 020 8818 7373.

Republic of Ireland: Merck Serono (Ireland) Limited, 4045 Kingswood Road, Citywest Business Campus, Dublin 24. Tel: 01 4687590.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. In the Republic of Ireland information can be found at www.hpra.ie. Adverse events should also be reported to Merck Serono Limited - Tel: +44(0)20 8818 7373 or email: medinfo.uk@merckgroup.com.

† Maximum of 20 days of oral dosing in the first 2 years with no further treatment required in the next 2 years.

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