Treatment with MAVENCLAD® (cladribine tablets) results in lymphocyte reduction and recovery following dosing in Years 1 and 2[1]

Adapted from Comi G et al. Mult Scler Relat Disord. 2019;29:168-174.

In a post-hoc analysis of CLARITY++, lymphopenia grades at specific time points during treatment with MAVENCLAD were analyzed

- The majority of patients had lymphocyte counts grade 0-1 throughout treatment[1-4]
- After completion of Yr 1 dosing, 82.2% patients had no lymphopenia or grade 1 lymphopenia (Yr 1, week 13)[3-4]
- After completion of Yr 2 dosing, 64.5% patients had no lymphopenia or grade 1 lymphopenia (Yr 2, week 12)[3-4]

No patients experienced Grade 4 lymphopenia at end of Year 1 or Year 2[3,4]

	Year 1, Week 13 (n=152)	Year 1, Week 48 (n=175)	Year 2, Week 12 (n=149)	Year 2, Week 48 (n=154)
Grade 0 or 1 (<LLN-0.8 x 10⁹ cells/L)	82.2%	89.1%	64.5%	88.3%
Grade 2 (0.8-0.5 x 10⁹ cells/L)	16.4%	10.9%	28.9%	10.4%
Grade 3 (0.5-0.2 x 10⁹ cells/L)	1.3%	0%	6.7%	1.3%
Grade 4 (<0.2 x 10⁹ cells/L)	0%	0%	0%	0%

During first 2 years of MAVENCLAD treatment[2]:

- 20%–25% Grade 3 or 4 lymphopenia
- <1% Grade 4 lymphopenia

Median duration of lymphopenia[5]:

- 6.0 weeks to improvement to Grade 2 or better
- 28.1 weeks to recovery to Grade 0 or 1

*4–5 days of at-home oral treatment: MAVENCLAD tablets are administered as 2 courses separated by 1 year (a maximum of 20 days of treatment). On treatment days, patient receives 1 or 2 tablets as a single daily dose, depending on body weight.[2]

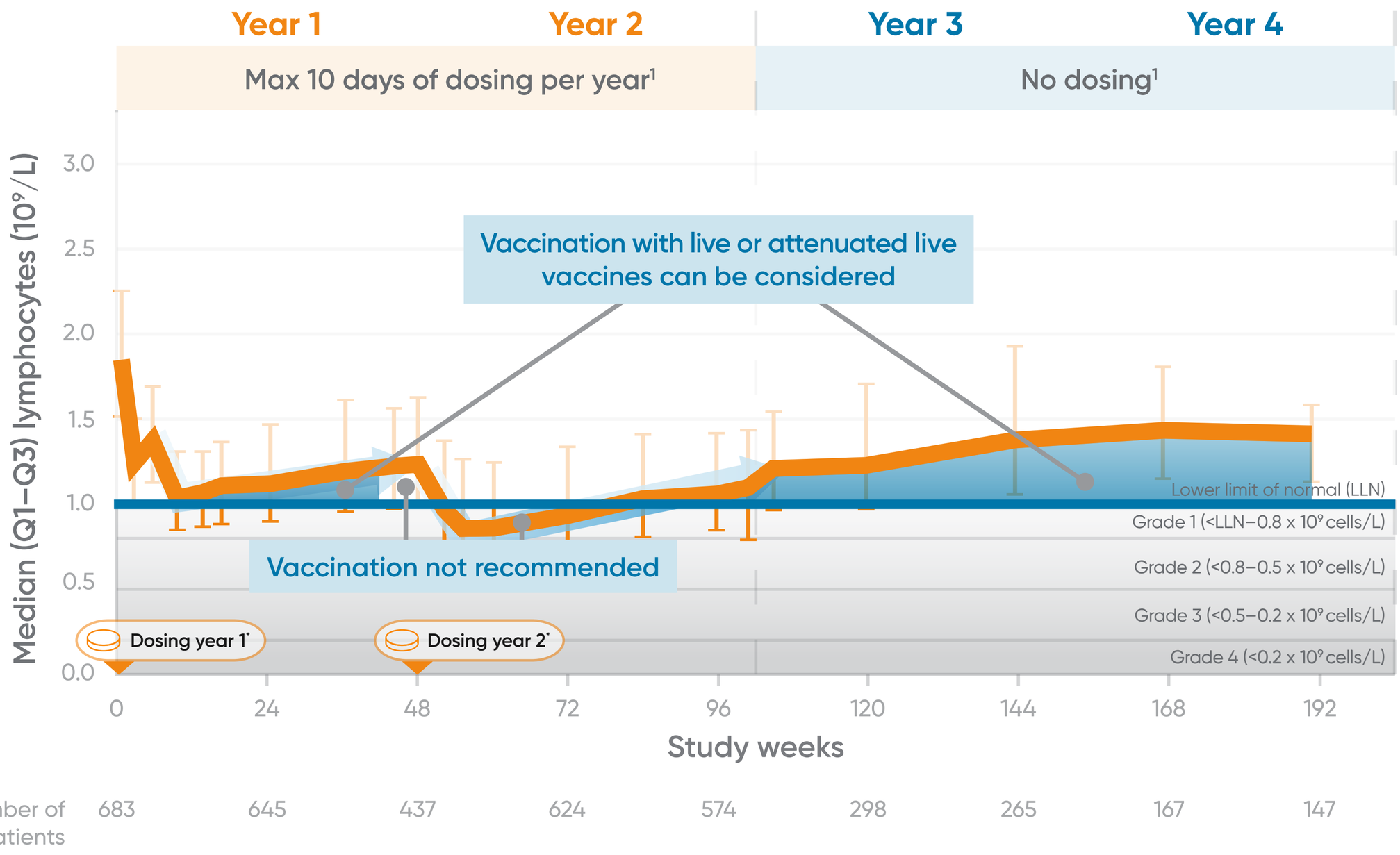
+ Monotherapy oral cohort (3.5mg/kg)

References: 1. Comi G et al. Mult Scler Relat Disord. 2019;29:168-174; 2. MAVENCLAD EU SmPC, 2020; 3. Comi G et al. Mult Scler Relat Disord. 2019;29:168-174. (Suppl Info); 4. Merck Serono CSS (Lymphocytes, WBC, CD4, CD8 Summary Year by Year linked with exposure); 5. Data on file. Merck 2.7.4 Summary of Clinical Safety

UK&IE/CLA/0620/0068 | Date of preparation: July 2020

MAVENCLAD® cladribine tablets

Vaccination with live or attenuated live vaccines can be considered when lymphocytes recover to normal[1,3]



Adapted from Comi G et al. Mult Scler Relat Disord. 2019;29:168-174.

Vaccination in the SmPC[1]:

- Treatment with MAVENCLAD should not be initiated within 4 to 6 weeks after vaccination with live or attenuated live vaccines because of a risk of active vaccine infection
- Vaccination with live or attenuated live vaccines should be avoided during and after MAVENCLAD treatment as long as the patient's white blood cell counts are not within normal limits
- The response to vaccines after treatment with MAVENCLAD has not been studied

MAVENCLAD is a convenient treatment option in today's world; with opportunities to consider vaccination†, short-course dosing, and lymphocyte monitoring that can be completed away from hospital clinics[1]

For highly active relapsing MS, think MAVENCLAD®.

Adapted from Comi G et al. Mult Scler Relat Disord. 2019;29:168-174.[2]

*4–5 days of at-home oral treatment: MAVENCLAD tablets are administered as 2 courses separated by 1 year (a maximum of 20 days of treatment). On treatment days, patient receives 1 or 2 tablets as a single daily dose, depending on body weight.[1]

†With live or attenuated live vaccines

References: 1 MAVENCLAD EU SmPC, 2020; 2. Comi G et al. Mult Scler Relat Disord. 2019;29:168-174; 3. Curry CV. Accessed May 5, 2020. https://emedicine.medscape.com/article/2085133-overview.
Please refer to your local Hospital Guidelines for Lymphocyte reference range.

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MAVENCLAD®
cladribine tablets

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. 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, 5 New Square, Bedfont Lakes Business Park, Feltham, Middlesex, TW14 8HA. Tel: 020 8818 7373.

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

Date of Preparation: January 2020 **Job No**: UK&IE/CLA/0818/0089(2)

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.

MAVENCLAD®
cladribine tablets