What are the potential benefits of MAVENCLAD®?

Clinical trial data has shown that MAVENCLAD®:

**Efficacy**
MAVENCLAD® is a disease-modifying therapy that can deliver clinical and radiological effects with a maximum of 20 days of oral treatment in the first 2 years. Almost 1 of 2 patients had no evidence of disease activity at the end of the 2-year study, after a maximum of 20 days of oral treatment.1-4

**Mechanism of Action (MOA)**
MAVENCLAD® depletes B and T lymphocytes and selectively reconstitutes the immune system with minimal impact on innate immune function. It was shown to induce a selective and transient lymphocyte depletion followed by a distinct pattern of lymphocyte reconstitution.1, 3-9

**Monitoring and Pregnancy Planning**
MAVENCLAD® provides a low monitoring burden compared to currently approved disease-modifying drugs for relapsing MS. Pregnancy planning can begin 6 months after the last dose in the second year of treatment.1, 10-13

What is the clinical evidence for MAVENCLAD®?

MAVENCLAD® use is supported by over 12 years of clinical experience in MS.3, 4, 14-18 Over 2,000 patients were included in the clinical programme, exceeding 10,000 patient-years of experience.3, 16, 18-21

MAVENCLAD® has a well-characterised safety profile, with 8 years of safety registry experience up to August 2017 and no reported cases of PML or risk of secondary autoimmunity.1, 18

At 2 years...

- ~4 out of 5* Free of relapses
- ~9 out of 10* Free of disability progression
- ~1 out of 2* No evidence of disease activity

At 4 years...

- ~7 out of 10* Remain relapse-free

*Patients treated with MAVENCLAD® 3.5 mg/kg in the CLARITY trial
How does MAVENCLAD® work?

MAVENCLAD® has an innovative mechanism of action that depletes B and T lymphocytes and selectively reconstitutes the immune system with minimal impact on the innate immune function compared to the adaptive immune system. MAVENCLAD® has been referred to as a selective example of an immune reconstitution therapy that works in two phases:1,3,5-9

THE SELECTIVE RECONSTITUTION IS BELIEVED TO EXPLAIN ITS DURABLE TREATMENT EFFECT BEYOND TOTAL LYMPHOCYTE COUNT RECOVERY AND ITS WELL-CHARACTERISED SAFETY PROFILE 23-25

How is MAVENCLAD® administered?

• MAVENCLAD® has a tailored weight-based dosing regimen. Administered as two annual treatment courses to a total of 3.5 mg/kg body weight, followed by no further active treatment with MAVENCLAD® in years 3 and 4.3
• MAVENCLAD® is taken orally for a maximum of 10 days in years 1 and 2, followed by observation in years 3 and 4.
• MAVENCLAD®'s unique posology may contribute to increased patient adherence.3

TAILORED DOSING REGIMEN

Example of weight-based treatment annually for 2 years, based on average weight of 67 kg for patients seen in CLARITY (maximum 10 days in each year)

YEAR 1 – 10 DAYS OF TREATMENT

WEEK ONE

Day 1 Day 2 Day 3 Day 4 Day 5

WEEK FIVE

Day 1 Day 2 Day 3 Day 4 Day 5

YEAR 2 – 10 DAYS OF TREATMENT

WEEK ONE

Day 1 Day 2 Day 3 Day 4 Day 5

WEEK FIVE

Day 1 Day 2 Day 3 Day 4 Day 5

Safety Profile

• MAVENCLAD® has a well-characterised safety profile, with 8 years of safety registry experience and no reported cases of PML\(^1\) or risk of secondary autoimmunity, up to August 2017.1,18
• The most clinically relevant adverse reactions were lymphopenia and herpes zoster.1
• The incidence rate of herpes zoster infection was more frequent in patients treated with MAVENCLAD® vs. placebo (0.83 vs. 0.20 [per 100 patient-years, respectively]).18
• Patients generally recovered to either normal lymphocyte counts or grade 1 lymphopenia within 9 months.1
• No conclusive evidence for an increased risk of malignancies compared to a matched reference population.

REFERENCES

4 Cook S et al. AAN 2016; [P3.058].
9 Sorensen P et al. EN 2009; [P399].
10 Soelberg-Sorensen P et al. EN 2010 [P442].
15 Soelberg-Sorensen P et al. EAN 2017; [P245].
17 Freedman M et al. AAN 2016; [P3.08].
18 Cook S et al. EAN 2017; [P3.5].
19 Giovannini G et al. AAN 2016; [P2.08].
20 Montalban X et al. AAN 2016; [P3.09].
21 PREMERE Clinical Trials registry. Available at: https://clinicaltrials.gov/ct2/show/NCT03013552 (accessed February 2017)
22 Reicke P et al. ECTRIMS 2009 [P846].
24 CSS Table, Figure 4.
25 CSS Table, Figure 12.

CONTACT

Erin Marie Beals
Head of Global Communications, Neurology and Immunology Communications
ErinMarie.beals@mercksero.com

For use with Media Representatives only.

The information contained in this document is provided to media representatives reactively upon request for general background information purposes only and is not intended to be published vis-à-vis the general public. The information contained is not intended for distribution in the USA. Any medical information is not intended as a substitute for informed medical advice. Information on products and devices mentioned in this document may vary by country.