

News Release

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NICE Recommends Cladribine Tablets for Highly Active Multiple Sclerosis

- **First multiple sclerosis (MS) therapy to achieve positive NICE recommendation in the shortest possible timeframe**
- **Investigational Cladribine Tablets has shown sustained clinical efficacy up to four years with a maximum of 20 days of oral treatment over two years**

Darmstadt, Germany, November 9, 2017 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom (UK) has issued a final appraisal determination (FAD) recommending investigational Cladribine Tablets (which is marketed as MAVENCLAD® in the UK) as an option for treating highly active multiple sclerosis in adults.¹ The recommendation limits the use of Cladribine Tablets to a person who has: rapidly evolving severe relapsing–remitting multiple sclerosis, that is, at least two relapses in the previous year and at least one T1 gadolinium-enhancing¹ lesion at baseline MRI *or* relapsing–remitting multiple sclerosis that has responded inadequately to treatment with disease-modifying therapy, defined as one relapse in the previous year and MRI evidence of disease activity. This decision comes only two months after the European Commission granted marketing authorization for Cladribine Tablets in August 2017.²

“We are delighted NICE and the Appraisal Committee have reached this decision and consider this an important step in enabling rapid patient access to Cladribine Tablets in England, Wales and Northern Ireland,” says Simon Sturge, Chief Operating Officer for the biopharma business of Merck KGaA, Darmstadt, Germany. “The positive conclusion NICE has reached is testament to the value, cost-



effectiveness and innovation Cladribine Tablets brings to the multiple sclerosis treatment paradigm.”

NICE, an independent organization recognized internationally as a role model for providing evidence-based guidance on health and social care, recommended Cladribine Tablets for patients with rapidly evolving severe relapsing–remitting multiple sclerosis* or relapsing–remitting multiple sclerosis that has responded inadequately to treatment with disease-modifying therapy**. NICE recommendations about the use of new medicines, medical technologies and diagnostics identify the most clinically- and cost-effective treatments available.³

“This expedited recommendation is unprecedented in multiple sclerosis and highlights the significant value Cladribine Tablets may offer the NHS and other healthcare systems. The ease of use, low monitoring and treatment burden of this short-course oral therapy will free up much-needed resources within the NHS,” said Gavin Giovannoni, Professor of Neurology at Barts and The London School of Medicine and Dentistry, Queen Mary University of London.

The European Commission (EC) granted marketing authorization for Cladribine Tablets 10mg for the treatment of highly active relapsing multiple sclerosis* (RMS)² in the 28 countries of the European Union (EU) in addition to Norway, Liechtenstein and Iceland in August, 2017. Cladribine Tablets is the first short-course oral therapy approved that shows it provides sustained disease control for up to four years with a maximum of 20 days treatment.

Cladribine Tablets is available for prescription in Germany and the United Kingdom. Merck KGaA, Darmstadt, Germany plans additional global filings for regulatory approval of Cladribine Tablets in other countries, including the United States.

About Cladribine Tablets

Cladribine Tablets is an investigational short-course oral therapy that is thought to selectively and periodically target lymphocytes thought to be integral to the pathological process of relapsing MS (RMS). Cladribine Tablets is currently under clinical investigation and not yet approved for any use in the United States and Canada.

* at least 2 relapses in the previous year and at least 1 T1 gadolinium-enhancing lesion at baseline MRI

** defined as 1 relapse in the previous year and MRI evidence of disease activity

In August 2017, the European Commission (EC) granted marketing authorization for Cladribine Tablets, marketed as MAVENCLAD[®], for the treatment of adult patients with highly active relapsing forms of multiple sclerosis (RMS) as defined by clinical or imaging features in the 28 countries of the European Union (EU) in addition to Norway, Liechtenstein and Iceland. Cladribine Tablets is currently under clinical investigation and not yet approved for the treatment for any use in the United States or Canada.

The clinical development program for Cladribine Tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a two-year Phase III placebo-controlled study following on from the CLARITY study, designed to evaluate the safety and efficacy of Cladribine Tablets over an extended administration for four years.
- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).
- The ONWARD (Oral Cladribine Added ON To Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding Cladribine Tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.
- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis Patients Who Have Participated in Cladribine Clinical Studies) study: interim long-term follow-up data from the prospective registry, PREMIERE, to evaluate the safety and efficacy of Cladribine Tablets

The clinical development program of Cladribine in MS comprises more than 10,000 patient years of data with over 2,700 patients included in the clinical trial program, and more than 10 years of observation in some patients.

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic, inflammatory condition of the central nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. It is estimated that approximately 2.3 million people have MS worldwide. While symptoms can vary, the most common symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

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About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 billion in 66 countries. Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany, holds the global rights to the „Merck“ name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

References:

¹ National Institute for Health and Clinical Excellence (NICE). Final Appraisal Determination Cladribine Tablets for treating relapsing-remitting multiple sclerosis. 2017. Available at: <https://www.nice.org.uk/>

² MAVENCLAD[®] Summary of Product Characteristics. August 2017. Available at: <https://www.medicines.org.uk/emc/medicine/34044.2017>

³ National Institute for Health and Clinical Excellence (NICE). What we do. Available at: <https://www.nice.org.uk/about/what-we-do>