

## News Release

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### **Merck KGaA, Darmstadt, Germany, Receives Approval (Updated Registration) for Cladribine Tablets in Australia**

- **First treatment in relapsing-remitting multiple sclerosis (RRMS) to show sustained clinical efficacy for up to 4 years with a maximum of 20 days of oral treatment over 2 years**
- **Updated registration follows recent approval of Cladribine Tablets in Europe and Canada**

Darmstadt, Germany, December 7, 2017 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the Therapeutic Goods Administration (TGA) has updated the registration including the indication, dosing and safety information of MAVENCLAD® (cladribine tablets) for the treatment of relapsing-remitting multiple sclerosis (RRMS) in Australia. As a result, MAVENCLAD® is now approved in Australia for the treatment of relapsing-remitting multiple sclerosis (RRMS) to reduce the frequency of clinical relapses and to delay the progression of physical disability. Following completion of 2 treatment courses, the Product Information states that no further treatment is required in years 3 and 4. The changes bring the Product Information<sup>1</sup> in line with the latest clinical trial evidence supporting Cladribine Tablets. Cladribine Tablets is the first and only oral short-course treatment to provide efficacy across key measures of disease activity in patients with RRMS, including disability progression, annualized relapse rate and magnetic resonance imaging (MRI) activity.

“Multiple sclerosis is a debilitating disease where new treatments are needed,” said Professor Bill Carroll, Clinical Professor of Neurology at the University of Western Australia and the Perron Institute and a consultant neurologist at the Sir Charles



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Gairdner Hospital as well as President-elect of the World Federation of Neurology. "Cladribine Tablets will be a welcomed treatment option for patients with the relapsing-remitting form of MS. As an oral therapy taken in two short courses over a 2-year period, Cladribine Tablets will be convenient for all eligible patients in Australia, including those who may not live close to their treating healthcare professional."

"We are pleased the Therapeutic Goods Administration has updated the Product Information for Cladribine Tablets in Australia to reflect additional clinical data," said Simon Sturge, Chief Operating Officer at the Biopharma business of Merck KGaA, Darmstadt, Germany. "Our next step is to work closely with the Australian government to bring this treatment advance to patients as quickly as possible."

Cladribine Tablets has been subject to a comprehensive clinical development program in multiple sclerosis (MS), that includes more than 10,000 patient years of data with over 2,700 patients included in the clinical trial programs,<sup>2</sup> and up to 10 years of observation in some patients.

Cladribine Tablets is thought to work by selectively targeting B & T lymphocytes followed by a distinct pattern of lymphocyte reconstitution, without continuous suppression of the immune system. Concomitant treatment with immunosuppressive or myelosuppressive agents is contraindicated. Patients are required to have hematological monitoring prior to and during therapy. Co-administration with potent ENT1, CNT3 and ABCG2 transporter inhibitors is not recommended. MAVENCLAD® should not be used in patients who have active chronic infections (TB, hepatitis) or are immunocompromised.

This registration update for Cladribine Tablets in Australia follows the recent approval of Cladribine Tablets in Europe and in Canada. MS affects more than 23,000 Australians with most people diagnosed between the ages of 20-40<sup>3</sup>. Merck, KGaA, Darmstadt, Germany plans additional filings for regulatory approval in other countries, including the United States.

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### About Cladribine Tablets

Cladribine Tablets is an investigational short-course oral therapy that is thought to selectively 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.

In August 2017, the European Commission (EC) granted marketing authorization for Cladribine Tablets, marketed as MAVENCLAD<sup>®</sup>, 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. In December 2017, Cladribine Tablets, marketed as MAVENCLAD<sup>™</sup> was approved in Canada for relapsing-remitting multiple sclerosis (RRMS).

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 Tablets 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 (MS)

Multiple sclerosis (MS) is an autoimmune, chronic and inflammatory condition that affects the central nervous system (CNS) and is the most common, non-traumatic, disabling neurological disease in young adults. Relapsing remitting MS (RRMS) is the most common form of MS, and around 85% of people with MS are diagnosed with this type.<sup>4</sup> The exact cause of MS is unknown but it is thought that the body's immune system attacks myelin, disrupting the information flow along the nerves. There is currently no cure for MS, but treatments are available to help slow the course of the disease.

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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 KGaA, Darmstadt, Germany“ name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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<sup>1</sup> Approved MAVENCLAD<sup>®</sup> Product Information (2017)

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<sup>2</sup> Merck KGaA, Darmstadt, Germany, data on file

<sup>3</sup> <https://www.msaustralia.org.au/what-ms>