AWMSG Secretariat Assessment Report – Limited submission

Fingolimod (Gilenya®▼) 0.25 mg and 0.5 mg hard capsules

Company: Novartis Pharmaceuticals UK Ltd

Licensed indication under consideration: A single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following groups of paediatric patients aged 10–17 years:

- patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy; or
- patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Date of licence extension: 22 November 2018

Comparator(s)

The comparators included in the company's submission are:

- Natalizumab (Tysabri®)
- Alemtuzumab (Lemtrada®)
- Cladribine (Mavenclad®).

Limited submission details

The limited submission criteria were met as this is a minor licence extension for use in children and young people aged 10 years and older.

Clinical effectiveness

- Relapsing-remitting multiple sclerosis (RRMS) is the most common type of MS and is characterised by periods of stability (remission) followed by episodes of exacerbations of symptoms (relapses). The condition is very rare in children aged 14 years or younger but more common in young people aged 15–18 years.
- The disease course of MS in children is similar to that in adults, however, children with MS reach higher disability states at a significantly lower age than patients with adult-onset MS. Paediatric-onset MS can affect school performance and cognitive ability, which can have a long-term, detrimental impact on the person. Current management of RRMS aims to reduce the frequency and severity of relapses and the rate of disease progression. The Association of British Neurologists recommends starting treatment as early as possible.
- Fingolimod is the first disease modifying therapy licensed for treating RRMS in

children and young people aged 10–17 years. Currently, in Wales, RRMS in young people aged 16 to < 18 years is treated by the same disease modifying treatments that are given to adults. RRMS in younger children (< 16 years) is treated in specialist paediatric neurology clinics in consultation with adult MS specialists. AWTTC-sought clinical experts indicated that beta interferon is a first-line option with other options such as natalizumab for active disease.

- The National Institute for Health and Care Excellence (NICE) recommends fingolimod as an option to treat highly active RRMS in adults only if they have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon. The All Wales Medicines Strategy Group (AWMSG) recommends it as an option for use in highly active RRMS for adults with rapidly evolving severe (RES) RRMS.
- The company's submission includes a phase III, multicentre, double-blind, randomised control trial (PARADIGMS) in 215 patients aged 10 to < 18 years with RRMS. The study compares the efficacy of oral fingolimod versus intramuscular beta interferon for up to two years.
- The primary endpoint was the annualised relapse rate (ARR), defined as the average number of confirmed relapses per year over the treatment period. In the sub-population of patients with highly active and/or RES RRMS, the adjusted ARR was [commercial in confidence text removed] in patients treated with fingolimod [commercial in confidence data removed] compared with those treated with beta interferon [commercial in confidence data removed]. The relapse rates in fingolimod-treated children and young people [commercial in confidence text removed] with highly active RRMS and RES RRMS.
- The reported overall safety profile of fingolimod in the PARADIGMS study was similar to that seen in adults; however, more cases of seizures, anxiety, depressed mood and depression were observed in the fingolimod arm versus the beta interferon arm and caution is required in this population. Long-term safety data are limited and there are uncertainties related to the small number of patients in the clinical trial, especially those < 12 years old and < 40 kg. An open-label, five-year extension study in the paediatric RRMS population is ongoing with the aim of providing further clinical efficacy and safety data for fingolimod.
- Fingolimod is an oral treatment that can be taken at home after the first dose and may provide a more convenient treatment option than natalizumab or alemtuzumab, both of which require intravenous infusion in hospital. Fingolimod may benefit children and young people with needle phobia.

Budget impact

- The company estimates that [commercial in confidence figure removed] children and young people aged 10–17 years in Year 1 (increasing to [commercial in confidence figure removed] in Year 5) have highly active RRMS and/or RES RRMS and are eligible for treatment with fingolimod. These numbers are broadly in line with expert opinion; however, the company did not account for patients who reach the age of 18 years leaving the patient cohort therefore the increase in patient numbers may be overestimated.
- The company model assumes that in the scenario without fingolimod being approved, the patient cohort ([commercial in confidence figure removed] patients in Year 1, increasing to [commercial in confidence figure removed] in Year 5) receive treatment with either natalizumab, alemtuzumab, cladribine or fingolimod. In the scenario in which fingolimod is recommended all patients in the cohort are assumed to receive fingolimod. There is uncertainty as to whether the proportions of patients receiving these treatments reflect current practice.
- The company-estimated net medicine acquisition cost using the patient access scheme for fingolimod is a saving of [commercial in confidence figure removed]

in Year 1 increasing to a cost of [commercial in confidence figure removed] in Year 5. In the company's model, patients were considered to commence treatments in Year 1. Patients receiving alemtuzumab and cladribine only incurred medicine acquisition costs in Year 1 and Year 2, leading to higher costs in the scenario without new medicine in the first two years versus later years. The resulting budget impact versus the scenario where all the cohort received fingolimod in each of the five years was therefore cost saving in Years 1 and 2, but a net cost in subsequent years. There is some uncertainty as to whether this reflects practice in Wales.

- Net resource implications (administration and monitoring costs) were estimated to total £5,709 in Year 1 decreasing to a saving of £19,739 in Year 5.
- A sensitivity analysis assuming the cohort switch from the most costly comparator, natalizumab to fingolimod resulted in an annual saving in medicine acquisition costs of [commercial in confidence figure removed] in Year 1, increasing to [commercial in confidence figure removed] in Year 5. A sensitivity analysis in which the cohort switch from receiving no treatment to using fingolimod resulted in an annual acquisition cost of [commercial in confidence figure removed] in Year 1, increasing to [commercial in confidence figure removed] in Year 5.

Additional information

- AWTTC is of the opinion that, if recommended, fingolimod (Gilenya®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipates that fingolimod (Gilenya®) may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 24 January 2019
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Fingolimod (Gilenya®) 0.25 mg and 0.5 mg hard capsules. Reference number: 2777. May 2019.