NICE National Institute for Health and Care Excellence

NICE guidance

Cladribine for treating active relapsing forms of multiple sclerosis

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Cladribine is recommended as an option for treating active relapsing forms of multiple sclerosis in adults, only:

- if they have active relapsing–remitting multiple sclerosis, and
- when high-efficacy disease-modifying therapies would be offered.

1.2 This recommendation is not intended to affect treatment with cladribine that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

Why the committee made these recommendations

This technology appraisal evaluates cladribine only for active relapsing–remitting multiple sclerosis. This does not include everyone it is licensed for.

High-efficacy disease-modifying therapies for active relapsing–remitting multiple sclerosis include ocrelizumab and ofatumumab. The aim of treatment is to reduce the number of relapses, slow the progression of disability, and maintain or improve quality of life.

Clinical trial evidence shows that cladribine reduces relapses and increases the time until disability progresses compared with placebo. Indirect comparisons suggest that the relapse rate with cladribine is similar to that of ocrelizumab and ofatumumab.

When compared with ocrelizumab and ofatumumab, the most likely cost-effectiveness estimate for cladribine is within the range that NICE considers an acceptable use of NHS resources. So, cladribine is recommended for people with active relapsing–remitting multiple sclerosis when high-efficacy disease-modifying therapies would be offered.

2 Information about cladribine

Marketing authorisation indication

2.1 Cladribine (Mavenclad, Merck Serono) is indicated for 'the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease as defined by clinical or imaging features'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for cladribine.

Price

2.3 The list price is £2,047.24 per 10 mg tablet (excluding VAT, BNF online, November 2024). Costs may vary in different settings because of negotiated procurement discounts.

3 Committee discussion

The evaluation committee considered evidence submitted by Merck Serono, a review of this submission by the external assessment group (EAG) and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Clinical need

3.1 Multiple sclerosis (MS) is a chronic, lifelong condition for which there is no cure. It causes progressive, irreversible disability, and many symptoms including pain, chronic fatigue, unsteady gait, muscle loss, speech problems, incontinence, visual disturbance and cognitive impairment. Most people have the relapsing–remitting (RR) form of MS, which is characterised by periods of new or worsened symptoms. RRMS breaks down further into active, highly active and rapidly evolving severe forms. Over time, RRMS will progress to secondary progressive MS for most people, which is characterised by progressive disability. For this technology appraisal, the committee evaluated cladribine only for people with active RRMS. This is because cladribine has already been evaluated for the highly active and rapidly evolving severe MS populations, and evidence for the secondary progressive MS population was not presented. The patient experts highlighted that RRMS is complex and unpredictable, and affects all aspects of life. They also explained that people with the condition have to plan extensively around their treatments. During the early stages of MS, people may find it difficult to care for their dependants or sustain their existing careers. In the later stages, they often need help from carers because of their accumulated disability. As MS progresses, it can worsen the quality of life for people with the condition and for their carers. The committee concluded that MS can have a substantial impact on quality of life.

Benefits of cladribine

3.2 Because MS is typically diagnosed when people are of child-bearing age, the patient experts highlighted the significance of a treatment, like cladribine, that may have fewer restrictions for family planning. They also highlighted that the low treatment administration and monitoring burden of cladribine offers particular benefit to people who:

- live far from specialist centres
- have insecure housing or are experiencing homelessness
- otherwise find it difficult to travel for treatment.

The committee heard that an oral treatment taken in 2 short courses over 2 years would be less disruptive than some available treatments. The company and clinical experts highlighted the long-acting effect of cladribine, which can delay relapses and the need for subsequent disease-modifying therapies (DMTs). The committee concluded that cladribine's dosing schedule has benefits compared with existing treatment options. It will consider these benefits, especially for people who would find it hard to travel for treatment, in its decision making.

Treatment pathway

Clinical management

3.3 In the NHS, DMTs are used to treat RRMS. The aim of treatment is to reduce the number of relapses, slow the progression of disability, and maintain or improve quality of life. The choice of therapy partly depends on the number of relapses and evidence of disease activity, as defined in each treatment's marketing authorisation. People are involved in shared decision making to discuss appropriate treatments to suit their lifestyles (such as, in terms of employment or family planning). The clinical experts explained that the NHS treatment algorithm for multiple sclerosis disease-modifying therapies informs prescribing decisions. As a treatment is found to be ineffective for someone, or relapse or disease

progression occurs, they may switch to an alternative treatment. Non-pharmacological treatments, such as physiotherapy and occupational therapy, are also used to manage the condition. The committee concluded that cladribine would be a welcome additional treatment option for people with MS.

Comparators

3.4 For people with active RRMS, the company submission compared cladribine with beta interferons, dimethyl fumarate, diroximel fumarate, glatiramer acetate, ocrelizumab, ofatumumab, ponesimod and teriflunomide. The clinical experts explained that ocrelizumab and ofatumumab are considered high-efficacy DMTs, and that these were the most relevant comparators for cladribine. While ponesimod is also considered high efficacy, they explained that it is less effective than ocrelizumab and ofatumumab, so it is rarely started in NHS practice. They noted that prescribing varies, with input from healthcare professionals and people with MS, to suit the needs and preferences of individuals. They added that, in NHS clinical practice:

- ocrelizumab and ofatumumab are the most commonly prescribed treatments for active RRMS
- ponesimod, dimethyl fumarate and diroximel fumarate may be used because they are taken orally
- glatiramer acetate and beta interferons are not routinely prescribed.

Consultation responses from the company and clinical consultees indicated that the oral DMTs are much less commonly prescribed. So, the committee concluded that the most appropriate comparators for cladribine were ocrelizumab and ofatumumab.

Clinical evidence

Clinical-effectiveness data sources

3.5 The main clinical evidence for cladribine was from the CLARITY and CLARITY-EXT trials. CLARITY was a randomised double-blind study of 1,326 people with active and highly active RRMS. It compared 3.5 mg/kg and 5.25 mg/kg doses of cladribine with placebo. The lower dose of 3.5 mg/kg was used in the company submission. The primary outcome was qualifying annualised relapse rate (ARR). Other clinical outcomes included the proportion of people who were relapse free, time to 3-month confirmed disability progression (CDP) and time to first qualifying relapse. Time to 6-month CDP was a post-hoc outcome. CLARITY-EXT was a 2-year extension study of CLARITY, in which the primary outcomes were safety and tolerability. Other secondary outcomes in CLARITY-EXT included qualifying ARR, time to first and second relapse, and time to 3-month CDP. The committee concluded that CLARITY and CLARITY-EXT were generalisable to the NHS.

Clinical effectiveness

3.6 Data from CLARITY showed a statistically significant 58% reduction in ARR with 3.5 mg/kg cladribine tablets at 96 weeks compared with placebo (0.14 compared with 0.34; $p<0.0001$). There was also a statistically significant delay in the time to first qualifying relapse with 3.5 mg/kg cladribine tablets compared with placebo (hazard ratio 0.45, 95% confidence interval 0.34 to 0.58; $p<0.0001$). Also, the results showed that statistically significantly fewer people had 3-month CDP and statistically significantly more people remained relapse free at 96 weeks with 3.5 mg/kg cladribine tablets compared with placebo. The clinical experts found it hard to draw direct comparisons between treatments because of the lack of head-to-head trials with cladribine. But they said that in their experience cladribine offers sustained remission from symptoms for some people with highly active RRMS who take it. Their experience in clinical practice aligns with cladribine being an effective DMT with a good safety and tolerability profile. The patient experts described cladribine as being considerably easier for them to take and adhere to than other treatments. They added that it substantially

improves quality of life because it helps them:

- avoid lengthy travel to appointments, which risks flareups
- remain in work
- better plan a family.

The committee concluded that cladribine leads to longer delays in time to qualifying relapse and a reduction in ARRs compared with placebo.

Network meta-analysis

3.7 Because there was no head-to-head evidence comparing cladribine with relevant comparators in the RRMS population, a network meta-analysis (NMA) was done for each outcome of interest for the whole RRMS population. The NMAs included 38 trials from between 1987 and 2022 and compared outcomes across cladribine and the comparator treatments in active RRMS. The company's NMAs were similar to NMAs done for previous NICE technology appraisals of treatment for RRMS, and produced comparable estimates to recent NICE technology appraisals in RRMS. Several randomised controlled trials contributed to the NMAs for each of the ARR (37 studies), 3-month CDP (15), 6-month CDP (17) and treatment discontinuation (25) sets of outcomes. The results were:

- There was a statistically significantly lower ARR with cladribine than with beta interferons, glatiramer acetate, placebo and teriflunomide. There was no statistically significant difference in ARR between cladribine and ocrelizumab, ofatumumab, dimethyl fumarate and ponesimod.
- There was a statistically significantly lower CDP with cladribine than with placebo. There were no statistically significant differences in CPD between cladribine and other DMTs.
- There was a statistically significantly lower probability of people stopping treatment with cladribine compared with interferon beta-1a (44 microgram). There were no statistically significant differences in treatment discontinuation between cladribine and the other DMTs.

The company acknowledged that differences between study characteristics (diagnostic criteria, study phase, blinding), populations (disease duration, treatment history) and outcomes definitions contributed to greater uncertainty in the results. This then challenged the reliability of NMA estimates. The EAG explained that these differences were a limitation. It thought that this uncertainty likely could not be overcome and advised interpreting the NMA results with caution. The company tried to address these differences by showing that baseline risk-adjusted NMAs had similar results. At the second committee meeting, the company presented baseline risk-adjusted NMAs for ARR, CDP and treatment discontinuation. The EAG explained that, compared with the unadjusted NMAs, the baseline risk-adjusted NMAs relied more on imputed data across outcomes. This was because several studies in each network lacked placebo arms, which led to a worse model fit. The committee preferred the better-fitting unadjusted NMAs. It acknowledged the uncertainty in the NMA results, noting that they were for the whole RRMS population, but concluded that the company's unadjusted NMAs were sufficient for decision making.

Economic model

The company's model structure

3.8 The company's model was a Markov transition model consisting of 11 health states (10 Expanded Disability Status Scale [EDSS] states for relapsing forms of MS, and death). The EAG agreed with the company's preference for an 11-state model not including secondary progressive MS and simpler than models previously used in RRMS NICE technology appraisals. There were 2 key features to the model:

- a natural history reference model that modelled the baseline transitions of people with MS who have not had treatment
- a treatment-adjusted model that incorporated treatment effects for cladribine and all comparators from the company's NMAs.

The treatment effects were applied to adjust progression through each of the

EDSS states using confirmed disability accumulation at 6 months. Relapses were modelled independently using ARR ratios from the NMAs. The committee noted that concerns have been raised about many of the assumptions made in the models used in previous NICE technology appraisals, including:

- the lack of treatment switching or sequencing
- the validity of the fixed waning assumptions
- the relevance of the source of mortality data to NHS clinical practice.

The committee concluded that the model structure and inputs broadly aligned with models used in previous technology appraisals on treatments for MS. But it thought that the model had considerable structural uncertainty.

Implementing subsequent treatments

3.9 Initially, in the company's model, it was assumed that people who stopped taking DMTs moved to the best supportive care arm. But, in the NHS, people who stop taking a DMT typically switch to an alternative DMT. The committee noted that the lack of treatment switching was an oversimplification that does not reflect NHS practice and that this was a structural uncertainty. In response to the draft guidance consultation, the company addressed the structural concerns. It did this by adding subsequent treatment scenarios in which a 'basket' of treatments could be applied, in place of best supportive care, when the initial treatment was stopped. The company acknowledged that the basket approach was a simplified approach to representing subsequent treatments. But it added that it effectively showed comparative benefits of treatments for active RRMS given the constraints of the model. The EAG supported using the basket approach while noting limitations, such as:

- side-effect profiles of basket treatments not being accounted for
- comparator treatments being their own subsequent treatments but not for cladribine
- treatment waning assumed to be the same as in first-line treatment.

The committee welcomed the basket adaptation to the model. The basket approach did not fully capture the complexity of MS treatment in the NHS. But it did represent an improvement on the single-treatment structure, and the cost-effectiveness estimates from scenarios reduced some of the uncertainty. Two basket options were provided. The first basket included the high-efficacy DMTs ocrelizumab, ofatumumab and ponesimod (weighted by market share). The second basket scenario included a weighted average of costs and benefits from dimethyl fumarate, diroximel fumarate, ocrelizumab, ofatumumab, ponesimod and teriflunomide. Clinical expert opinion was that basket 1 (high-efficacy DMTs only) was more representative of the NHS. The committee concluded that the scenario using basket 1 at second line, after either cladribine or its comparators, was helpful for decision making.

Source of natural history data

3.10 The model used the British Columbia Multiple Sclerosis (BCMS) registry (used in previous NICE technology appraisals for MS) as a source of natural history data. The clinical experts explained that the BCMS registry data may not be representative of the MS population in the NHS especially for people whose RRMS is considered active and not highly active. In recent decades, treatment and care for MS has improved prognosis, so progression to more significant disability (higher EDSS states) is less common and slower. The committee recalled that the BCMS registry data for disability progression was collected between 1980 and 1995. The committee noted its disappointment that the continued reliance on an untreated population (and historic data sources) was a feature of the model structure. Alternative models used internationally (such as, by The Netherlands' National Health Care Institute) have overcome this issue. Also, it thought that the modelling of EDSS state transitions was implausible because of the high proportion of people in higher EDSS states. The clinical experts added that mortality events are less common than in the BCMS registry data. They also said that people with MS today have a mortality profile that is much closer to that of the general population than that of historical MS populations. People with MS often die of causes not related to MS. After the first committee meeting, the committee asked the company to use more recent data, such as from the UK MS Register, or to validate that the BCMS registry data:

- represents the active MS population in the NHS
- does not include data of people with highly active RRMS at baseline.

The company reviewed alternative data sources for the untreated MS population. Studies indicated that the disability progression of the untreated MS population has not changed substantially over time. They also showed that the BCMS registry data has a comparable disability progression trajectory to the more recent UK-based University of Wales Multiple Sclerosis database. The company was unable to request and access UK MS Register data in time for the second committee meeting. The committee welcomed the additional BCMS registry data validation. But it was disappointed to not have analysis using the more recent UK MS Register data, and was concerned that the transitions to higher EDSS states for the active RRMS population seemed high. The company provided health-state occupation graphs that showed how quickly people progressed in the model. It also provided additional scenario analyses to evaluate the BCMS data with slower disability progression scenarios. The EAG could not find further appropriate data sources and agreed with the company's justifications for continued use of the BCMS registry data. It could not apply the slower progression to its preferred assumptions. The committee concluded that it would have preferred more recent datasets, such as the UK MS Register, for the untreated population. But it added that it would, in this instance, accept the use of BCMS registry data for decision making. It welcomed the use of alternative MS models that are not reliant on historic data for an untreated population.

Treatment discontinuation probabilities

3.11 In the treatment-adjusted model, annualised probabilities represented the chance of stopping individual treatments. In the company's initial base case, annualised treatment discontinuation probabilities were derived from the NMA for comparators and from CLARITY for cladribine. Treatment discontinuation probabilities varied for 0 to 1 years, 2 to 9 years, and 10 years and over. Because cladribine was administered in years 1 and 2, the only discontinuation modelled by the company for cladribine was between those years. The EAG thought that

real-world evidence would be more generalisable to the NHS than an NMA of randomised controlled trials. Also, the EAG used a broader definition of treatment discontinuation, which considered overall treatment persistence. The EAG assumed that people stop treatment if they take a different DMT. So, if someone had 2 years of cladribine, then started taking a different treatment, this counted as cladribine discontinuation in the EAG's model, but not in the company's model. The EAG said treatment discontinuation had been underestimated for cladribine because people may switch to another DMT. But as it was modelled, the benefits would still be accrued for cladribine. The clinical experts thought that the EAG's treatment discontinuation probabilities were an overestimate, and the company's probabilities were an underestimate. They thought that the treatment waning aspect of the modelling, which captured a decline in the treatment effect over time, was confounding. This was because people within their care would have a DMT for as long as it worked and then switch to another treatment. People would not stay on a partially effective treatment. The company and EAG were aligned on applying treatment waning. The clinical experts acknowledged that some people continue to get the full treatment benefit of the drug over a long time period. But added that other people experience progression or relapse.

The committee agreed that switching to another treatment should be considered cladribine discontinuation and preferred treatment discontinuation estimates from the company's NMA. It recommended using time to next treatment data from the long-term CLASSIC-MS study, which has over 10 years of follow-up data, to model treatment discontinuation for cladribine and any comparators when applicable. In response to the draft guidance consultation, the company used CLASSIC-MS for cladribine and the estimates from its NMA for comparators' treatment discontinuation. The EAG supported adopting CLASSIC-MS data because of its long-term follow up and used it for cladribine treatment discontinuation. But the EAG chose to apply the relative effects from the company's NMA to the newly adopted CLASSIC-MS estimate for cladribine discontinuation. It stated that applying the NMA hazard ratios of comparators to the CLASSIC-MS value for cladribine ensures internal consistency. The committee concluded that it preferred the EAG's new approach to modelling treatment discontinuation probabilities for cladribine and comparator DMTs.

Mortality rates

3.12 In the company's initial base case, the same mortality rate was applied to people with MS, regardless of their level of disability (EDSS status). A scenario explored EDSS-specific mortality rates using Pokorski (1997). Pokorski relied on earlier analysis of Canadian data collected up to 1985. The EAG preferred to use mortality rates that differed by EDSS state. The clinical experts explained that, with new treatments and improved care, mortality rates for people with MS have improved in recent years. They said people with MS now rarely die from MS. The committee concluded that people in higher EDSS states have a higher mortality risk than people in lower states. So, mortality rates should have varied by EDSS state. The committee was concerned that the current natural history model, which overpredicted occupation of the high EDSS states over time, would overpredict mortality using variable mortality rates. It requested graphs of health-state occupation to understand and appraise the model transitions. In response to the draft guidance consultation, the company adopted the committee's preferred source, Harding et al. (2018), and applied EDSS-specific mortality rates. The company's new base case used Harding mortality rates for EDSS 4 to 9, and continued to use Pokorski for EDSS 0 to 3 because these were not reported in Harding. Scenarios were provided with Pokorski only and a more recent study from Iceland, Eliasdottir et al. (2023).The clinical experts were concerned that the Harding et al. mortality ratio in EDSS 9 seemed very high and in EDSS 4 to 6 was slightly too high. The committee welcomed the more recent studies. But it was concerned that Eliasdottir et al. referred to EDSS state at study baseline, which risked double counting progression and mortality. Although the committee was aware of the experts' reservations, it concluded that the standardised mortality ratios (SMR) from Harding et al. were the most relevant for the model structure. It noted that the apparently high SMR for people with EDSS 9 would apply to a small proportion of people with MS in the NHS. Also, high SMRs are expected when a condition is associated with significant mortality and, at the same time, people of the same age and sex in the general population experience a very low mortality rate. The committee concluded that Harding et al. would improve generalisability of the model outputs to the NHS population. It reflected that some of the mortality rates concerns stemmed from model transitions driven by the natural history data and that alternative model structures may present fewer challenges.

Self-injection training for comparator treatments

3.13 The company's base case included 3 hours of nurse time to teach people to inject themselves with injectable DMTs. The EAG said that this training is typically provided by company-sponsored nurses, so is not a cost to the NHS. The clinical experts confirmed that training was provided by company-sponsored nurses for ofatumumab but that companies did not provide training for older treatments (such as beta interferons) because people do not often start treatment with these anymore. Also, the support provided by company-funded nurses may stop in the future. The committee concluded that the model should have reflected current practice. So, the cost of injection device training for patients should not have been included. This was subsequently implemented in the model after draft guidance consultation.

Cladribine monitoring costs

3.14 The company's initial base case included lower monitoring costs for people taking cladribine than did the EAG base case. It included 1 MRI scan in the first year of treatment and 0 MRI scans in the second year of treatment. The EAG's base case included 1 MRI scan in both the first and second years of treatment. Also, the company's base case included 1 neurology appointment in the second year of treatment, while the EAGs base case included 2 appointments. The clinical experts said that people would typically have 1 MRI scan during the first 2 years of cladribine treatment (typically in the second year rather than the first year). They also said that people would have 1 neurology appointment each year. The committee preferred the company's approach of including 1 MRI scan and 2 neurology appointments in total for the 2-year period of active cladribine treatment. In response to the draft guidance consultation, the company updated its base case to incorporate this preference.

Monitoring costs for glatiramer acetate and beta interferons

3.15 The company's base case included higher monitoring costs for people taking glatiramer acetate and beta interferons in the first year of treatment than the EAG's base case. The company's model included 2 neurology appointments, and

the EAG's base case included 0 appointments. The clinical experts said that people would typically have 1 appointment in the first year when taking a DMT. The committee concluded that 1 neurology appointment should be included in the model. But glatiramer acetate and beta interferons were not thought to be relevant comparators, so were not included after the draft guidance consultation.

Cost effectiveness

The committee's preferred cost-effectiveness assumptions

3.16 The committee's preferred assumptions for the cost-effectiveness modelling of cladribine for active RRMS were to:

- use the EAG's assumption for basket 1 (high-efficacy DMTs) to model second-line treatment (see section 3.9)
- include the waning assumption agreed by the company and EAG (see section 3.11)
- use the EAG's treatment discontinuation probabilities assumption, using CLASSIC-MS for cladribine and hazard ratios from the company's NMA indexed on the CLASSIC-MS cladribine value to derive comparator treatment discontinuation probabilities (see section 3.11)
- use the EDSS-specific mortality rate assumption agreed by the company and EAG, using Pokorski (1997) for EDSS 0 to 3 and Harding et al. (2018) for EDSS 4 to 9 (see section 3.12)
- use the EAG's assumption to exclude nurse-led self-administration costs for injectables because the analysis should reflect NHS clinical practice (see section 3.13)
- use 1 MRI scan and 2 neurology appointments across the first 2 years of cladribine to capture accurate monitoring costs in line with NHS clinical practice (see section 3.14)
- remove beta interferons, dimethyl fumarate, diroximel fumarate, glatiramer acetate, ponesimod and teriflunomide as comparators (see section 3.4 and

section 3.15).

Equality

3.17 The committee heard that MS disproportionately affects women more than men. Also, it is diagnosed in younger people. The committee noted that the issue of different disease prevalence cannot be addressed in a technology appraisal. The committee also noted that MS has significant lifelong effects on family planning, employment and financial decision making. The burden of some treatments can be challenging for some, for example:

- people who have insecure housing or are experiencing homelessness
- members of the travelling community
- people who find travel more difficult such as people with lower incomes or disabled people.

The committee considered the benefits of cladribine, that is the low treatment administration and monitoring burden for these population groups and communities, in its decision making.

Assessment of cost effectiveness

3.18 The committee decided that the relevant comparators for cladribine in the active RRMS population were ocrelizumab and ofatumumab. After the draft guidance consultation, the EAG's revised base case, which used the committee's preferred assumptions (see section 3.16) and the costs relevant to the NHS, showed that cladribine was an effective use of NHS resources compared with each of ocrelizumab and ofatumumab. Cladribine produced fewer quality-adjusted life years than either of these treatments and was cost saving, so cladribine was cost-effective in the South-West quadrant of the cost-effectiveness plane.

Conclusion

Recommendation

3.19 The committee concluded that the modelling was not ideal for the complexities of active RRMS in the NHS, but it was able to come to a decision. It concluded, that cladribine was a cost-effective treatment and recommended it for people with active RRMS who would be offered high-efficacy DMTs. If the reason for not offering someone with active RRMS high-efficacy DMTs is because they aim to become pregnant, cladribine can still be offered.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has an active relapsing form of multiple sclerosis and the healthcare professional responsible for their care thinks that cladribine is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Dr Charles Crawley
Chair, technology appraisal committee B

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Alexandra Sampson and Sammy Shaw
Technical leads

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