Plegidry for the treatment of RRMS in adults

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As a first-line treatment in the management of RRMS, Plegidry offers the convenience of a reduced injection schedule and more flexibility overall.

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The latest NICE guidance on the management of relapsing-remitting multiple sclerosis (RRMS) does not include the use of disease-modifying drugs, which are the subject of several technology appraisals. NICE’s 2002 appraisal of interferon beta proposed one of the first risk-sharing strategies to be agreed by the NHS as the only means by which this treatment could meet its value for money threshold.

There is no single treatment pathway for the initial treatment of RRMS. In 2009, the Association of British Neurologists recommended interferon beta or glatiramer acetate as first-line therapy for RRMS that is not rapidly evolving. In practice, clinicians and patients agree on the choice of first-line therapy – interferon beta or glatiramer acetate (Copaxone) by injection, or teriflunomide (Aubagio) orally or alemtuzumab (Lemtrada) by intravenous infusion – based on route of administration, adverse effects and storage requirements.

Four brands of interferon beta are licensed for the treatment of RRMS. Interferon beta-1a is available as Avonex and Rebif in prefilled pens; Avonex is administered once weekly by intramuscular injection and Rebif three times weekly subcutaneously. Interferon beta-1b is available as Betaferon and Bextavia, both of which are supplied as powder and solvent for reconstitution and injected subcutaneously on alternate days.

The addition of polyethylene glycol to the interferon beta-1a molecule (pegylation) doubles its half-life to approximately 78 hours, allowing a longer dose interval. Peginterferon beta-1a is licensed for the treatment of adults with RRMS and supplied as a single-use prefilled pen containing 125µg in 0.5ml. Treatment is initiated with a dose of 63µg followed by 94µg at two weeks, then 125µg at four weeks and every two weeks thereafter.

There is little clinical experience in elderly people or patients with hepatic impairment; no dose adjustment is recommended in patients with renal impairment. The pen should be stored in a fridge and warmed for 30 minutes before use.

Clinical trial

Peginterferon beta-1a was evaluated in the double-blind ADVANCE trial, in which 1512 adults with RRMS (mean age 37) were randomised to treatment given every two or (not reported here) every four weeks or to placebo. Patients had mild to moderate neurological impairment (mean Expanded Disease Severity Scale score, EDSS, 2.46), with a mean number of relapses in the previous year of 1.5. Eighty-three per cent of patients had not
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It is a refashioned interferon beta-1a, differing from the existing interferons in its injection schedule; requiring only fortnightly injections as opposed to weekly (Avonex) or three times a week (Rebif), and dosage; 125µg in Plegridy versus 30µg in Avonex and 44µg in Rebif. The reduced injection frequency is its main benefit and will improve patient adherence to treatment, making it possible to achieve the expected therapeutic outcome.

The efficacy data from the first year of the ADVANCE trial (Plegridy every two weeks or four weeks versus placebo), indicates that it is similar to that of existing interferons in both relapse reduction and disability progression.1 Plegridy showed a 35.6 per cent reduction in annualised relapse rate in the two-week dosing group, and 27.5 per cent in the four-week dosing group compared to placebo. The risk of progression (confirmed over 12 weeks) was reduced by 38 per cent in both groups.

Beyond one year, results from the trial show that initial treatment efficacy of Plegridy was maintained, but with greater efficacy observed in the every two weeks injection group compared to every four weeks injection group.2 The tolerability of Plegridy is similar to that of beta interferon-1a, side-effects such as injection site reactions, flu-like symptoms and headaches were the most frequently reported in the clinical trial.

Overall, Plegridy has its place as a first-line treatment in the management of RRMS, particularly in those with low to moderate disease activity, where the benefits of Plegridy outweigh the risks. For those already on interferon therapy, the convenience of a reduced injection schedule offers more flexibility overall.

References

Declaration of interests
None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

Place in therapy
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Ten per cent of placebo recipients did not complete one year’s treatment, half due to adverse events. Fourteen per cent of patients discontinued peginterferon beta-1a, of which adverse events accounted for 32 per cent.

At 48 weeks, the adjusted annualised relapse rate was significantly lower with peginterferon beta-1a than placebo (0.256 vs 0.397), equivalent to a 39 per cent reduction in the risk of relapse. Peginterferon beta-1a was associated with a significantly lower incidence of new or newly enlarging T2 hyperintense lesions compared with placebo and significantly reduced the mean number of Gd-enhancing lesions and new hypointense T1 lesions. It also reduced the risk of disability progression over one year by 38 per cent. The reductions in annualised relapse rate and disability progression were maintained during the second year of treatment (see Figure 1).

Adverse effects
The incidence of treatment-related adverse events was 53 per cent with placebo and 90 per cent with peginterferon beta-1a, with severe events reported by 11 and 18 per cent respectively. The most frequent events reported with active treatment were injection site reactions, flu-like symptoms, pyrexia, headache and myalgia.

References
1. NICE CG186. October 2014.

Declaration of interests
None to declare.

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Figure 1. Time to first confirmed relapse over two years