## Version History

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<th>Policy Title</th>
<th>Drugs for MS. Drug facts box – Interferon beta 1b for secondary progressive MS (SPMS)</th>
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<td><strong>Version</strong></td>
<td>1.0</td>
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<tr>
<td><strong>Author</strong></td>
<td>West Midlands Commissioning Support Unit</td>
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<tr>
<td><strong>Publication Date</strong></td>
<td>Jan 2013</td>
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<td><strong>Review Date</strong></td>
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<tr>
<td><strong>Supersedes/New</strong></td>
<td>(Further fields as required by local organisations)</td>
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## Previous Versions

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Drugs for multiple sclerosis

Summaries of key information and evidence for efficacy and safety

January 2013

Drug Facts Box for Interferon beta 1b for secondary progressive MS (SPMS)

<table>
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<th>What is this drug for?¹,²</th>
<th>To reduce the progression of MS</th>
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<tr>
<td>Who is this drug for?¹,²</td>
<td>Interferon beta-1b (Betaferon, Extavia): Adults with a single demyelinating event with an active inflammatory process; adults with relapsing-remitting MS; adults with secondary progressive MS with active disease</td>
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</table>
| Who should not be taking this drug?¹,² | Patients under age 12
Pregnant women
Patients with a history of sensitivity to interferon beta, human albumin or any excipients |
| How is this drug administered?¹,² | By subcutaneous injection |
| What dose of this drug is administered?¹,² | 250 µg |
| How often is this drug administered?¹,² | Every other day |
| What is the cost of this drug? | Betaferon: £39.78 for one 300-µg vial
Extavia: £39.78 for one 300-µg vial |
| What are the adverse reactions associated with this drug? | Most common: injection-site reactions, infection, influenza-like symptoms |
| Licensing timeline | Launched in UK in 1995 (Betaferon) and 2008 (Extavia) |

Other information:

Treatment with interferon beta should be initiated by a physician experienced in the treatment of MS.¹,²

NICE has published a Technology Appraisal (TA32, 2002)³ advising that a recommendation to use glatiramer acetate and beta interferon could not be justified, based on benefits and costs at the time. However, patients on treatment with these drugs at the time of publication of the TA had the option to continue until they and their consultant considered it appropriate to stop.

In 2002, the NHS entered into a risk-sharing arrangement with manufacturers that enabled both glatiramer acetate and interferon beta to be available to all patients with relapsing-remitting MS, and those with secondary progressive MS in which relapses are the dominant clinical feature, who meet criteria developed by the Association of British Neurologists.⁴

Studies

Summary of methods

Two multicentre, double-blind RCTs compared the efficacy and safety of interferon beta-1b 250 µg SC every other day with placebo for the treatment of secondary progressing MS (n = 718 and 939).⁵,⁶ (One trial also included a group given 160/µm².) The planned duration of the trials was three years, but both were terminated after a planned interim analysis after at least two years. The primary clinical outcome measures were the time to confirmed progression to disability in one trial and the probability of progression to disability by study endpoint in the other trial. Secondary endpoints included the proportion of patients with confirmed progression and the change in a disability score.
Quality of the trials
The design of the trials was fairly good, being double-blind, randomised and controlled and having a Jadad score of 3. Both trials were sponsored by the manufacturer.

Main results
In one trial, interferon beta-1b was significantly more effective in delaying progression of disability by all outcome measures. In the other study, there was no significant effect of interferon beta-1b on any of the outcomes related to progression of disease, although a significant effect on relapse rate was found with the higher dose of interferon compared with placebo. A combined analysis suggested that differences in criteria for disease progression and baseline disease activity might account for the differences in results between the two studies.

Adverse events
The most common adverse events seen with interferon beta-1b were injection-site reactions and influenza-like symptoms.

References


Table 1. Interferons beta-1a and -1b for SPMS in RCTs using clinical endpoints: study design and results

| Study                                | Inclusion criteria                                                                                                                                                                                                 | Exclusion criteria                                                                                                                                                                                                 | Treatment arms (n)                                                                                                                                                                                                 | Main outcomes (interferon vs. placebo)                                                                                                                                                                                                 |
|--------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| European SG (ESG, 1998)\(^5\)        | • Aged 18 to 55  
• Clinically definite MS  
• Period of deterioration sustained for ≥ 6 months  
• EDSS score 1 to 3.5  
• ≥ 2 relapses or ≥1.0 point increase in EDSS in prior 2 years                                                                                                        | • Prior treatment with interferon or other immunomodulatory treatment                                                                                                                                                                                           | Interferon beta-1b 8 million IU (360)  
Placebo (358)  
Dose titration: 4 million IU for first 2 weeks  
Duration of study: at least 2 years for interim analysis                                                                                         | • Time to confirmed progression of disability (EDSS): 644\(^*\) vs. 403 days  
• Probability of progression with interferon vs. placebo at 3 years: OR 0.63 [95% CI 0.46 to 0.85]  
• Proportion of patients with confirmed progression: 38.9\(^*\)\(^*\) vs. 49.7%  
• Odds of becoming wheelchair-bound: 0.66 [0.47 to 0.93]  
• EDSS at endpoint: 5.57 vs. 5.84 ns  
• Mean annual relapse rate: 0.44\(^*\)\(^*\) vs. 0.64  
• The most common adverse events with interferon beta 1b included injection-site reactions, flu-like symptoms, hypertonia and hypertension |
| North American SG (NASG, 2004)\(^6\)  | • Aged 18 to 65  
• Clinically definite relapsing-remitting MS  
• EDSS score ≤ 3.0 to 6.5  
• ≥ 2 relapses in prior year                                                                                                                               | • Prior treatment with interferon or other immunomodulatory treatment except corticosteroids                                                                                                              | Interferon beta-1b 250 µg (317)  
Interferon beta-1b 160 µg/m² (314)  
Placebo (308)  
Duration of study: 3                                                                                                                                       | • Time to confirmed progression of disability: ns  
• Proportion of patients with confirmed progression: ns  
• Change in mean EDSS score: ns |
| reported Intention-to-treat analysis | 2 years | years (early termination after interim analysis) | • Mean annual relapse rate: 43% lower with interferon beta-1b

The most common adverse events with interferon beta 1b included injection-site reactions and flu-like symptoms |

MS, multiple sclerosis; RCT, randomised controlled trial; RFSS, Regional Function System Score; IM, intramuscular; SC, subcutaneous; OR, odds ratio

* p < 0.05, ** p < 0.01, *** p < 0.001 vs. placebo; ns, not significant; CI, confidence interval