### Version History

<table>
<thead>
<tr>
<th>Policy Title</th>
<th>Drugs for MS.Drug facts box – Glatiramer Acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version</td>
<td>1.0</td>
</tr>
<tr>
<td>Author</td>
<td>West Midlands Commissioning Support Unit</td>
</tr>
<tr>
<td>Publication Date</td>
<td>Jan 2013</td>
</tr>
<tr>
<td>Supersedes/New</td>
<td>(Further fields as required by local organisations)</td>
</tr>
</tbody>
</table>

### Previous Versions

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Drugs for multiple sclerosis

Summaries of key information and evidence for efficacy and safety

January 2013

Drug Facts Box for Glatiramer Acetate

<table>
<thead>
<tr>
<th>What is this drug for?</th>
<th>To reduce the development of clinically definite MS and the relapse rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who is this drug for?</td>
<td>Adults who have experienced a well-defined first clinical episode and are at high risk of developing clinically definite MS Ambulatory adults with relapsing-remitting MS</td>
</tr>
<tr>
<td>Who should not be taking this drug?</td>
<td>Patients under age 12 Pregnant women</td>
</tr>
<tr>
<td>How is this drug administered?</td>
<td>By subcutaneous injection</td>
</tr>
<tr>
<td>What dose of this drug is administered?</td>
<td>20 mg</td>
</tr>
<tr>
<td>How often is this drug administered?</td>
<td>Once daily</td>
</tr>
<tr>
<td>What is the cost of this drug?</td>
<td>One pack of 28 prefilled syringes each containing 20 mg in 1 ml solution (one dose) costs £513.95.</td>
</tr>
<tr>
<td>What are the adverse reactions associated with this drug?</td>
<td>Most common: injection-site reactions, infection, influenza, anxiety, depression, headache, vasodilatation, dyspnoea, nausea, rash, arthralgia, back pain</td>
</tr>
<tr>
<td>Licensing timeline</td>
<td>Launched in the UK in April 2003</td>
</tr>
</tbody>
</table>

**Other information:** Initiation of treatment with glatiramer should be supervised by a neurologist or a physician experienced in the treatment of MS.

NICE has published a Technology Appraisal (TA32, 2002) 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.

**Studies**

**Summary of methods**

Each of the two licensed indications is supported by one multicentre, double-blind, randomised, placebo-controlled trial: the PreCISe trial in patients with a clinically isolated syndrome (duration nine months, n = 481) to assess the effect on subsequent definite MS, and another trial in patients with relapsing-remitting MS (duration two years, n = 251). The second trial was extended for a further one to 11 months. The primary outcomes were the time to clinically definite MS (first trial) and the relapse rate (second trial). The review supporting the NICE TA assessed only the trial on relapsing-remitting MS.

**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, with a power calculation and using intention-to-treat analysis. The trials were
sponsored by the manufacturer.

Main results
In the trial of patients with a first clinical episode, the time for 25% of patients to convert to clinically definite MS was significantly longer with glatiramer than with placebo: 722 days vs. 336 days, and the risk of conversion was lower by about 45%.\textsuperscript{4}
In the trial of patients with relapsing-remitting MS, the rate of clinical relapse after two years was significantly lower with glatiramer than with placebo: about 1.2 vs. 1.7.\textsuperscript{5}

Adverse events
The most commonly reported adverse events with glatiramer reported in the trials were injection-site reactions and immediate post-injection reactions.

References


<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Treatment arms (n)</th>
<th>Duration of study</th>
<th>Main outcomes (glatiramer vs. placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>glatiramer 20 mg (243)</td>
<td>Treatment given by subcutaneous injection daily</td>
<td>time for 25% of patients to convert to clinically definite MS: 722 vs. 336 days*** (fewer than 50% of patients in either group converted)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>placebo (238)</td>
<td>Duration of study: up to 36 months</td>
<td>risk of conversion to clinically definite MS for glatiramer vs. placebo: HR 0.55 [95% CI 0.40 to 0.77]***</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>number of patients having a second attack: 24.7% vs. 42.9%*** (NNT = 6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Most common adverse events with glatiramer: Injection-site reactions, immediate post-injection reactions (lymphadenopathy, urticaria, influenza-like illness, vomiting)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Most common adverse event with glatiramer: Injection-site reactions</td>
</tr>
</tbody>
</table>

**PreCISe (Comi et al., 2009)\(^a\)**  
Biogen Idec and Elan Pharmaceuticals  
Double-blind RCT  
Multicentre  
n = 481  
Jadad score: 3  
Power calculation ✅  
Intention-to-treat analysis ✅  
Sponsored by the manufacturers  

- Aged 18 to 45  
- Having one unifocal neurological event with onset not more than 90 days prior to enrollment  
- Positive brain MRI (≥ 2 cerebral lesions ≥ 6 mm in diameter  
- Use of experimental drugs, beta interferon or chronic corticosteroids within 6 months  
- Relapse between screening and baseline visit  
- Pregnancy or breastfeeding  
- Relapse between screening and baseline visit  
- Pregnancy or breastfeeding  

**Johnson et al., 1995\(^b\)**  
Double-blind RCT  
Multicentre  
n = 251  
Jadad score: 3  
Power calculation ✗  
Intention-to-treat analysis ✅  
Sponsored by the manufacturers  

- Aged 18 to 45  
- ≥ 2 relapses in year prior to study entry  
- EDSS score 0 to 5.0  
- ≥ 1Gd+ lesion on T1-weighted MRI at study entry  
- Previous use of glatiramer, immunosuppressants  
- Pregnancy or lactating, insulin-dependent diabetes mellitus, positive HIV, evidence of Lyme disease, or using aspirin or NSAIDs  

**Main outcomes**  
Primary  
- rate of clinical relapse after 2 years: 1.19 ± 0.13 vs. 1.68 ± 0.13 **  
- more patients taking glatiramer improved and more patients taking placebo worsened (using EDSS score)**  

**Secondary**  
- time for 25% of patients to convert to clinically definite MS: 722 vs. 336 days*** (fewer than 50% of patients in either group converted)  
- risk of conversion to clinically definite MS for glatiramer vs. placebo: HR 0.55 [95% CI 0.40 to 0.77]***  
- number of patients having a second attack: 24.7% vs. 42.9%*** (NNT = 6)  

Most common adverse events with glatiramer: Injection-site reactions, immediate post-injection reactions (lymphadenopathy, urticaria, influenza-like illness, vomiting)  

MS, multiple sclerosis; RCT, randomised controlled trial; MRI, magnetic resonance imaging; EDSS, Expanded Disability Status Scale; Gd, gadolinium-enhancing
* $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$ vs. control; CI, confidence interval