

## National Horizon Scanning Centre

# Glatiramer acetate (Copaxone) for a single demyelinating event with an active inflammatory process

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This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

## **Glatiramer acetate (Copaxone) for a single demyelinating event with an active inflammatory process**

### **Target group**

- Clinically isolated syndrome (CIS) - a single demyelinating event with an active inflammatory process with the patient episode carrying a high risk of becoming clinically definite multiple sclerosis (CDMS).

### **Background**

Clinically isolated syndrome (CIS) is the earliest clinical presentation of relapsing-remitting multiple sclerosis (RRMS). In CIS, there is an acute attack suggestive of demyelination (e.g. optic neuritis), which lasts at least 24 hours in one or more sites in the central nervous system (CNS).

Individuals who experience a CIS may or may not go on to develop MS. A diagnosis of CDMS is made once there is evidence of two separate demyelinating episodes (clinical or MRI)<sup>1</sup> or the person develops new signs and symptoms.

### **Technology description**

Glatiramer acetate (Copaxone) is an immunomodulating drug administered by subcutaneous (SC) injection at a dose of 20mg per day in a prefilled syringe. It is a random polymer (average molecular mass 6.4 kD) composed of four amino acids that are found in myelin basic protein. It is thought to act by modifying immune processes that are currently believed to be responsible for the pathogenesis of MS and shifting the population of T-cells from pro-inflammatory Th1 cells to regulatory Th2 cells that suppress the inflammatory response.

Glatiramer acetate is currently licensed for the reduction in frequency of relapses in ambulatory patients with RRMS. In clinical trials this was characterised by at least two attacks of neurological dysfunction over the preceding two year period. Glatiramer acetate is not recommended by NICE for the treatment of MS in the NHS in England and Wales but is available through the risk-sharing scheme (RSS)<sup>2</sup>.

### **Innovation and/or advantages**

Glatiramer acetate is a new class of therapy for this indication. There is evidence from trials that glatiramer acetate reduces the risk of converting to MS by half and delays time taken to a second event indicative of CDMS.

### **Developer**

Teva Pharmaceuticals Ltd.

### **Availability, launch or marketing dates, and licensing plans:**

In phase III clinical trials.

### **NHS or Government priority area:**

This topic is relevant to:

- The Long-term Neurological Conditions National Service Framework (2008).

### Relevant guidance

- NICE technology appraisal in development. Cannabinoids for the treatment of the symptoms of multiple sclerosis. Suspended (date of issue to be announced)<sup>3</sup>.
- NICE technology appraisal. Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis. 2007 (review date: June 2010)<sup>4</sup>.
- NICE technology appraisal. Multiple sclerosis - beta interferon and glatiramer acetate. 2002<sup>5</sup>.
- NICE clinical guideline. Management of multiple sclerosis in primary and secondary care. 2003<sup>6</sup>.

### Clinical need and burden of disease

MS is the most common neurological disorder among young adults and causes considerable disability in this group. Onset is usually between 20 and 40 years of age.

MS takes the following forms:

- RRMS: characterised by episodes of neurological dysfunction interspersed with periods of stability.
- Secondary progressive MS (SPMS): in which progressive neurological disability occurs later in the course of the disease.
- Primary progressive MS (PPMS): in which progressive neurological disability occurs from the outset.

The incidence of MS is 3.5 to 6.6 people per 100,000 population each year, equivalent to about 1,820 to 3,380 new cases in England and Wales<sup>7</sup>. The prevalence is between 100 to 120 per 100,000 population, equivalent to 52,000 to 62,400 people in England and Wales<sup>6</sup>. In 85% of young adults who develop MS, onset is with an acute CIS of the optic nerves, brainstem, or spinal cord<sup>8</sup>.

### Existing comparators and treatments

Interferon beta-1a (Avonex) and interferon beta-1b (Betaferon) are the only licensed therapies for CIS.

### Efficacy and safety

Trial code	NCT00666224 <sup>9</sup> : glatiramer acetate vs. placebo; randomised phase III with open label extension
Sponsor	Teva Pharmaceutical Industries Ltd.
Status	Ongoing, not recruiting
Location	USA, South America, Australia, New Zealand, Europe (including UK).
Design	Randomised, double blind, placebo control.
Participants in trial	n=481; age (31.1±6.8 years), enrolled within 90 days of a single unifocal clinical attack (index attack) 2 or more cerebral lesions highly suspicious of MS on the MRI: no corticosteroids within the 30 days prior to MRI. Randomised to SC glatiramer acetate 20mg per day or placebo.  *Following interim analysis, the double-blind phase was stopped early and all subjects offered open label therapy with glatiramer acetate and continued follow-up as planned in the original protocol <sup>10</sup> .
Follow-up	Three years double blind, then an additional 2 years open label.
Primary outcome	Time to CDMS, as determined by Poser criteria (occurrence of second clinical attack).
Secondary	Clinical and MRI parameters.

outcomes	
Key results	Risk of conversion to CDMS: 25% with glatiramer acetate vs. 43% with placebo ( $p < 0.0001$ ). Time to 25% of patients in each study group converting to CDMS: 722 days with glatiramer acetate vs. 336 days with placebo ( $HR = 0.55$ ; $p = 0.0005$ ).
Expected reporting date	Results of the double blind phase were presented in April 2008 <sup>10</sup> .
Adverse effects	The most common adverse effects associated with glatiramer acetate administered for RRMS in the pivotal clinical trials were: injection site reactions, chest pain, flu syndrome, asthenia, back pain, headache and pain <sup>a</sup> .

### Potential or intended impact – speculative

#### Patients

- |   |   |   |
|---|---|---|
| <input checked="" type="checkbox"/> Reduced morbidity: delay of diagnosis of CDMS                 | <input type="checkbox"/> Reduced mortality or increased survival                    | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease | <input checked="" type="checkbox"/> Other: Delay or prevention of diagnosis of CDMS | <input type="checkbox"/> None identified  |

#### Services

- |   |  |   |
|---|--|---|
| <input checked="" type="checkbox"/> Increased use: specialist monitoring of therapy | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input type="checkbox"/> Decreased use  | <input type="checkbox"/> Other:                          | <input type="checkbox"/> None identified            |

### References

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<sup>a</sup> Electronic medicines compendium

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