**NICE STA: Natalizumab for the treatment of multiple sclerosis**
**ACD-Industry Commentator : Merck Serono Ltd**

On behalf of Merck Serono Ltd, please find herewith, our comments on the NICE ACD with regards to the NICE Single Technology Appraisal for natalizumab in the treatment of multiple sclerosis. Our comments fall under points 1 and 2 of the general headings requested:

***i) Whether you consider that all of the relevant evidence has been taken into account;***

a) **Paragraph 2.3. Cost of technology considerations**

Paragraph 2.3 includes cost considerations. Here the drug cost of £14,730 is reported as the cost for the introduction of this technology to the NHS. It is also important to assess other relevant comparative costs which may have an impact on the relevant cost effectiveness of such as:

- Monitoring of immunogenicity
- Monitoring of hypersensitivity
- Infusions
- Bed occupancy
- MRI scans
- Nursing care

b) **Paragraph 3.2: Assessment of the suboptimal therapy patient population group**

The ITT group from the AFFIRM study may not be a suitable proxy for the suboptimal group, as they qualified by the McDonald criteria and therefore earlier/milder patients would not have been treated with beta interferon.

c) **Paragraph 3.3: QoL Assessment**

Presented information suggests improvement in QoL measured by the SF36 instrument but not by the MSQLI instrument. This raises questions as to the validity of; the MSQLI instrument, how the data was collected, or the overall findings. It is rare to find results in which a general QoL questionnaire showed significant findings where these could not be replicated in the disease specific equivalent.

d) **Paragraph 3.5: Modeling considerations and Adverse events**

All therapies require management of potential side effects. In the case of interferons, it is mainly limited to liver enzyme monitoring at treatment initiation as well as concomitant medication with paracetamol to manage flu like symptoms, which tend to regress over time.

Natalizumab will require close monitoring of patients in order to rule out potential PML. Frequent MRI as well as CSF will be required. This should be included in the model as well as the fact that interferons and glatiramer acetate are self-administrated therapies, whereas natalizumab requires patients to travel to infusion facilities.

e) **Paragraph 3.11: Modeling considerations and improvements in EDSS**

The company pharmacoeconomic model allows for improvements in the EDSS. It is not clear how this was modeled for the beta interferon component in this model.

f) **Clinical data assessed**

The clinical benefits of natalizumab rely on post hoc analysis and relatively small sample sizes. Proper randomized, prospective studies in both indications (in the appropriate population) remain to be conducted to document natalizumab benefits.

***ii) whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate;***

g) **Comparator therapy**

Interferons as well as glatiramer acetate are not indicated for the treatment of the defined RES population of patients and the only treatment that has been approved for a very similar population is mitoxantrone, hence comparison should be made with Standard of Care in England and Wales and with mitoxantrone.