Neutralizing antibodies (NAbs) have received considerable attention from both the scientific and marketing communities. Many of the DMTs used to treat MS are proteins. This includes the interferons (Avonex, Betaseron, Extavia and Rebif), Copaxone and Tysabri. Occasionally, the body treats these medications as foreign proteins and it develops antibodies against them. Antibodies are proteins that the body makes to fight bacteria, viruses and toxins. Many antibodies against DMTs bind to areas of the medication that does not interfere with their function. These binding antibodies are not of clinical importance. However, some of the antibodies bind to parts of the medication that block its function. These are called neutralizing antibodies and they can interfere with the effectiveness of the DMT.

Comparisons of NAbs are difficult because these rates were determined during the course of different studies, performed on different populations at different times and different severities of MS. More importantly, the methods used to measure the antibodies and the timing of sampling differ between studies, and the cutoffs used to determine a positive result differ. Examples of differences in the percent of patients with positive NAbs in large phase III studies include:

- Avonex: 14%
- Betaseron: 35%
- Copaxone: NA
- Mitoxantrone: NA
- Rebif: 24% at 22ug dose, 12.5% at 44ug dose
- Tysabri: 6% (see below for comments)

Several factors that make comparisons of NAbs challenging have already been mentioned. However, some additional factors must also be considered. One factor is that the rate of NAbs does not remain constant over time. The rate increases over the first 18-24 months of treatment before decreasing. Most studies of interferons were of 2 years duration which means that they were discontinued at the time that NAbs were just starting to have their maximal effect. Another factor affecting NAbs is that they can revert to normal rather quickly after an initially positive test. For this reason, NAbs should not be considered positive unless two tests are positive, three months apart.

The clinical importance of NAbs has also been called into question. In early studies, patients who were positive for NAbs had a much higher rate of MS disease activity, similar to the disease activity of those in the placebo arms of studies. However, some recent studies have questioned this finding with some studies indicating no effect of NAbs of the effectiveness of the disease.

Copaxone has antibodies binding the medication in most patients who receive it, but these do not appear to block the effect of the medication. Thus, NAbs do not play a role in the selection of this medication. Mitoxantrone does not appear to lead to NAbs. Tysabri has a low rate of NAbs. Patients on Tysabri who develop NAbs appear to have a lower rate of success with the
medication. The role of testing for NAbS in those using Tysabri has not been determined at this point.

More importantly, it must be remembered that NAbS are only one of many factors that determine the effectiveness of a medication. Other issues such as dosage, frequency, method of administration and effectiveness of the medication also contribute. The question of which medication is best should not be based on the presence of NAbS, but should be based on the overall effectiveness of the medication. We strongly advise that patients make decisions on which DMT to use based on factors other than the presence of NAbS. We believe that only head-to-head studies of medications can accurately predict which one is stronger. Information about head-to-head studies is available on our website.