

## MabThera<sup>®</sup> in rheumatoid arthritis

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### What is rheumatoid arthritis?

Rheumatoid arthritis (RA) is one of the most common autoimmune diseases, affecting 1% of adults worldwide. A progressive, systemic disease, it is characterised by inflammation of the membrane lining the joints, which ultimately leads to irreversible joint destruction and disability. Primarily affected are joints of the hands, feet, elbows, knees and neck, although the eyes, lungs or blood vessels can also be involved.

As yet, there is no cure and the cause is unknown, though women are twice as likely to be affected as men<sup>1</sup>. What has been established is that progressive, permanent joint damage occurs early on in the disease, long before the onset of visible changes, such as joint deformity.

### What is MabThera?

MabThera (rituximab), the first and only selective B cell therapy in RA, provides a fundamentally different treatment approach targeting a key player in the pathogenesis of RA. This approach offers lasting treatment success for RA patients, providing outstanding effects on structural damage, joints and fatigue with an unprecedented dosing interval in a cost-effective manner, resulting in greater freedom for patients.

### What role can MabThera play in the treatment of RA?

There are a number of treatments available to manage RA, including those that address the symptoms and slow the progression of the disease. The most frequently prescribed RA biologic therapy currently are the TNF inhibitors. However, up to 40% of patients treated with TNF inhibitors (T cell targeted biologic therapy) experience either an inadequate response or are intolerant to such therapies.<sup>1</sup>

MabThera is unique, specifically targeting the B cell – part of the immune system, which is a key factor in causing inflammation associated with RA. B cells may trigger certain cellular processes, including generation of auto-antibodies (such as “rheumatoid factor”) that research suggests may contribute to RA. By targeting the B cell, MabThera provides patients who have had an inadequate response to initial TNF inhibitor therapy with an alternative treatment option.

### **How does MabThera work?**

MabThera works by binding to a protein (called the CD20 antigen) on the surface of B cells, where it then recruits the body’s natural defences to attack and deplete the selected B cells. By selectively targeting a sub-set of B cells, MabThera is thought to break the cycle of RA, preventing effects that cause the disease symptoms and leading to long-term benefit for the patient. As neither stem cells nor plasma cells are affected by MabThera, B cells are restored after therapy and acquired immunity remains intact.

### **How is MabThera administered in RA and in what dosage?**

MabThera is administered as a course of two 1000mg infusions two weeks apart. With an interval between courses of six to 12 months according to disease activity, it offers an unprecedented duration of response to patients.

The efficacy provided by MabThera has been found to be independent of glucocorticoids that are recommended to be given before MabThera to reduce the incidence of infusion reactions.

A study presented at the American College of Rheumatology last year found that after the first treatment course of MabThera, every point (1.0) that DAS28<sup>2</sup> increased before a subsequent course was given, resulted in a 0.28 higher DAS score at week 12 after the second course. This indicates that repeat MabThera treatment courses should be given before a patient experiences an increase in disease activity.

### **How effective is MabThera as an RA treatment?**

The Phase III study REFLEX (Randomized Evaluation of Long-term Efficacy of rituximab in RA) identified that MabThera provides a significant and clinically meaningful improvement to patients who have had an inadequate response to TNF inhibitors. Of those patients treated with MabThera and methotrexate (MTX), it was identified that over half of patients achieved ACR20<sup>3</sup>, with 27% of patients achieving ACR50 and 12% achieving ACR70. Results further indicated that the progression of joint destruction was also reduced (joint erosion and progression of joint space narrowing being 50% lower compared to placebo). Patients treated with a repeat course of MabThera experienced improved efficacy compared to their initial course (remission rates doubling from 6% to 12% and 25% of patients reaching ACR70 following a third course of MabThera).

### **How safe is MabThera?**

MabThera's safety has been well demonstrated, with 2,438 patient-years of follow-up collected. The results have remained consistent across the trials, with no increase in serious infections following long-term use; in fact, the rate of any adverse events and infusion reactions has been shown to decrease with subsequent courses.

### **How cost effective is MabThera?**

The cost effectiveness of MabThera is favourable, with average annual treatment costs being lower than those of any other biologic agent. There are also lower associated treatment costs due to MabThera's unprecedented treatment intervals that allow less frequent clinic visits than other RA infusion treatments.

***For more information and images of MabThera, B cell therapy and RA, visit [www.mabthera-ra.com](http://www.mabthera-ra.com)***

## References

1. Moreland, L.W. Targeted Biologic Therapies for Rheumatoid Arthritis. (last accessed on 04.05.05)  
<http://video.medscape.com/pi/editorial/cmecircle/2004/3415/flash/moreland/transcript.html>
2. Disease activity is measured by a Disease Activity Score (DAS), where low disease activity is defined as  $DAS28 \leq 3.2$  and remission is defined as  $DAS28 \leq 2.6$
3. The ACR response is a standard assessment used to measure patients' responses to anti-rheumatic therapies, devised by the American College of Rheumatology (ACR). It requires a patient to have a defined percentage reduction in a number of symptoms and measures of their disease. For example, a 20%, 50% or 70% level of reduction (the percentage of reduction of RA symptoms) is represented as ACR20, ACR50 or ACR70. An ACR70 response is exceptional for existing treatments and represents a significant improvement in a patient's condition.