NICE advice

Remsima (infliximab biosimilar) for subcutaneous injection for managing rheumatoid arthritis

Evidence summary
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Product overview

The content of this evidence summary was up-to-date in July 2020. See summaries of product characteristics (SPCs), British National Formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites for up-to-date information.

Remsima for subcutaneous injection (Celltrion Healthcare Hungary Kft) is a biosimilar monoclonal antibody of infliximab that inhibits the activity of tumour necrosis factor (TNF)-alpha. It has a marketing authorisation for managing rheumatoid arthritis in combination with methotrexate.

Likely place in therapy

As with all biologic disease-modifying antirheumatic drugs (DMARDs) for rheumatoid arthritis, Remsima (subcutaneous) would be prescribed and initiated in secondary care. Unlike intravenous infliximab, which is usually administered in secondary care rheumatology clinics, Remsima (subcutaneous) can be self-administered at home if the person, family member or carer has been given the appropriate training.

In practice Remsima (subcutaneous) is most likely to be used in people:

- who are already established on intravenous infliximab
- with stable disease but who have difficulty attending hospital appointments
- in whom the risk of attending hospital for intravenous infusions outweighs the benefits.

It may also be beneficial for people who are starting on infliximab who have not used a biologic before or who are switching from a biologic with a different mechanism of action to the tumour necrosis factor (TNF)-alpha inhibitors.

There are no data on people switching to Remsima (subcutaneous) from Remsima (intravenous) at doses higher than 3 mg/kg or frequencies of administration higher than every 8 weeks, and there are no data on people switching from other infliximab products to Remsima (subcutaneous).

Factors for decision making

Effectiveness

Evidence was from an unpublished phase 3 study (n=343) in people with rheumatoid arthritis, which was included in the European public assessment report (EPAR) for Remsima (subcutaneous). For the primary endpoint of change of DAS28-CRP (disease activity score 28-C-reactive protein) from baseline to week 22, the evidence showed non-inferiority of Remsima (subcutaneous) compared with Remsima (intravenous). The analysis of other efficacy endpoints showed that Remsima (subcutaneous) was generally comparable in terms of disease activity measured by DAS28-CRP, DAS28-ESR

(DAS28-erythrocyte sedimentation rate) and ACR (American College of Rheumatology) response up to week 54, compared with Remsima (intravenous).

Safety

The safety profile of Remsima (subcutaneous) compared with Remsima (intravenous) in people with rheumatoid arthritis was assessed in a randomised, phase 3 non-inferiority trial. The safety profile of Remsima (subcutaneous) was similar to the safety profile of the intravenous formulation; however, the study was powered for non-inferiority and not for safety outcomes.

The incidence of anti-infliximab antibodies following Remsima (subcutaneous) was comparable to Remsima (intravenous) and had no significant impact on efficacy and the safety profile.

Localised injection site reactions associated with Remsima (subcutaneous) were predominantly mild to moderate and included: erythema, pain, pruritus, swelling, induration, haematoma, oedema, bruising, coldness, irritation, paraesthesia, ulcer, urticaria, haemorrhage, rash and scab. Most of these reactions occurred immediately or within 24 hours of subcutaneous injection and resolved spontaneously without any treatment.

Limitations of the evidence

The data reported in the EPAR have some limitations. Firstly, they come from a study that has not yet been published in a peer-reviewed journal. The study duration was short. Although the whole trial was 54 weeks in duration, only the first 30 weeks of the study directly compared Remsima (subcutaneous) with Remsima (intravenous). However, the treatment arms were identical until week 6, by which time the main part of the response was already achieved. Although the study was powered to measure non-inferiority, after 22 weeks of treatment the Remsima (subcutaneous) arm showed an improvement of 0.27 points in DAS28-CRP compared with the intravenous arm, although this difference is not considered clinically significant.

Unlike the dosing of Remsima (intravenous), which is adjusted according to bodyweight, Remsima (subcutaneous) is given at a fixed dose of 120 mg for all adults. People with a body mass index (BMI) of 35 or over were not included in the study, and there were only 7

people weighing over 100 kg in the Remsima (subcutaneous) group. Therefore, efficacy of Remsima (subcutaneous) is not known in people with a BMI of 35 or over and evidence is limited in people who weigh over 100 kg. A subgroup analysis conducted by the authors showed no significant difference in outcomes in people of different BMIs; however, the study was not powered for such subgroup analyses.

No patient-oriented outcomes were reported. Subcutaneous administration is known to be preferable for some people, but it is possible that subcutaneous administration could affect treatment adherence. It is not possible to determine the effects of non-adherence from this study design.

Person-centred factors

Infliximab is usually given by intravenous infusion in a hospital setting, which poses potential logistical problems such as travel, time, expense, time off work and childcare. All of these could pose a barrier to the uptake of intravenous infliximab or its ongoing use. Some homecare providers offer intravenous infliximab, but expert advisers have suggested that the uptake of this option is low.

Remsima (subcutaneous) allows patients, or their family members or carers, to administer the treatment themselves at home, provided they have received training. However, injection site reactions and dexterity problems may reduce uptake. The frequency of injections is higher with Remsima (subcutaneous), which is administered every 2 weeks, compared with Remsima (intravenous), which is every 8 weeks.

Resource implications

The cost of prescribing Remsima (subcutaneous) for managing rheumatoid arthritis will vary by locality. Therefore, it is not possible to show the overall resource impact.

A resource impact tool allows localities to use their own figures. See the resource impact assessment for a more detailed assessment of the budget impact of this medicine.

See the full evidence review for more information.

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