PrescQIPP Community Interest Company

Subcutaneous Infliximab prescribing

Nationally over £700 million is spent annually on the top 5 most frequently used biologics in rheumatology, gastroenterology and dermatology, of which approximately £80 million is for infliximab.[1]

The European Medicines Agency has recently authorised the first subcutaneous (s.c.) formulation of infliximab (Remsima®) for use in Rheumatoid Arthritis (RA),[2] with licence extensions for inflammatory bowel disease (IBD) anticipated mid-2020. This bulletin reviews the place in therapy of s.c. infliximab and offers guidance and support materials for organisations considering the prescribing of s.c. infliximab as a QIPP project.

The availability of a subcutaneous biosimilar of infliximab will give patients the freedom to administer infliximab themselves at home. This could free up capacity in secondary care by providing an alternative subcutaneous option to s.c. adalimumab and in the case of RA, s.c. etanercept.

Recommendations

- Review locally whether s.c. infliximab is the most cost-effective formulation, considering contract prices as well as locally charged/agreed activity costs.
- Switching suitable patients to s.c. infliximab could help reduce capacity problems at providers. As with all switches, these should be tailored to the individual patient and should take capacity at homecare providers into account as well.
- Ensure that prescribing of s.c. infliximab is in line with its licence and relevant NICE guidance, taking into account that there is currently no data on switching from another brand of infliximab to s.c. infliximab.
- A cost calculator is available here https://www.prescqipp.info/our-resources/bulletins/bulletin-264-subcutaneous-infliximab/ for local commissioners and providers to compare costs using the tariffs charged locally. Where applicable, costs used in the calculator are split based on patient weight, where this affects dose and therefore costs.

National Guidance

Infliximab (as an infusion) has been licensed for over a decade and has been recommended by NICE as a first line biologic in the treatment of a range of immune-mediated inflammatory diseases, including RA and IBD. NICE is currently undertaking an evidence review of s.c. infliximab.

Infliximab is only one of a wide range of biologics (from different therapeutic classes) licensed and recommended by NICE, some of which are administered via infusion, some via subcutaneous injection and some orally. The recommendations on individual agents in RA and IBD have been summarised in NICE guidelines[3-5] and treatment pathways.[6-8]

The choice of agent is generally guided by a combination of clinical factors, patient choice, cost, likely adherence and local infusion capacity.[9,10] NICE generally recommends in their guidance that if more than one treatment is suitable, the least expensive should be chosen to make the best use of NHS resources. This takes into account administration costs, dosage and price per dose. On this basis, adalimumab and infliximab (both available as biosimilars) are currently considered first line choices of anti-TNFs for RA and IBD, with the addition of etanercept as an alternative product in RA.

Guidelines from the British Society for Rheumatology are in line with the recommendations from NICE on the use of biologics, stipulating that patients should be assessed for co-morbidities as these influence the choice of biologic that is most suitable for the patient.[9]

For both ulcerative colitis and Crohn's disease the choice of biologics is more limited, but the first line choice in treatment-naive patients should, according to the British Society of Gastroenterology (BSG), still be determined by clinical factors (including co-morbidities and safety data), patient preference, cost, likely adherence and local infusion capacity.[10]

Infliximab, adalimumab and ustekinumab are all recommended by NICE as potential first-line biologics in Crohn's disease, with vedolizumab recommended after anti-TNF failure or if anti-TNFs are contra-indicated. However, anti-TNF therapy with infliximab or adalimumab is likely to remain the initial choice of biologic for Crohn's disease, until more data is available in support of using other biologics preferentially to an anti-TNF, according to the BSG.[10]

NICE recommended first line choices of biologics in ulcerative colitis are the anti-TNFs infliximab, adalimumab, golimumab, tofacitinib and vedolizumab. NICE is currently reviewing ustekinumab in moderate to severe ulcerative colitis. In practice, golimumab does not have a significant place in therapy when considering the relative costs associated with the different anti-TNFs and the conflicting data on relative efficacy of golimumab, infliximab and adalimumab.[10] Although more expensive compared with infliximab and adalimumab, vedolizumab has demonstrated increased efficacy compared to adalimumab in a head-to-head trial in patients with ulcerative colitis.[11] It is therefore posed as an alternative first line agent by the BSG.[10] There is no data available to assess whether the increased efficacy is matched with a higher cost-effectiveness when factoring in the higher cost of vedolizumab to the NHS compared to adalimumab.

Clinical effectiveness and safety

Comparability studies have been undertaken to compare safety and efficacy of the intravenous (i.v.) biosimilar Remsima® (CT-P13) with the originator Remicade®, the outcome of which informed the decision to authorise the i.v. preparation.

Marketing authorisation for the s.c. formulation was granted based on the data from an initial (part 1) 54-week phase 1 / phase 3 study and the subsequent randomised controlled trial (part 2), demonstrating non-inferiority of the s.c. preparation of CT-P13 compared to the i.v. preparation over a period of 30 weeks in patients with active RA. Outcome data of these studies have been published in the Summary of Product Characteristics (SmPC)[12] and as part of abstracts presented at conferences.[13,14]

In part 2 of the study, patients with active RA received two infusions of infliximab (3mg/kg) two weeks apart, followed from week six onwards by either a maintenance dose of 120mg infliximab every two weeks via s.c. injection or a 3mg/kg dose every eight weeks via infusion. Patients who received the infusion up until week 30 were then switched to the s.c. preparation at week 30 for further analysis up to week 54. In both treatment arms methotrexate was given concomitantly.

Of the 357 patients enrolled in the trial, 343 went on to receive either the infusions or s.c. injections. The s.c. formulation was found to be non-inferior to the i.v. formulation, demonstrating similar efficacy scores (DAS28, ACR20/50/70 and EULAR-CRP responses) at week 30 as well as a similar safety profile.[12]

Outcome data for the trials in IBD have yet to be published, with the first outcome data presented at conferences and symposia in the first quarter of 2020.[15] The dose and frequency of administration in the clinical trials were: two infusions of infliximab (5mg/kg) two weeks apart, followed from week six onwards by a maintenance dose of 120mg (<80kg) or 240mg (≥80kg) every two weeks via s.c. injection. However, the expected licensed maintenance dose for IBD will be 120mg every two weeks with an option to escalate the dose to 240mg every two weeks as required.[16]

For the IBD trials CT-P13 was used for both the i.v. and s.c. preparations.[15] There is no data available on switching from a different brand of infliximab to s.c. Remsima®.[12]

Patient factors

Choice of agent is generally guided by a combination of clinical factors, patient choice, cost, likely adherence and local infusion capacity. NICE generally recommends in their guidance that if more than one treatment is suitable, the least expensive should be chosen (taking into account administration costs, dosage and price per dose) to make the best use of NHS resources.[3-5]

On this basis, infliximab and adalimumab (both available as biosimilars) are currently considered first line choices for both RA and IBD.[3-5]

A wider range of biologics is licensed for RA and co-morbidities.[3,6] This may therefore play a bigger part in determining the initial choice of biologic for an individual patient with RA compared with a patient with IBD.

Infliximab is only licensed in RA when used in combination with methotrexate, which may not be appropriate for all patients.[12]

In Crohn's disease, the BSG recommends use in combination with a thiopurine due to increased efficacy and suggests using infliximab in combination with methotrexate as there are indications that this may reduce immunogenicity.[10]

Cost comparison

Due to the sensitivity of pricing information, a direct price comparison based on current contract prices cannot be published in this bulletin. A cost calculator has been developed for local organisations to enable comparisons based on the latest contract or acquisition costs and is available here https://www.prescqipp.info/our-resources/bulletins/bulletin-264-subcutaneous-infliximab/

Switching options

Switching from infliximab infusions to s.c. injections in patients responding well to infliximab and who are willing and able to self-administer, could increase capacity in day units and reduce the number of hospital visits needed.

Subcutaneous infliximab offers an alternative s.c. treatment option to other first-line anti-TNFs.

Guidelines for RA[17] and IBD[10] already recommend switching to either a different class of biologic or alternative anti-TNF if there is an indication for discontinuing first-line treatment. Whether clinically more appropriate to switch to an alternative anti-TNF or different class of biologic depends on numerous factors, including whether the reason for discontinuation was intolerance, loss of efficacy (and after what time) and what the drug / antibody concentrations in the blood are. Significant savings by avoiding more expensive biologics as second-line treatment are therefore unlikely.

During the Current COVID-19 pandemic, NICE have recommended the following in their COVID-19 rapid guideline: rheumatological autoimmune, inflammatory and metabolic bone disorders:[18]

"Assess whether patients having intravenous treatment can be switched to the same treatment in subcutaneous form. If this is not possible, discuss with the patient an alternative subcutaneous treatment."

Switch Savings

Based on current contract prices and average costs of administration of i.v. infliximab charged to commissioners, it is unlikely that the availability of s.c. infliximab will generate significant monetary savings at this point in time. It could even be more costly for certain patient cohorts, but this will need to be assessed using local tariff information. However, the introduction of s.c. infliximab could help reduce capacity problems where they have been identified.

Summary

The introduction of a subcutaneous version of infliximab is unlikely to dramatically change the initial choice of anti-TNF. It is unlikely to produce significant savings to local budgets but will give patients an additional option of a product that can be self-administered and could help reduce local capacity issues.

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Additional resources available	Bulletin	https://www.prescqipp.info/our-resources/bulletins/bulletin-264-subcutaneous-infliximab/
	Tools	

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