

Regional Medicines Optimisation Committee Briefing Best Value Biologicals: Adalimumab Update 6

Biosimilar versions of the original biological medicine adalimumab (brand name Humira®) have been introduced in the NHS as part of a formal framework agreement dated 1 December 2018, after the patent for Humira® expired in October 2018. This briefing provides important details for ongoing implementation of best value adalimumab products.

This briefing provides a regular update for provider trusts, clinicians and commissioners on adalimumab. Implementing best value biological medicines enables the NHS to continue to improve patient care and provide new treatments now and into the future. It is a key element of NHS England's Medicines Value Programme.

The framework agreement has been put in place for a one year period from 1st December 2018, so the briefing considers the position and issues arising to date, and looks forward to 2020.

1. Review and context

Adalimumab provides major clinical benefits to patients with severely debilitating diseases and NHS England is working closely with patient groups and clinical service providers as new medicines are made available to ensure that high quality patient care is maintained. Clinicians are responsible for the decision to prescribe a biological medicine, in consultation with individual patients.

NHS England issued guidance to trusts and CCGs recommending in the 'Commissioning Framework for Biological Medicines (including biosimilar medicines)' that nine out of 10 new patients should be started on the best value biological medicine within three months of a biosimilar launch and at least eight out of ten existing patients should be switched to the best value biological medicine within 12 months.

In May 2019, NHS England updated the 'what is a biosimilar' guide. This document is available on the NHS England website: <https://www.england.nhs.uk/publication/what-is-a-biosimilar-medicine/>. It provides an update for key clinical and non-clinical stakeholders about the role of biosimilar medicines in the NHS in England and to support the safe, effective and consistent use of all biological medicines, including biosimilar medicines, to

the benefit of patients. It includes a detailed summary of guidance and evidence so is an excellent resource for investigating any issues in further detail.

2. Procurement update

The UK market has the following biosimilar products available in addition to the originator product Humira® by AbbVie: Amgen’s Amgevita®, Biogen’s Imraldi®, Mylan’s Hulio® and Sandoz’s Hyrimoz®.

It is anticipated that Fresenius Kabi’s product Idacio® will be a new entrant to the market and details are included in section 9 below. This product is not currently incorporated in any NHS England contract.

In planning the 2018 procurement, it was recognised that all trusts should retain access to the originator product during the period of the first framework, in addition to their allocated first-line biosimilar. The framework therefore ensures that Humira® is available in all parts of the country. Some clinicians and patient groups fed back the need to have access to a citrate-free biosimilar product for some patients, and a citrate-free biosimilar option in all trusts. If the first-line biosimilar medicine isn't clinically appropriate for the patient they will then have access to one of the other products available. The current contract is as detailed below.

Outcome of tender: Market access awards by region:

Regional Group	1 st line 40mg biosimilar	2 nd line 40mg biosimilar	20mg/0.4ml biosimilar	Originator award
East Midlands	Biogen/ Imraldi®	Amgen/ Amgevita®	Amgen/ Amgevita®	AbbVie/ Humira®
East of England				
South East				
Thames Valley and Wessex				
South West				
North East	Amgen/ Amgevita®	N/A		
North West				
Yorkshire and Humber				
North London	Sandoz/ Hyrimoz®	Amgen/ Amgevita®		
West Midlands				
South London	Mylan/ Hulio®; But best value biological: AbbVie / Humira®			

The first line treatment in each contract is to be the treatment of choice, but if individual patients require a citrate free formulation this is available. This is a clinical decision on an individual patient basis as detailed in section 6 below.

The current contract is set to run until 30 November 2019 with options to extend the duration of the contract. Discussions concerning the next contract are currently underway and a decision will be made regarding the future arrangements in due course.

3. Biosimilar uptake at month 6, end May 2019

Uptake of biosimilar adalimumab at the end of month 6 indicates that 63.6% of patients are on biosimilar adalimumab (see figure below). It is therefore estimated that approximately 35,000 patients have received the biosimilar products. The current uptake of best value adalimumab is higher than this for two reasons:

- This uptake is based on financial data so there is a time lag between the homecare provision of the adalimumab injection and the reporting of financial information.
- South London remain on the originator product as this is the best value biological product for that area

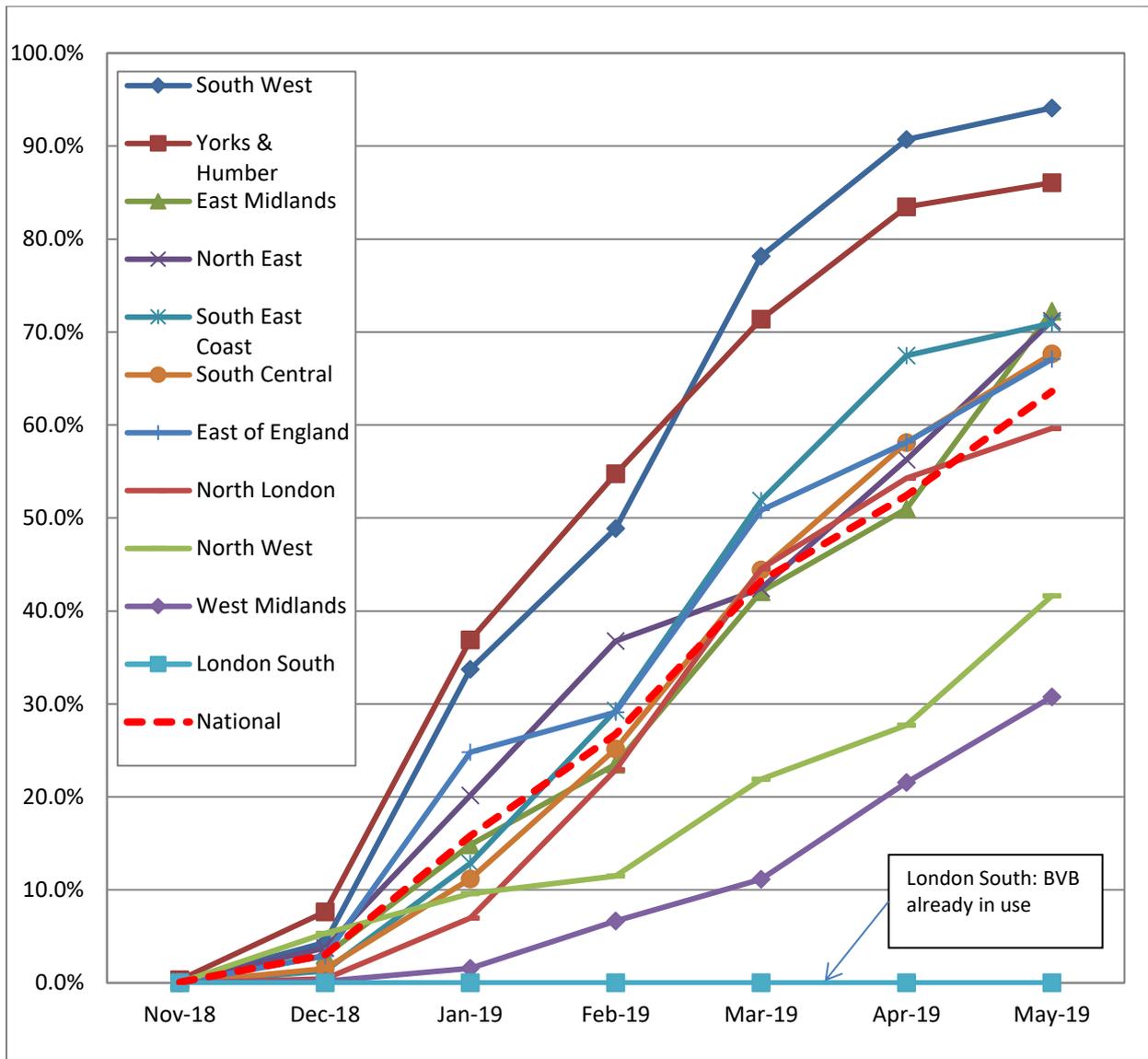
The transition to best value adalimumab has enabled substantial amounts of funding to be redirected into supporting better patient care. The overall financial saving to the NHS in 2018/19 was £98m, and the total saving is expected to be £308m by the end of 2019/20.

Trusts are encouraged to take a proactive approach, using the materials shared on the SPS website, ensuring good engagement with patients in the shared decision making process.

Figure 1

Monthly analysis of regional uptake of biosimilar adalimumab products (Note: London South best value biological already in use)

(Source: Define® data)



4. Feedback from patients and clinicians

There has been regular ongoing communication with patient groups and clinicians, and close attention is being paid to any perceived adverse reactions. Patient groups are currently undertaking helpful further work to assess patient experience.

Feedback has been that on some occasions consent has not been sought, and in some cases patients only received written correspondence with no face to face or telephone conversations. Patient dissatisfaction has been reported to patient groups, with concerns raised about side effects and the lack of support from clinical teams.

One clear message is therefore variation in communication with patients. Clear, verbal communication is an important element of high quality patient care and shared decision

making. Patient experience is one of the three key parts of clinical quality (alongside clinical safety and clinical effectiveness). Any changes should have regard to shared decision making as discussed in the NHS England website: <https://www.england.nhs.uk/shared-decision-making/>. No changes in therapy should be implemented without patient agreement.

Discomfort at the injection site reported by number of patients has been documented with all products. This discomfort has not been directly linked to the citrate content of the injection, and injection technique, speed of injection and temperature of the injection have all been shown to influence the discomfort or pain experienced. Support should therefore be provided to patients to ensure that any such discomfort is limited.

We have noted that there is a very low level of reporting through the yellow card MHRA adverse reaction reporting process, so please ensure that any adverse events are reported.

Anyone unsure of how to report adverse events should be directed to www.mhra.gov.uk/yellowcard or to the British National Formulary (BNF) section 'Adverse reactions to drugs'. Paper copies of yellow cards are also available at the back of any BNF.

It should be noted that all of the biosimilar adalimumab products are new medicines and are therefore under additional monitoring (they have an inverted black triangle symbol (▼) displayed in their package leaflet and summary of product characteristics, together with a short sentence explaining what the triangle means). It does not mean that these medicines are unsafe but that all suspected adverse drug reactions for these products should be reported.

5. Clinical Advice

The Regional Medicines Optimisation Committee has been asked to provide advice for circumstances in which the patient needs to switch from the selected biosimilar to an alternative product.

Section 4.5 of the [NHS England 'What is a Biosimilar' guide](#) should be noted; this clarifies the position regarding the use of biosimilar products.

In order to address the specific question regarding 'biosimilar to biosimilar' switching the following statement has been produced by the Regional Medicines Optimisation Committee.

This statement does not address any switching of biosimilar products on a regular basis (back and forth between different biosimilars), as such an approach would require direction from the Medicines and Healthcare products Regulatory Agency. It should also be noted that products are to be prescribed by brand name and substitution by pharmacy is not permitted.

Biosimilar to Biosimilar Switching – Statement agreed by RMOG South May 2019

Evidence from clinical trials and increasing experience from clinical practice supports that a single switch from an originator to a biosimilar is not associated with any significant risk or loss of efficacy.

If a patient transferred from an originator product to a biosimilar does not tolerate the biosimilar, clinicians may need to consider switching back to the originator product ('reverse switch') or switching to an alternative biosimilar ('cross-switching'). Currently studies are lacking on the safety and efficacy of switching from one biosimilar to another, and this is primarily a clinical decision.

Theoretical concerns are of immunogenicity. Two published multiple switch studies have been identified, one with a biosimilar etanercept and one with a biosimilar adalimumab. In both studies the biosimilar and reference product were switched several times in one of the treatment arms.

The safety, efficacy and immunogenicity profiles of the switched and non-switched arms were similar. Therefore although data are limited, these multiple switching studies do not reveal any concerns that suggest such switches will affect safety or efficacy.

Since clinical evidence on the safety of multiple switches is scarce, future studies and patient monitoring in registries are needed to provide more data.

References:

1. Griffiths CEM et al. The EGALITY study. *Br J Dermatol* 2017; 176(4): 928-38.
2. Blauvelt A et al. Phase III randomized study of the proposed adalimumab biosimilar GP2017 in psoriasis: impact of multiple switches. *Br J Dermatol* 2018; 179: 557-558.

Therefore, from a clinical perspective:

- where severe discomfort at the injection site is of significant concern, transition to another product may be appropriate. (The impact of excipients such as citrate is considered in section 6 below).
- Where disease flares occur after switching to a biosimilar these are unlikely to reflect a failure of the biosimilar. Disease flares and a lack of sustained response happen commonly during treatment with the same product. Logically any lack of responsiveness (regardless of a recent switch) should prompt a discussion about

changing the drug completely to a different biologic agent, but reverting to the originator drug is a possible initial step. If a flare is due to disease progression rather than lack of effect of the biosimilar (which is likely to be the majority of cases), going back to the originator will not make much difference and sooner or later the patient will move on to a different biologic agent.

Since publishing the RMOc position, a real world study (abstract just published), showed that switching between multiple biosimilar infliximab products was not associated with increased immunogenicity. Patients (n=265) were switched to a biosimilar and followed up for 3 years. At year 2, 140 patients were switched to a second biosimilar infliximab while 26 remained on the first biosimilar and 55 reverted back to the originator. Analysis showed that the number of biosimilars received did not affect antidrug antibodies development.

Reference: Lauret A, Moltó A, Abitbol V, et al. Effects of successive switches to different biosimilars infliximab on immunogenicity in chronic inflammatory diseases in daily clinical practice. Presented at: The European League Against Rheumatism European Congress of Rheumatology 2019, June 12-15, 2019; Madrid, Spain. Abstract OP0227.

6. Citrate content

To recap the advice on citrate content, the Regional Medicines Optimisation Committees (RMOcs) have advised the following on prescribing in this context:

Patient groups and clinicians told us that the availability of a citrate-free biosimilar was important to them as citrate can sometimes be associated with discomfort on injection. The procurement strategy ensures that each hospital group has access to a citrate-free formulation for situations where this is required.

Patient experience in this context is variable, and the evidence for the direct effect of citrate on injection site reaction is very limited. For this reason it is difficult to define clear prescribing criteria for citrate-free products. Clinicians should therefore consider the most appropriate and cost-effective treatment for each patient when making a prescribing decision. Some citrate-free formulations may be 'second line' treatments, so clinicians will need to decide with patients which formulation is most appropriate in such circumstances.

It is therefore expected that if a biosimilar is considered the most clinically appropriate biological treatment for a patient, the standard approach for trusts and CCGs will be to prescribe the first line biosimilar in accordance with the regional contract. Local commissioning arrangements in this context are to be agreed with CCGs.

7. Reference pricing

The National Tariff Payment System provides a mechanism by which a centrally determined reference price may be set by NHS England, and its use required by commissioners and NHS providers. This is detailed in the following document on the NHE England website:

<https://www.england.nhs.uk/publication/reference-prices-for-adalimumab-letter-from-matthew-swindells/>.

It is intended that the reference price will cover the cost of the best value product, any use of second line biosimilars (where applicable) and the cost to hospitals of switching patients to the best value biological medicine. The reference price will be how commissioners reimburse providers for adalimumab, instead of the previous 'pass through' arrangement in which the actual cost of the drug has been reimbursed.

The National Tariff rules, and thus the reference price for adalimumab, are mandatory:

- The NHS Standard Contract requires the provider, through Service Condition 39.1, to source adalimumab through the national Adalimumab Framework.
- The Contract also requires the commissioner, through Service Condition 36.1, to pay the provider in accordance with the National Tariff.
- The National Tariff rules on local prices for high-cost drugs says that the price must be the reference price if there is one.
- NHSE have explicitly published a reference price in the letter at <https://www.england.nhs.uk/wp-content/uploads/2019/04/reference-prices-for-adalimumab-letter.pdf>.

Further details are incorporated in the FAQ published by NHS England in June, appended below

For queries about reference prices contact england.biosimilars@nhs.net

8. Ordering process

The majority of orders for adalimumab injection are being managed and processed appropriately, but please note the following important point regarding use of FP10 prescription :

- We have noted that some adalimumab usage is being processed by the FP10 prescription route.

- This should not happen as it will result in the list price being paid rather than the NHS discounted price.
- We assume that in these circumstances the FP10 prescriptions are mainly being used as homecare orders.
- If any prescribers are using FP10 prescriptions please can this cease and use hospital orders instead.

9. Product update

The following Adalimumab biosimilars have now been launched in the UK, and were included in NHS England’s procurement exercise:

- Amgevita® (Amgen)
- Hulio® (Mylan/Fujifilm Kyowa Kirin)
- Hyrimoz® (Sandoz)
- Imraldi® (Samsung Biogen).

A simplified comparison of the different adalimumab products is as tabulated below. This includes a new entrant to the market from Fresenius Kabi which is not yet incorporated in any NHS England contracts:

Company	Product name	Licences	20mg strength available	Citrate excipient	Latex free pen device	Latex free prefilled syringes	EMC link for further product details
Abbvie	Humira®		Yes	No	Yes	Yes	Humira
Amgen	Amgevita®	Same as Humira®	Yes	No	No – contains latex	Yes	Amgevita
Mylan / Fujifilm Kyowa Kirin	Hulio®	Same as Humira®	No	No	Yes	Yes	Hulio
Samsung Biogen	Imraldi®	Same as Humira®,	No	Yes	Yes	Yes	Imraldi
Sandoz	Hyrimoz®	Same as Humira®	No	Yes	No – contains latex	No – contains latex	Hyrimoz
Fresenius Kabi	Idacio®	Same as Humira®	No, but in 40mg vial	Yes	Yes	Yes	EPAR

10. Homecare

Detailed advice has been provided in previous briefing notes regarding good practice in the context of homecare management. Further information is available from the National Homecare Medicines Committee (NHMC), or please email regional pharmacist contact below.

All products are available through multiple homecare providers so a choice of provider is available. There has been ongoing close communication with all homecare companies and it is clear that progress is good with any issues arising are being addressed.

For Pharmacy managed switching programmes there have been anecdotal reports of clinicians not being aware of the exact date of the first prescription for the biosimilar. If the adalimumab switching programme is being managed by the pharmacy team, please liaise closely with and communicate clearly to the clinical teams so that the date of the initial prescription for a new product is documented in patients' medical records in a timely manner.

11. Registries

As detailed in the previous adalimumab bulletin, the three main registries that are relevant to the prescribing of adalimumab in the UK are:

- British Association of Dermatologists' Biologic and Immunomodulators Register (BADBIR)
- UK Inflammatory Bowel Disease (IBD) Registry
- British Society of Rheumatology (BSR) Biologics Registry.

At present each of the four adalimumab biosimilar manufacturers have signed up to some, but not all, of these. For any biologic, submitting data to a range of registries is understandably desirable from a clinical standpoint, but it is not mandatory.

As part of the licensing process, all originator biologics and biosimilars have to submit a post-marketing risk management plan. This plan typically includes submitting data to one biologics registry as well as completing one, or more, long-term studies post-launch. This approach is designed to pick up any significant safety concerns, over and above those seen with the originator product, post-launch. The non-submission of patient data to any one registry should not be seen as a barrier to biosimilar adoption in that patient cohort.

12. Supporting materials in one place

Interim findings from a survey exploring the experiences of patients being switched to biosimilar versions of adalimumab, highlights variation in:

- quality of communication/information patients receive in advance of and during a consultation;
- patients consent being sought before transitioning; and,
- the level of shared decision making taking place

Supporting materials including previous briefings, the [toolkit for best value biological implementation](#) and [information resources for patients](#) are available on the Specialist Pharmacy Service's (SPS) website: www.sps.nhs.uk/adalimumab.

Please register to receive email updates.

Shared decision making supporting materials are available on the NHS England website: <https://www.england.nhs.uk/shared-decision-making/>

13. Contact us

RMOC regional pharmacist (NHSE/NHSI) contact details:

- South East and South West – Stephen.brown17@nhs.net
- London - richard.goodman@nhs.net
- Midlands and East - richard.seal1@nhs.net
- North - michelecossey@nhs.net

The South RMOC is leading work on biological medicines.

All resources are shared via the [Specialist Pharmacy Service's website](#)

Annex 1: NHS England FAQ

June 2019

Gateway ID: 08720

INTRODUCTION

Biosimilar versions of the original biological medicine adalimumab (brand name Humira®) were introduced in the NHS as part of a formal framework agreement from 4 December 2018 after the patent for Humira® expired in October 2018. This FAQ provides important details for implementation of best value adalimumab products.

In 2017/18, adalimumab cost the NHS over £400 million, and it is the biological medicine on which we spend most in our hospitals.

More than 46,000 patients are being prescribed the drug for severe hospital treated conditions such as rheumatoid arthritis, inflammatory bowel disease and psoriasis.

During 2018, NHS England worked closely with the national groups that represent the majority of patients who are being treated with adalimumab, including the National Rheumatoid Arthritis Society, the National Ankylosing Spondylitis Society, the Psoriasis Association and Crohn's & Colitis UK.

We also worked with professional bodies including the British Association of Dermatology, the British Society of Gastroenterology, the British Society of Rheumatology, the Neonatal Paediatric Pharmacists' Group, the Royal College of Nursing and the UK Clinical Pharmacy Association.

Supporting materials including previous briefings, a [toolkit for best value biological implementation](#) and [information resources for patients](#) are available on the Specialist Pharmacy Service's (SPS) website: www.sps.nhs.uk/adalimumab

Implementing best value biological medicines enables the NHS to continue to improve patient care and provide new treatments now and into the future. It is a key element of NHS England's Medicines Value Programme, which is aimed at continuing to give people the medicines they need and want, making the best use of the NHS' budget, and ensuring the NHS remains a world leader in the use of medicines.

OVERVIEW

NHS England ran the procurement for adalimumab in a way that was aimed at both getting the best price and supporting a thriving market. As a result of the tender, no one supplier of adalimumab was awarded the whole market. Suppliers had incentives to offer their best price at the point of tender, and access to the market was awarded on the basis of the competitiveness of their prices.

For the purposes of the tender, hospital trusts were divided into eleven regional groups. Each hospital trust with a region has been allocated a list of adalimumab products and invoice prices; this list includes the first line biosimilar, the originator Humira®, and a second line citrate-free biosimilar (if the first line biosimilar contains citrate).

For trusts in practice, the process is as follows:

- The clinician in consultation with a patient selects and prescribes the most appropriate product for the patient, specifying the brand name.
- The hospital pharmacy receives and processes the prescription, ensuring that suitable arrangements are in place for the supply to be made, generally through a homecare company.
- The invoice is sent to the trust hospital pharmacy, and payment is made to the supplier at the set invoice price.
- The trust recharges the commissioner(s) at the set reference price (instead of the previous arrangement in which the ‘pass through’ charge has generally been the invoice price of the medicine).
- The difference between the invoice price (paid) and the reference price (received) is retained by the trust as reimbursement for the work involved in transitioning to the best value biological.

Q1 WHY WASN'T A STANDARD COMMERCIAL MEDICINES UNIT FRAMEWORK USED FOR THIS PROCUREMENT?

Previous frameworks for biosimilars have included all brands on an unranked framework. Consequently, trusts have tended to switch to the lowest-cost biologic for valid financial reasons, but other companies have struggled to gain market share.

The tender strategy for this procurement therefore had two key objectives:

- Plurality – to ensure plurality of supply for adalimumab over the longer term, and to signal to the wider market the NHS’ support for best value biologics; and

	<ul style="list-style-type: none"> • Best price – to achieve competitive prices from suppliers for the benefit of taxpayers and patients. <p>This is a first step towards development of a sustainable market. This means that no one supplier of adalimumab will be awarded the whole market but it provides a strong incentive for suppliers to offer their best price at the point of tender, with competitive suppliers gaining a greater share of the market than those which price less competitively.</p> <p>A lotting strategy was devised to encourage competitive bids and ensure that all biosimilar companies gained a place on the framework if they submitted a compliant bid. In order for bidders to be awarded a place on the framework agreement, a two-stage process was used, involving a guaranteed share element for offers below a specified threshold price, and the use of a second stage in which the remaining share was allocated based on price ranking.</p> <p>Trusts also have the option to use their own homecare or other dispensing arrangements as companies were instructed to offer two prices: one to incorporate delivery to the patient’s home through a homecare company, and a second price which excludes the homecare service.</p>
Q2	WHAT IS A REFERENCE PRICE?
	<p>The 2017/18 and 2018/19 National Tariff Payment System (Page 118) provided a mechanism by which a centrally determined reference price could be set by NHS England, and its use required by commissioners and NHS providers.</p> <p>The reference price applies to the best value product and any use of second line biosimilars (where applicable). It has been set at a level to allow clinical cover the cost to hospitals of switching patients to the best value biological medicine. This will be how providers charge commissioners for adalimumab injection, instead of the previous ‘pass through’ arrangement in which the actual cost of the drug was reimbursed.</p>
Q3	WHEN WILL THE REFERENCE PRICE APPLY?
	<p>NHS England consulted on a proposed change to Local pricing rules: for high-cost drugs, devices and listed procedures (Rule 5) as contained within the National Tariff payment system.</p>

NHS England also consulted on changes to the NHS Standard Contract, under which providers are required to purchase adalimumab from the relevant approved sub-regional supplier under the NHS England framework.

The outcomes of both the NHS Standard Contract consultation, and the National Tariff consultation require the use of a reference price from 1 April 2019. These changes took effect from 1 April 2019.

Q4 WHAT IS THE REFERENCE PRICE FOR OUR REGION?

From 1 April 2019, NHS England expects CCGs to require trusts to use the adalimumab suppliers allocated to their regional group, at the corresponding supplier invoice price. Reference prices will be used to reimburse providers for adalimumab 20mg and 40mg from 1 April 2019 and replace any current pass-through payments.

A reference price for the 20mg and 40mg has been set for the 2019/20 financial year at:

Strength	Reference price regional groups (except South London)	Reference price regional group South London
20 mg dose	£1,775.00 per patient a year (pro rata) including homecare costs.	£1,775.00 per patient a year (pro rata) including homecare costs.
40 mg dose	£3,550.00 (£136.54 per dose) per patient a year (pro rata) including homecare costs.	£3,662.23 (£140.86 per dose) per patient a year (pro rata) including homecare costs.

The reason for the different reference price for South London is to ensure that these trusts are not disadvantaged by the regional arrangements.

In situations where a dose is prescribed which differs from those listed above, the reference price to be paid is to be calculated on a pro rata basis.

Q5 IS THERE A SEPARATE REFERENCE PRICE FOR SECOND LINE TREATMENTS?

The reference price for each regional group applies to all 40mg adalimumab brands. It will be the choice of the provider and clinician, in consultation with the patient, which of the brands allocated to their region they wish to use but

	<p>the reference price and therefore reimbursement from CCGs will be the same. The by 'dose' price covers the different dosing schedules for the 40mg products.</p>
Q6	<p>WHY DO SOME REGIONAL GROUPS HAVE A SECOND LINE BIOSIMILAR AND OTHERS DON'T?</p>
	<p>Each regional group has been awarded access to: (a) Humira®; and (b) a first line biosimilar (either citrate-containing or citrate-free). In those groups where the first line biosimilar is citrate-containing they will also have access to a second line citrate-free biosimilar.</p> <p>This is because national patient groups and clinicians told us that for some patients the availability of a citrate-free biosimilar was important as citrate can be associated with injection site discomfort and local reactions.</p>
Q7	<p>WHY IS THE SECOND LINE BIOSIMILAR MORE EXPENSIVE THAN THE FIRST LINE BIOSIMILAR IN MY REGION?</p>
	<p>One of the features of the tender was that second line biosimilars would be priced higher than the first line products. This was intended to incentivise uptake of the best value biologic for each regional group, helping to support market share for a wider range of suppliers and encourage more competitive pricing.</p> <p>However, the reference price covers the cost of both first and second line biosimilar products ensuring patients are able to access a citrate-free product and providers are fully reimbursed for this where clinically required. If more than one treatment is suitable, the best value biological medicine should be chosen.</p> <p>Note that where clinically required, patients may transition directly from the originator product to a citrate-free biosimilar even if this is not the lowest-priced product for the region.</p>
Q8	<p>WHEN SHOULD THE SECOND LINE CITRATE FREE PRODUCTS BE PRESCRIBED?</p>
	<p>The Regional Medicines Optimisation Committees (RMOCs) have advised the following:</p> <p><i>Citrate content:</i></p>

Patient groups and clinicians told us that the availability of a citrate-free biosimilar was important to them as citrate can sometimes be associated with discomfort on injection. The procurement strategy ensures that each hospital group has access to a citrate-free formulation for situations where this is required.

Patient experience in this context is variable, and the evidence for the direct effect of citrate on injection site reaction is very limited. For this reason it is difficult to define clear prescribing criteria for citrate-free products. Clinicians should therefore consider the most appropriate and cost-effective treatment for each patient when making a prescribing decision. Some citrate-free formulations may be ‘second line’ treatments, so clinicians will need to decide with patients which formulation is most appropriate in such circumstances.

As detailed in the RMOG advice, the evidence linking citrate content to injection site reactions is very limited. The studies are small, with significant methodological limitations, and other factors such as differences in needle gauge may also have made an impact. Any differences in discomfort at the injection site were short-term.

It is therefore expected that the standard approach for trusts and CCGs will be to prescribe the first line biological in accordance with the regional contract.

Where it is important for an individual patient to receive the second line agent to meet individual needs, this course of action is available. Local commissioning arrangements in this context are to be agreed with CCGs. Uptake will be monitored on an ongoing basis and any unusual prescribing patterns will be reviewed.

Q9 A HOSPITAL IN ANOTHER REGIONAL GROUP IS GETTING BETTER PRICES. CAN WE BUY FROM THAT GROUP?

As with generic products, those suppliers who offered the best prices have been given access to a larger proportion of the market. This means that invoice prices are different between regions.

The reference price in each region is set to cover the cost of first and second line biosimilars but it does mean that some providers have more potential to make savings than others. NHS England and NHS Improvement will be working together to ensure that it is clear what potential for savings there is at provider level.

There is a requirement for suppliers to only provide their products to the regions to which they have been allocated, and this will be monitored.

As specified in the NHS Standard Contract, providers are required to purchase adalimumab from the relevant approved sub-regional supplier under the NHS England framework.

The tender framework will be in place for a year from 1 December 2018 to 1 December 2019, with an option to extend, during which time the impact on prescribing, patients and the market will be reviewed.