North Central London
Joint Formulary Committee

# JOINT FORMULARY COMMITTEE (JFC) – MINUTES

**Minutes from the meeting held on Thursday 28th January 2016**
**Room 6LM1, Stephenson House, 75 Hampstead Rd**

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|---|---|---|---|
| **Present:** | Prof L Smeeth | NCL JFC Vice-Chair | **(Chair)** |
| | Ms R Clark | NHS Camden, Head of Medicines Management | |
| | Mr P Gouldstone | NHS Enfield, Head of Medicines Management | |
| | Ms P Taylor | NHS Haringey, Head of Medicines Management | |
| | Dr A Stuart | NHS Camden, GP Clinical Lead Medicines Management | |
| | Dr M Kelsey | Whittington, DTC Chair | |
| | Ms W Spicer | RFH, Chief Pharmacist | |
| | Dr R Kapoor | UCLH, Consultant Neurologist | |
| | Mr A Shah | RNOH, Chief Pharmacist | |
| | Dr C McGuiness | JFC Patient Partner | |
| | Dr R Sofat | UCLH, Consultant Clinical Pharmacologist | |
| | Dr R Urquhart | UCLH, Chief Pharmacist | |
| | Mr T James | MEH, Chief Pharmacist | |
| | Mr B Sandhu | NEL CSU, Assistant Director Acute Services | |
| | Mr B MacKenna | NHS Islington, Deputy Head of Medicines Management | |
| **In attendance:** | Mr J Minshull | NCL JFC, Support Pharmacist | |
| | Ms I Samuel | RFH, Formulary Pharmacist | |
| | Mr P Bodalia | UCLH, Principal Pharmacist | |
| | Mr A Barron | NCL JFC, Support Pharmacist | |
| | Mr E Hindle | MEH, Formulary Pharmacist | |
| | Ms S Sanghvi | UCLH, Formulary Pharmacist | |
| | Mr G Purohit | RNOH, Deputy Chief Pharmacist | |
| | Ms H Mehta | NMUH, Formulary Pharmacist | |
| | Dr H Amer | UCLH, Clinical Pharmacology Registrar | |
| | Mr A Heffer | WH, Medicines Information Pharmacist | |
| | Dr S Naik | UCLH, Consultant Endocrinologist | |
| | Dr M Cohen | RFH, Consultant Endocrinologist | |
| **Apologies:** | Ms H Taylor | WH, Chief Pharmacist | |
| | Dr R Fox | RNOH, DTC Chair | |
| | Mr C Daff | NHS Barnet, Head of Medicines Management | |
| | Dr R Breckenridge | UCLH, DTC Chair | |
| | Mr A Dutt | NHS Islington, Head of Medicines Management | |
| | Dr A Tufail | MEH, DTC Chair | |
| | Prof R MacAllister | NCL JFC Chair | |
| | Mr J Paszkiewicz | NEL CSU, Senior Prescribing Advisor | |

## 2. Meeting observers

Prof Smeeth welcomed the applicants and observers to the meeting.

## 3. Minutes of the last meeting

Item 6 should be updated to "Oct-15, MEH approved bevacizumab intravitreal for Coats' disease and familial exudative vitreoretinopathy".

The minutes were otherwise accepted as an accurate record of the meeting.

## 4. Matters arising

### 4.1 Tiotropium Respimat (Appeal)

The Committee considered an appeal for tiotropium Respimat for severe asthma based on the provision of new evidence and because the original approval had recommended using an inhaler device outside its product license (Handihaler) when a device was available to be used within its licence (Respimat).

Mr Minshull explained that the three papers received in the appeal request did not demonstrate how Respimat device was preferable to Handihaler device in severe asthma. Only one study (Hohfeld *et al*, 2013) was a head to head study of the Respimat and Handihaler, but this was a study designed to demonstrate that there was no clinically significant difference between these two devices with regards to systemic exposure to the drug. It was not looking at deposition in the lungs and did not cover asthma patients.

It was raised that GMC Prescribing Guidance directs prescribers to use a licensed product where one exists and can meet patient needs. Unlicensed medicine should only be used if a licensed product doesn't exist, where a licensed product wouldn't meet the needs of the patient, or as part of a "properly approved research project". It was decided on these grounds that the licensed Respimat inhaler should be approved for use in severe asthma.

## 5. Declarations of relevant conflicts of interest

Dr Cowen declared he had consulted and given presentations for Eli Lilly (item 7.2 and 7.3), Novo Nordisk (item 7.3 and 7.4), AstraZeneca (item 7.3), Sanofi (item 7.3), Takeda and Janssen-Cilag Ltd.

Mr Gouldstone declared he had attended an Advisory Board for Novo Nordisk (item 7.3 and 7.4).

## 6. Local DRT recommendations / minutes

| Month | DTC site | Drug | Indication | JFC outcome |
|---|---|---|---|---|
| Feb-11 | UCLH | Thyrotropin alpha | As part of the ablation and detection of residual thyroid cancer for patients who cannot safely discontinue thyroid hormones therapy | Added to NCL Joint Formulary |
| Jun-15 | RFH | SonoVue Contrast Agent | Diagnostic agent characterization of liver lesions | Added to NCL Joint Formulary |
| Nov-15 | RFH | Sacubitril/valsartan **(early access scheme)** | Heart failure with reduced ejection fraction in patients who remain symptomatic despite maximum therapy | RFH only |
| Dec-15 | RFH | Peginterferon beta-1a (Plegridy®) | Relapsing-remitting multiple sclerosis in-line with NHS England Commissioning | Added to NCL Joint Formulary |
| Nov-15 | WH | Artesunate | Malaria | Added to NCL Joint Formulary |
| Nov-15 | WH | Riamet (artemether-lumefantrine) | 1. IV to PO switch therapy from IV Artesunate for severe P. falciparum malaria<br>2. First line treatment for uncomplicated P. falciparum malaria<br>3. Second-line treatment for P. vivax | Added to NCL Joint Formulary |

## 7. New Medicine Reviews

### 7.1 Dermatonics (urea 25%) topical cream for hard foot skin in high risk diabetic patients

The committee heard an application to use Dermatonics (urea 25%) Once Heel Balm® topical cream for anhidrotic, fissured, calloused and hard foot skin in high risk diabetic patients to reduce risk of ulceration. Ten percent of the diabetic population is expected to have an ulcer at some point, and mortality rate following ulceration is high (up to 50% within 5 years of having an ulcer).

Physiological urea is involved in hydration of corneocytes and in the maturation of stratum corneum. In diabetic patients, autonomic neuropathy impairs the release of sweat, thus impeding this process. Callus formation may exacerbate the problem by compressing epidermal cells, stimulating the overproduction of keratinized tissue. Use will be restricted to patients with level 3 or level 4 foot skin, as defined by the Young Townson Footskin Scale (calloused or calloused and cracked skin), who require extensive intervention from the Podiatry Service.

NICE Guideline 19 (Diabetic foot problems, August 2015) recommends that a Foot Protection Service should be available to give advice about and provide skin care of the feet for any patient with moderate to high risk of developing diabetic foot problems, however it doesn't specify the nature of this skin care. The guideline did not compare effectiveness for different skin moisturisation strategies and did not make any recommendations on choice.

There is no single urea containing cream available across NCL formularies; however Calmurid cream (10% urea, 5% lactic acid) is available on two formularies. A range of urea containing creams are prescribed in primary care. Calmurid requires twice daily application, therefore Dermatonics Once Heel Balm may be more convenient for patients as used once daily. Deramtonics Once Heel Balm is approximately half the price of Calmurid (based on a cost per 100 gram application) and would require application of half as much cream (as once daily rather than twice daily). Diabetic patients do not routinely apply emollient to their feet when not visiting the podiatrist, and experience difficulty adhering to multiple daily applications of emollient.

The limitations of the efficacy evidence available for this product was noted, specifically that it was limited to small, poorly designed studies that measured efficacy outcomes that are not patient related (e.g. electrical resistance within the stratum corneum). Studies available suggest that urea 25% cream is does have a statistically significant impact on improving moisture in the skin when compared to baseline, and that there may be an improvement in favour of urea 25% cream when compared to other urea containing creams. It was also noted that the evidence did not try to assess impact on clinically meaningful outcomes such as ulceration or amputation rate, though a statistical review submitted by the manufacturer suggested that every £1 spent on Dermatonics could reduce spend on ulceration treatment by £12, extrapolated from evidence that Dermatonics removed all calluses from a group of 100 patients within 11 days. Of the three studies presented, only one was in patients with diabetes.

There is no SPC for Dermatonics, therefore adverse effects are not reported as robustly as with licensed medicines. The manufacturer reports that there have so far been no reports of sensitivity to Dermatonics. An SPC is available for Balneum Plus Cream which contains 5% urea indicates that there are no common or very common side effects reported with this. Skin burning sensation, erythema, pruritis and application site pustules are uncommon side effects of the 5% cream. Contact dermatitis, urticarial, rash and pustular rash have all been reported though the frequency is unknown.

Despite the acknowledged limitations with the evidence, it was anticipated that appropriate use of urea cream may reduce the incidence of diabetic foot complications and is likely to be relatively safe. It was agreed that Dermatonics Once Heel Balm should be added to the formulary under evaluation for one year, for initiation by the Podiatry Service for patients with diabetic foot at high risk of ulceration.

Decision: Under evaluation
Prescribing: GP Prescribing following initiation by Podiatry Service
Tariff status: In tariff
Funding: GP
Fact sheet or shared care required: No
Audit required: Follow up patients who are prescribed Dermatonics to establish impact on use of Podiatry Service, ulceration and amputation rates. Review of impact on primary care prescribing to be presented.

## 7.2 Dulaglutide in Type 2 diabetes Info.

An application was heard for the inclusion of dulaglutide as a treatment option for Type 2 diabetes (T2DM), in line with NICE NG28 recommendations for glucagon-like peptide-1 receptor agonists (GLP-1RAs). The application had received broad support from consultants across NCL.

There are two GLP-1RAs on the NCL Joint formulary; once-daily liraglutide 1.2mg and once-weekly exenatide MR 2mg (in line with NICE TA203 & TA248 respectively). Since publication of NICE NG28 both TAs were removed.

AWARD-6 was a 26-wk, open-label, multinational, non-inferiority RCT to investigate the safety and efficacy of once-weekly dulaglutide 1.5mg versus once-daily liraglutide 1.8mg. Adult patients with an HbA1c 7-10%, BMI ≤45kg/m2 who were receiving a stable dose of metformin (≥1500mg/day) for >3 months were eligible. The primary endpoint, reduction in HbA1c from baseline, was -1.42% and -1.36% for dulaglutide and liraglutide respectively, the estimated treatment difference was -0.06% (95% CI: -0.19 to 0.07) which indicates non-inferiority. Body weight reduced by -2.90Kg and -3.31Kg for dulaglutide and liraglutide respectively, the estimated treatment difference was +0.71Kg (95% CI: +0.17 to +1.26Kg).

AWARD-1 was a 26-wk, parallel-group, multinational RCT to investigate the safety and efficacy of once-weekly dulaglutide versus placebo and twice-daily exenatide (comparison of dulaglutide 1.5mg to exenatide was open-label). Adult patients with a BMI ≤45kg/m2 and HbA1c 7-11% on monotherapy or 7-10% on combination OADs were eligible. Eligible patients entered a 12wk lead-in period whereby OADs other than MET/PIO were discontinued and MET/PIO were up-titrated, only patients with HbA1c >6.5% were eligible for randomisation. Results found reductions in HbA1c from baseline to week 26 were -1.51% and -0.99% for dulaglutide 1.5mg and exenatide respectively; the estimated treatment difference was -0.55% (95% CI: -0.66 to -0.39) thereby achieving superiority against exenatide. Body weight reduced by -1.30Kg and -1.07Kg for dulaglutide 1.5mg and exenatide respectively, the estimated treatment difference was not significant (-0.24Kg [95% CI: -0.88 to +0.41Kg]).

With regards to safety, there were no incidences of severe hypoglycaemia in either trial and overall hypoglycaemia events were not statistically different between arms. GI side-effects were higher with dulaglutide 1.5mg than with exenatide and comparable to liraglutide 1.8mg however overall withdrawal rates due to adverse effects was similar.

The annual cost of dulaglutide, liraglutide 1.2mg and exenatide MR were equivalent.

The Committee heard from the clinical experts that dulaglutide is likely to deliver cost-savings compared to liraglutide as costs are fixed at the liraglutide 1.2mg equivalent dose. Furthermore dulaglutide is expected to offer a superior patient experience as dosing is once-weekly, the device is patient friendly and suitable for needle-phobic patients. Specific advantages for dulaglutide over exenatide MR 2mg include being licensed with insulin, licensed with CrCl >30mL/min (rather than >50mL/min) and does not cause skin nodules.

The experts informed the Committee that the NICE continuation criteria (≥1% reduction in HbA1c and ≥3% reduction in body weight) was not always adhered to; if a patient had a substantial response in HbA1c without the >3% reduction in body weight then the drug would be continued. Flexibility may also be afforded to patients in whom hypoglycaemia would have significant occupational issues.

The Committee agreed that dulaglutide was the preferred GLP-1RA as dulaglutide was likely to be at least as effective as liraglutide 1.2mg and exenatide MR in terms of HbA1c control and weight loss, was price parity, would prevent liraglutide 1.8mg use, and offered a superior patient experience. The alternative cheaper GLP-1RA (exenatide BD and lixisenatide) were not equivalent in efficacy therefore are not recommended.

The Committee agreed that there was a strong rationale for minimising the number of drugs on formulary within a class and agreed with the clinical experts that practical experience of using dulaglutide was required before a switch was considered. It was agreed that all new patients initiated on GLP-1RA should be prescribed dulaglutide and if experience is positive at 6 months, all GLP-1RA patients should be switched to dulaglutide. Exenatide MR and liraglutide 1.2mg would remain on formulary for existing patients during the evaluation period.

It was agreed that a shared care guideline was required for dulaglutide therefore prescribing could not commence until the shared care guideline was agreed.

***Actions: Mr Barron, Dr Cowen and Dr Nair to develop a NCL shared care guideline. Mr Barron should disseminate letters to all Diabetologists in NCL.***

Decision: Approved
Prescribing: Specialist initiation with continuation by GP
Tariff status: In tariff
Funding: GP funding
Fact sheet or shared care required: Shared care
Audit required: No

## 7.3 GLP-1 receptor agonists and insulin in Type 2 diabetes

The Committee reviewed the evidence for GLP-1RAs when used in combination with basal insulin.

There are two conceivable places in therapy for this combination; those inadequately controlled on GLP-1RA (and require insulin for the first time) and those who are inadequately controlled on basal insulin (and would otherwise require insulin intensification).

For those inadequately controlled on GLP-1 receptor agonists; one trial randomised patients to insulin detemir or 'no detemir' if subjects failed to achieve HbA1c <7% after a 12 week liraglutide 1.8mg run-in period. At week 26, the estimated treatment difference for HbA1c for 'detemir vs 'no detemir' was -0.52% (95% CI: -0.68 to -0.36), weight was +0.79Kg (95% CI: 0.08 to 1.49) and the mean detemir dose was 39.5iU/day. In the randomized phase, no major hypoglycaemia occurred and minor hypoglycemia rates were 0.286 and 0.029 events per PYE with and without insulin detemir respectively.

For those inadequately controlled on basal insulin; one study compared GLP-1RA to up-titrated basal-insulin and one study compared GLP-1RA to a once-daily bolus insulin.

A 30 week, double-blind, multinational RCT investigated the safety and efficacy of exenatide 10mcg BD versus placebo in patients who were receiving glargine. Adult patients with a BMI ≤45kg/m2, HbA1c between 7-10.5% on >20iU glargine were eligible. Patients were randomised to receive twice-daily exenatide or placebo; the glargine doses were not adjusted for the 1st 5 weeks, at week 6 the basal dose could be adjusted according to the treat-to-target algorithm. The estimated treatment difference for Hba1c between exenatide and placebo was -0.69% (95% CI: -0.93% to -0.46%). The estimated treatment difference for weight was -2.7Kg (95% CI: -3.7% to -1.7%). There was no difference in hypoglycaemia. Discontinuation due to AE was higher with exenatide than with placebo (9% vs 1%).

A 26 week, open-label, multinational, RCT investigated the efficacy and safety of liraglutide versus once-daily NovoRapid in patients with T2DM on a background of basal insulin. Patients who had completed a preceding degludec trial on once-daily degludec with an HbA1c ≥7% were eligible. The estimated treatment difference for Hba1c between liraglutide and NovoRapid was -0.32% (95% CI: -0.53% to -0.12%). Estimated treatment difference for weight was -3.75Kg. Confirmed hypoglycaemia for liraglutide and NovoRapid was 1.0 and 8.15 episodes per PYE (estimated rate ratio: 0.13 [95% CI: 0.08 to 0.21]). There were no episodes of severe hypoglycaemia. Discontinuation rates were 14% and 16% for liraglutide and OD NovoRapid respectively with withdrawal due to AE being higher for liraglutide (6% vs 1%).

Real-world evidence from the Associate of British Clinical Diabetologists (ABCD) indicates that HbA1c reductions of -0.8% and weight loss of -2.9Kg when liraglutide was added to a basal insulin. Furthermore approximately 40% of liraglutide use was in combination with insulin.

The experts informed the Committee that concordance to once-daily bolus insulin can be poor which prevents successful HbA1c lowering. Furthermore hypoglycaemia is more likely in some patients groups, including the elderly in whom minor hypoglycaemia can lead to falls and hospitalisation. It was noted that there was no RCT evidence to support GLP-1RA + insulin use in the elderly population.

The Committee voted and agreed that GLP-1RAs can be used in combination with insulin however the precise place in therapy was still to be agreed as part of the NCL Type 2 Diabetes treatment algorithm. The choice of GLP-1RA should be in-line with the NCL Joint Formulary.

Decision: Approved
Prescribing: Secondary care or IPU initiation with continuation by GP with ongoing specialist support
Tariff status: In tariff
Funding: GP funding
Fact sheet or shared care required: Shared care
Audit required: No

## 7.4 iDegLira (Xultophy®) in Type 2 diabetes

An application was heard for iDegLira as an alternative separate basal insulin and GLP-1RA injections. The application has received broad support from consultants across NCL.

The Committee heard that iDegLira is a combination of liraglutide and insulin degludec. The pre-filled pen administers 'dose steps' corresponding to 1 unit of degludec and 0.036mg of liraglutide per 'dose step'.

The EMA report the relative bioavailability of insulin degludec being very similar when administered as part of iDegLira versus degludec administered concomitantly with liraglutide. However the relative bioavailability of liraglutide when administered as part of iDegLira versus liraglutide administered concomitantly with degludec was 0.89 (90% CI: 0.83 to 0.97), and the ratio of $C_{max}$ was 0.74 (90% CI: 0.66 to 0.84), indicating an 11% lower AUC and a 26% reduction in $C_{max}$.

DUAL II was a 26-week, multinational, double-blind RCT to investigate the efficacy of iDegLira and degludec. Adults patient with T2DM and HbA1c 7.5-10.0%, BMI ≥27Kg/$m^2$ and a stable basal insulin dose of 20-40iU/day in combination with MET±SU were included. At randomisation, participants discontinued their pre-randomisation insulin and all OADs except MET. iDegLira was initiated at 16 'dose steps' and degludec was initiated at 16iU; both doses were adjusted according to a titration algorithm. For the primary endpoint, the estimated treatment difference in HbA1c between iDegLira and degludec was -1.1% (95% CI: -1.3 to -0.8%). After 26 weeks, the mean daily dose was 45 dose steps of iDegLira (45iU degludec + 1.62mg liraglutide) and 45iU degludec. 65.3% of patients on iDegLira required the maximum dose of 50 dose steps (no further titration possible) compared to 67.5% on degludec. The treatment difference for change in body weight was -2.5Kg (95% CI: -3.2 to -1.8Kg). There were no differences in confirmed, severe or nocturnal confirmed hypoglycaemia.

DUAL V (abstract only) was a 26-week, multinational, open-label RCT to investigate the efficacy and safety of iDegLira and glargine. Adults patient with T2DM and HbA1c 7.0-10.0%, BMI ≤40Kg/m2 and a stable glargine dose of 20-50iU/day were included. Exclusion criteria are unknown. Patients were randomised to once-daily iDegLira +MET or continued glargine up-titration +MET. Initial doses were 16 dose steps for iDegLira and pre-trial dose for glargine (mean 32iU). For the primary endpoint, the estimated treatment difference in HbA1c between iDegLira and up-titrated glargine was -0.59% (95% CI: -0.74 to -0.45%). The treatment difference for change in body weight was -3.20Kg (95% CI: -3.77 to -2.65Kg). The rate of confirmed hypoglycaemia was lower with iDegLira than glargine (rate = 2.23 PYE vs 5.05, ratio 0.43 [95%CI = 0.30-0.61]). A lower proportion of patients completed the study with iDegLira than glargine (90% vs 95%).

Novo Nordisk produced an naïve indirect-comparison and found a statistically significantly greater reduction in HbA1c with 38 dose steps of iDegLira (38iU degludec + 1.4mg liraglutide) vs liraglutide 1.8mg + 36iU basal insulin (-1.68% vs -1.33%, p=0.009). The Committee heard that perceived 'superiority' of iDegLira is likely due to the larger number of units of insulin being administered and that the comparator is 33.3% detemir which is known to be less potent than glargine and degludec. The claim of superiority was therefore dismissed.

The Committee heard that the SMC had approved iDegLira on the grounds of cost-minimisation versus Lantus® + liraglutide 1.8mg. This analysis was not considered relevant in NCL because liraglutide 1.8mg is not recommended for use, the comparator costs were not biosimilar glargine and the analysis assumed no wastage of iDegLira which is known not to be the case (e.g. 38 dose steps + 2 'airshots' per dose = 7.5 doses from each pen, thereby wasting 0.72mg from the incomplete dose left in the pen and 0.5mg wasted with 'airshots').

The experts disputed the wastage claim as the 'airshots' contain a mixture of air and active drug, and that patients do not have to discard part doses. It was agreed that iDegLira was likely to be more expensive that Abasaglar + liraglutide 1.2mg however this budget pressure would be minimised by preferentially using iDegLira for patients with a low baseline basal insulin dose (<35iU). Patient experience of a once-daily injection compared to two daily-injections would be enhanced.

The Committee agreed that patient convenience was an important consideration however disagreed that concordance would differ significantly between once-daily iDegLira compared to once-daily basal + once-weekly GLP-1RA (e.g. dulaglutide). Diabetes specialist nurses have previously confirmed that patients would typically discard incomplete doses therefore iDegLira would represent a certain incremental cost at doses >29 dose steps.

The Committee concluded that the benefit of reducing the injection frequency by one per week was inadequate to justify the incremental cost. The Committee therefore did not recommend adding iDegLira to the NCL Joint formulary.

## 7.5 Liraglutide in Type 1 diabetes

This item was deferred.

## 8. Guidelines

### 8.1 Statin prescribing & lipid modification guideline

The Committee reviewed the recommendations in the statin and lipid modification guidance and requested that the following comments be noted and minor amendments be made:

- Lipid profiles should be measured at baseline and 3 months. Consider measuring every 12 months thereafter (or after 6 months if the dose/statin changes)
- AST is not routinely monitored by clinicians, therefore LFT monitoring should be changed just to request "monitor transaminases". This will be lab specific
- It was agreed to keep statement that LFTs should only be measured after 12 months if clinically indicated
- The recommendation to start atorvastatin 40 mg daily rather than 80 mg daily in secondary prevention/familial hypercholesterolaemia was accepted
- The Committee is not aware of any evidence of benefit for treating lipids to target in primary prevention, therefore the Chair will feed back to NICE that these targets are not appropriate.
- The wording around co-enzyme Q10 and plant sterols needs to be amended to clarify that, although there is limited evidence of benefit, there is also no evidence of harm. Therefore, these drugs should not be prescribed, however, if patients want to purchase over the counter there is no evidence of harm in this.

The guideline should be submitted for approval by Chair's action following these amendments.

***Actions: Ms Sanghvi to seek clarification from NICE on rationale for including a target in primary prevention.***

## 9. Etanercept biosimilar

Etanercept (Benepali®) is a recombinant human TNF inhibitor. A "biosimilar" such as Benepali® is essentially the same substance as an originator biologic medicine (in this case etanercept (Enbrel®), with minor difference due to the natural variability caused by their complex nature and the manufacturing process. Benepali® will be available at the start of February, and is expected to cost approximately 33% less than Enbrel®. Benepali® will be available for supply through home care companies.

Biosimilar etanercept has recently received a marketing authorisation based on its equivalence to Enbrel®. Efficacy was established based on 24-week interim results from a 52-week, phase III, randomised, double-blind trial of patients with rheumatoid arthritis (RA). Patients were included if they were aged 18–75 years, and active RA diagnosis of 6 months to 15 years prior to screening. Major exclusion criteria included previous treatment with any biologic, lymphoproliferative disease history, HF, active TB, and pregnancy or breast-feeding. The primary endpoint was ACR20 response rate at week 24. Immunogenicity was measured in all patients with anti-drug antibodies (ADAs) and neutralising antibodies (Nabs). Based on previous etanercept studies showing an Etanercept biosimilar (Benepali®, Biogen): Rheumatoid Arthritis

481 patients (80.7%) were included into the per-protocol analysis (75 patients were excluded due to protocol deviations), with 78.1% achieving ACR20 response (primary efficacy end point) in Benepali® arm versus 80.3% in Enbrel® arm at 24 weeks. This mean difference of 2.2% (95% CI -9.41% to 4.98%) demonstrated non-inferiority of Benepali® to Enbrel® (using the wide, FDA recommended -15% to 15% margin).

The overall safety profiles of Benepali® and Enbrel® were determined to be similar, with 55.2% Benepali® arm patients experiencing at least one TEAE, compared to 58.2% in the Enbrel® arm. Upper respiratory tract infection, elevated alanine aminotransferase, nasopharyngitis and headache were the most frequently reported TEAEs. Discontinuations occurred in 5% of Benepali® patients and 6.4% of Enbrel® patients. Fewer injection site reactions were reported in the Benepali® arm (0.3%) than in the Enbrel® arm (2.4%).

It was highlighted that Benepali® is not yet available to replace Enbrel® in all patient groups due to the absence of a 25 mg preparation, which is expected to be launched in Q3 2016.

The Committee agreed that Benepali® should be added to the Joint Formulary for use within the licensed indication for Enbrel® for both new and existing patients. It was identified that a patient information leaflet on biosimilars has been developed by the London Procurement Partnership, and that this should be adopted by NCL organisations.

Decision: Approved
Prescribing: Secondary care only
Tariff status: PbR excluded
Funding: CCG funding
Fact sheet or shared care required: No
Audit required: No

**10. HSCIC prescribing costs charts**

This item was included for information only. Any questions should be directed to Mr Minshull.

**11. JFC Work Plan**

This item was included for information only. Any questions should be directed to Mr Barron.

**12. NCL Evaluation writing guide & Guideline templates**

The 'Writing Guide for North Central London evaluation' was approved. Templates were also approved for drug evaluations, guidelines and abbreviated guidelines.

**13. Terms of Reference**

Mr Minshull agreed to email all Committee members with the questions contained within the agenda pack. Mr Minshull would collate the responses and bring back to the February meeting.

**14. Next meeting**

Thursday 25th February 2016, Room 6LM1, Stephenson House, 75 Hampstead Rd.

**15. Any Other Business**

Nil