North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 21 October 2019
G12 Council Room, South Wing, UCL, Gower Street, WC1E 6BT

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Dr M Kelsey	WH, DTC Chair	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr S Semple	MEH, Chief Pharmacist	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Ms I Shaban	Islington CCG, Deputy Head of Medicines Management	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	Mr C Daff	Barnet CCG, Head of Medicines Management	
In attendance:	Dr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Barron	NCL MEP, Project Lead	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr F Master	RFL, Formulary Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Dr J Sun	UCLH, Foundation Year 2 Doctor	
	Mr J Fullerton	Specialist Registrar in Clinical Pharmacology	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Mr F Ismail	NEL CSU, Contracting and Commissioning Pharmacist	
	Ms A Patel	UCLH, Specialist Pharmacist - Oncology	
	Dr J Panicker	NHNN, Consultant Neurologist	
	Prof M Ehrenstein	UCLH, Consultant Rheumatologist	
	Dr M Heightman	UCLH, Consultant Respiratory Physician	
	Prof K Moore	RFL, Professor of Hepatology	(telephone)
	Ms N Taherzadeh	RFL, Specialist Pharmacist - Gastroenterology	
Apologies:	Ms K Davies	NEL CSU, Deputy Director Medicines Management	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Prof D Hughes	RFL, Consultant Haematologist	
	Ms L Reeves	C&I, Chief Pharmacist	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Dr S Yardley	CNWL, Consultant in Palliative Medicine	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Mr T Dean	Patient Partner	
	Dr A Sell	RNOH, DTC Chair	
	Mr A Dutt	Islington CCG, Head of Medicines Management	

2. Meeting observers

The Committee welcomed Mr Ismail (NEL CSU, Contracting and Commissioning Pharmacist), Ms Patel (UCLH, Specialist Pharmacist - Oncology) and Ms Taherzadeh (RFL, Specialist Pharmacist – Gastroenterology) as observers of the meeting.

3. Minutes of the last meeting

The minutes were accepted as an accurate reflection of the meeting

4. Matters arising

Nil

5. JFC Work Plan & outstanding actions

These items were included for information only. Any questions should be directed to Ms Kassam.

5.1 Erenumab for chronic migraine prophylaxis (negative FAD)

NICE have determined that erenumab is not cost-effective for preventing migraine in adults who have at least 4 migraine days per month. In November 2018, JFC approved a pre-NICE free-of-charge (FOC) scheme for erenumab for chronic migraine, after failure or contraindication to Botox®, however suspended the approval in January 2019 following a negative NICE Appraisal Consultation Document (ACD). The Committee agreed to review their approach to reviewing pre-NICE FOC schemes following publication of revised RMOC guidance.

5.2 Proposed RAG rating summary for JFC evidence summaries

The Committee agreed to adopt a Red-Amber-Green (RAG) rating summary for both written drug evaluations and verbal presentations; the RAG ratings will include an assessment of efficacy, comparative efficacy, safety, convenience and cost.

5.3 Integrating NHS Pharmacy and Medicines Optimisation programme

Dr Bodalia updated the Committee on the NHS England Programme of Integrating Pharmacy and Medicines Optimisation (IPMO) and progress within NCL. As agreed previously with the CEO Provider Group, the IPMO programme currently sits within the Provider Productivity workstream of the North London Partners STP governance structure and acts as a cross-cutting theme in enabling each STP Programme and their implementation of the Long Term Plan. Regional transformation will be led by the NCL Pharmacy Leadership Group with detailed discussions delegated to an IPMO Steering Group. To facilitate the programme, an inaugural NCL IPMO workshop took place in June with a follow-up workshop scheduled for 7th November. The strategy and actions of the Steering Group and the Workshops report into the NCL Medicines Optimisation Committee.

Separate to this, the CEO Provider Group has established a Medium Term Financial Strategy (MTFS) plan, with an established MTFS Programme Team led by Mark Hackett. The MTFS aims to reduce the financial deficit in North London within the current financial year, bringing accounts within the planned control target. As medicines represents a high area of spend within the NHS budget across a range of setting and systems, Dr Bodalia and Ms Butt (NCL Medicines Efficiency Programme) have been asked for medicines related strategies for deliverable cost savings in this financial year. Items 10 and 11 of this agenda have been brought to ensure potential strategies align with the medicines governance process.

6. Declarations of relevant conflicts of interest

No additional declarations were noted for the new medicine applications.

7. Local DTC recommendations / minutes

7.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
RFL	Aug-19	Oral dexamethasone (0.6mg/kg single dose, maximum 16mg dose)	Moderate – severe wheeze and acute asthma in patients aged 1 month – 18 years (first-line therapy)	Decision: RFL only† Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

UCLH	Sept-19	Imatinib (appeal)	Neo-adjuvant therapy prior to surgical resection for pigmented villonodular synovitis/ tenosynovial giant cell tumour if tumour shrinkage was considered to potentially reduce the morbidity of surgery.	Decision: UCLH only, subject to protocol development. Prescribing: Secondary care Tariff status: Excluded from tariff Funding: Locally agreed chemotherapy tariff Fact sheet or shared care required: No
UCLH	Sept-19	Intravenous ketamine	Difficult-to-sedate patients in ICU when other sedative agents are less suitable due to individual patient factors	Decision: Added to NCL Joint Formulary; subject to local DTC approval‡ . Restricted to ITU only. Prescribing: Secondary care Tariff status: in tariff Funding: Trust Fact sheet or shared care required: No
UCLH	Oct-18	Pollinex® Grasses + Rye and Pollinex® Trees	Grass/tree-pollen seasonal allergic rhinitis requiring treatment with subcutaneous immunotherapy for patients over 6 years old	Decision: Added to NCL Joint Formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
RNOH	Jul-19	Citric acid (0.6mol/L) for administration via nebuliser	Cough Reflex Testing as an additional component of dysphagia assessment	Decision: RNOH only Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

† RFL have incorporated oral dexamethasone into their treatment pathway as a 1st line setting due to poor tolerance of oral prednisolone, the shorter treatment duration with dexamethasone and treatment cost. The 2019 SIGN/BTS asthma guidance recommend that oral dexamethasone is used 2nd line for patients who cannot tolerate oral prednisolone. Oral dexamethasone is available as a liquid, the treatment course is less expensive than prednisolone liquid. The WH are undertaking an evaluation of oral dexamethasone to establish tolerability and the requirement for a repeat dose in primary care after 48 hours in children who do not tolerate oral prednisolone.

‡ Already on formulary at RFL. UCLH require a local protocol to be approved before adding to local formulary.

7.2 Not approved

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Sept-19	Intravenous ketamine	Treatment of status asthmaticus in ICU	Decision: Not approved
UCLH	Sept-19	Sublingual/subcutaneous ketamine	Chronic intractable pain in the ambulatory setting	Decision: Not approved
UCLH	Sept-19	Aspirin lysine	NSAID exacerbated respiratory disease	Decision: Not approved

8. New Medicine Reviews

8.1 Compassionate access scheme: Nivolumab and Ipilimumab for mismatch repair deficient/ microsatellite instability-high metastatic colorectal cancer (Applicant: Prof J Bridgewater, UCLH)

The Committee considered a compassionate access scheme *in absentia* for nivolumab in combination with ipilimumab for patients with mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC).

Checkmate-142 is a Phase II, non-randomised, open-label study of nivolumab, and nivolumab combinations in DNA mismatch repair–deficient (dMMR) or microsatellite instability–high (MSI-H) mCRC with disease progression following at least one systemic therapy. In November 2018, the Committee approved a similar scheme for nivolumab monotherapy using data from the monotherapy arm of the Checkmate-142 study.

For this application, efficacy data consists of a single-arm of Checkmate-142 (n=119) which administered nivolumab 3 mg/Kg and ipilimumab 1 mg/Kg every three weeks for 4 doses; patients continued on nivolumab monotherapy at 3mg/kg every two weeks thereafter. The primary outcome of 'investigator report objective response rate' was 54.6% [95% CI: 45.2 to 63.8%], of which 4 patients had a complete response. The secondary outcome of 'blinded and independent objective response rate' was 49% [95% CI: 39.5 to 58.1%], of which 5 patients had a complete response. The median time to response was 2.8 months, 12-month progression-free survival was 71% [95% CI: 61.4 to 78.7%] and 12-month overall survival of 85% [95% CI: 77.0 to 90.2%]. There were improvements in patient reported outcomes in symptoms, global health status and functioning. Median follow up was only 13.4 months and there was a small increase in discontinuation rate compared to nivolumab monotherapy. An assessment of the comparative safety and efficacy between nivolumab monotherapy and nivolumab in combination with ipilimumab was not possible as patients were not randomly allocated between treatment arms and no power calculations were undertaken.

The compassionate access scheme is only available to patients who have failed on or intolerant to other recommended systemic therapies, therefore the only alternative treatment is compassionate-access nivolumab monotherapy. The applicant for nivolumab monotherapy was asked to comment on this application and agreed combination therapy was likely to be the more effective however stated nivolumab monotherapy may be preferred for some patients due to the likely lower adverse effects profile and for those in whom ipilimumab is cautioned (such as those with a history of colitis).

The Committee agreed that despite the lack of comparative data, nivolumab in combination with ipilimumab was likely to be therapeutically useful for patients with a rare condition and limited treatment options. In summary, the Committee approved the use of nivolumab and ipilimumab for dMMR/MSI-H mCRC.

Decision: Approved
Prescribing: Secondary care only
Tariff status: N/A
Funding: Free of charge (Compassionate Access Scheme)
Fact sheet or shared care required: N/A

8.2 Botulinum toxin (Botox®) to treat urinary retention due to a disorder of the urethral sphincter (Applicant: Dr J Panicker, UCLH)

The Committee considered an application to inject botulinum toxin A into the urethral sphincter for patients with urinary retention secondary to Fowler's Syndrome or Detrusor Sphincter Dyssynergia.

Fowler's syndrome

The pathophysiology of Fowler's Syndrome is poorly understood, patients present with painless urinary retention with no neurologic or anatomic aetiology. Patients typically report concurrent pain, functional neurological symptoms, psychological symptoms and chronic opioid use. Experts believe Fowlers Syndrome may represent a distinct subgroup of patients with dysfunctional voiding due to failure of urethral sphincter relaxation, however this has not been proven. Standard of care for urinary retention secondary to Fowler's Syndrome is Sacral Nerve Stimulation (SNS) +/- intermittent self-catheterisation.
Botulinum toxin is proposed to be an alternative to SNS for patients in whom SNS is not recommended, including:

- Multiple comorbidities
- Unresponsive to SNS
- Suffering complications following SNS
- Patient undecided to undergo SNS
- Interim treatment for patients on the waiting list for SNS

NHNN have ten years of experience in using botulinum toxin in this capacity, although this use has been off label.

The Committee considered a single centre, uncontrolled, 10-week, open-label, pilot study (n=10) of women with Fowler's Syndrome. Inclusion criteria were elevated urethral pressure profile, increased sphincter volume, and abnormal electromyography. Subjects received one peri-urethral injection with botulinum toxin A into the external urethral sphincter. For patients with complete urinary retention (n=5), the outcome of interest was restoration of voiding. For patients with impaired voiding (n=5), the outcome of interest was a ≥ 50% improvement in maximum urinary flow rate. Secondary outcomes included post-void residual urine volumes (PVR) and International Prostate Symptom Score (IPSS). Of the women in complete retention, 80% were spontaneously voiding by week 10. Of the women with impaired voiding, 60% reported an improvement in maximum urinary flow rate of >50% by week 10. At baseline, the mean PVR was 260 mL compared to 89 mL at week 10. All patients required self-catheterisation at baseline however 7 had stopped by week 10. The IPSS improved over 10 weeks. The applicant clarified that patients underwent an assessment of medication history and were advised not to change their medications during the study however data was not collected.

The Committee noted small size, short term (only 1 injection), un-blinded, uncontrolled, single-centre nature of the study which made the long-term safety and efficacy of repeat-dose botulinum toxin A difficult to establish. The methodology behind the reporting "mean PVRs" was considered questionable as it excluded observations for all patients in complete retention; the median improvement in PVR for patients with readings at both week 0 and week 10 results in a less remarkable difference between the measures pre- and post-injection (only -58 mL).

The Committee heard from Dr Panicker that the application is limited to those in whom SNS is inappropriate and where self-catheterisation is difficult and painful due to a tight sphincter. The applicant informed the Committee that SNS, although standard of care, is associated with disadvantages including repeat follow-up due to leg pain, lead breakage and the need to return for battery replacement. Experience at NHNN to date is that injection with botulinum toxin A is without major adverse effects. All decisions to initiate botulinum therapy require an assessment of medication and an MDT discussion (inclusive of a psychologist).

Detrusor Sphincter Dyssynergia (DSD)

Sphincterotomy is standard-of-care for the management DSD secondary to inadequate sphincter relaxation. Botulinum toxin A is requested as an alternative to sphincterotomy as the latter is associated with haemorrhage.

There are no head-to-head comparisons of botulinum toxin with alternative surgical options. A Cochrane review to evaluate surgical method of managing neurogenic bladder dysfunction included 4 RCTs (n=142) using botulinum toxin alone, or in combination with other treatments. A meta-analysis was not considered appropriate due to the variation in trial protocols and comparators. The evidence of limited quality suggested that botulinum toxin confers benefit with regard to increasing voided urine volume, lowering detrusor pressure, and decreasing PVR. The review failed to provide robust evidence in favour of any of the surgical treatment options, due to the limited availability of eligible trials, the variability in the interventions, limited duration of follow-up (average of 8 months) and small trial size.

In terms of safety, The Committee heard from Dr Panicker that the rate of stress incontinence with treatment is 0.02% in addition to transient localised pain and bleeding.

The cost for botulinum toxin for both applications was £7,200 inc. VAT, excluding activity cost, for 15 patients per year (assuming 12 weekly injections).

In camera, the Committee acknowledged that alternative to surgery and self-catheterisation are desirable however agreed that the limited data, the study limitations and the absence of long-term safety

information raised major concerns. Theoretical risks associated with repeated injection into the urethral sphincter include loss of sphincter innervation and nerve dysfunction.

In summary, the Committee agreed that botulinum toxin A injections into the urethral sphincter should only take place as part of a placebo/sham-controlled, blinded, randomised trial to ensure adequate safety and governance whilst the effectiveness and safety of repeat injections is determined.

Decision: Not approved

8.3 Spiolto® Respimat (tiotropium and olodaterol) for moderate to severe COPD (Applicant: Dr M Heightman, UCLH)

The Committee considered an application for a combination inhaler, consisting of a long-acting muscarinic antagonist (LAMA) and long-acting beta2-agonist (LABA) in a Respimat® device to treat moderate to severe COPD. Due to the recent update to NICE COPD guidance, LAMA/LABA combination therapy will be the most commonly used regular inhaled therapy for COPD patients.

Buhl et al (n=5,163) report two multicentre, international, 52-week, double-blind, parallel group randomised controlled trials. Participants were aged ≥40, had moderate to severe COPD, were current or formers smokers, and had a post-bronchodilator FEV1 of ≤80% than the predicted value and an FEV1/FVC <0.7. Participants were allocated to one of five groups, using daily doses of olodaterol 5µg monotherapy, tiotropium 2.5µg monotherapy, tiotropium 5µg monotherapy, tiotropium 2.5µg and olodaterol 5µg combination inhaler or tiotropium 5µg and olodaterol 5µg combination inhaler (Spiolto) – all administered via the Respimat device. The results for the groups using unlicensed devices were not reported. Spiolto demonstrated statistically significant improvements versus tiotropium monotherapy and olodaterol monotherapy in both studies in the 'change from baseline in trough FEV1' and the 'change from baseline in the area under the curve between 0 to 3 hours'; however the difference did not exceed the minimum important difference for either of these first two co-primary outcomes. In the third co-primary outcome, in a combined analysis of both studies, Spiolto demonstrated statistical significance in reducing the St. Georges Respiratory Questionnaire (SGRQ) versus tiotropium monotherapy (difference of −1.2 [95% CI −2.3 to −0.2]) and olodaterol monotherapy (difference of −1.7 ([95% CI −2.8 to −0.6]).

The adverse effect profile of Spiolto is well known as tiotropium and other LABA inhaled therapies are used widely in NCL.

The use of Spiolto is cost-minimising compared to dual separate LAMA and LABA inhalers and is price-neutral compared to the other LAMA/LABA combination device on formulary (Anoro® Ellipta). The evidence-review underpinning NICE NG115 identified LAMA/LABA devices to have the highest probability of being ranked best for outcomes compared to all mono- and combination inhaled therapies. The budget impact associated with the change in practice as advised in the updated NICE guideline (which includes the change in inhaler use from 'predominantly LAMA' to 'predominantly LABA/LAMA') is expected to be £32,000 per annum in NCL by 2024.

The Committee heard from Dr Heightman that 1 in 5 patients prefer a pressurised device, which is currently not an option on formulary and the 'Breathe Easy' group identified the Respimat device as the 3rd most preferred device out of all available (the first two being the Ellipta device and the pMDI device).

In camera, the Committee were supportive of adding a LAMA/LABA pressurised device to the NCL Joint Formulary. In summary, the Committee approved Spiolto for patients with COPD who are limited by symptoms, or has exacerbations despite treatment with SABA or SAMA, and who do not have asthmatic features or features suggesting steroid responsiveness.

Decision: Approved
Prescribing: Primary and Secondary care
Tariff status: In tariff
Funding: Hospital and CCG
Fact sheet or shared care required: No

8.3.1 RRP stable COPD treatment guideline

The RRP stable COPD treatment guideline was discussed together with the rationalisation of inhaler choices on the NCL Joint Formulary (please refer to agenda item 8.3.2).

8.3.2 Rationalisation of inhaler choices on the NCL Joint Formulary

In September 2019, the Committee requested that the number of inhaled therapies for COPD on the NCL Joint Formulary be rationalised, and also asked for clarification as to who would be responsible for reviewing patients started on *triple therapy* after 3 months, in accordance with NICE guidelines.

The Committee reviewed a proposal to update the NCL Joint Formulary in line with choices recommended in the updated Responsible Respiratory Prescribing (RRP) 'Stable COPD treatment guideline' and the JFC 'Adult Asthma Inhaler Choice'. LAMA and LABA monotherapy were removed for initiation in COPD though could be continued for patients already on treatment. Inhaled corticosteroid and LABA combination devices not in the scope of one or both of these guidelines would have restrictions against their use applied for the relevant indication.

For the second action, the RRP 'Stable COPD treatment guideline' was amended with the instruction that the initiating clinician should perform a review after three months of therapy, with the review based on symptomatic response. The updated RRP table COPD guideline would be uploaded to the NCL MON website.

9. Guideline: Chronic Spontaneous Urticaria

This item was deferred to the November 2019 JFC meeting.

9.1 Eligibility criteria for omalizumab and the role of montelukast

This item was deferred to the November 2019 JFC meeting.

10. Biosimilar Teriparatide (Terrosa® and Movymia®)

10.1 Teriparatide treatment duration (18 months versus 24 months treatment)

The Committee considered a request to extend the duration of teriparatide therapy commissioned in North Central London from 18 months to 24 months.

Teriparatide (Forsteo®) was first approved by the EMA in 2003. The pivotal study underpinning the marketing authorisation was expected to last 36 months however was cut short (median treatment duration: 19 months) in response to a two-year study in rats, which found treatment- and dose-related occurrence of malignant metastatic osteosarcoma. In contrast, a follow-up rat study did not signal an increased risk of osteosarcoma, and no cases were identified in human studies therefore the EMA were satisfied of a positive risk/benefit with 18-months of teriparatide. NICE approved teriparatide in 2005 and subsequently CCGs routinely commissioned 18-month courses of teriparatide. In 2007, a license extension was granted to use teriparatide for osteoporosis in men. In 2009, the EMA reviewed the below two studies and amended the label to increase treatment duration to up to 24-months

EUROFORS was a 2-year 2-stage randomised controlled trial which recruited women ≥ 55 years old, who were at least two years post-menopausal, with a T-score ≤-2.5 for BMD at lumbar spine, total hip or femoral neck and had at least one documented vertebral or non-vertebral fracture. All women were given teriparatide for 12 months and then entered one of two substudies. Substudy 1 randomised women 3:1:1 to teriparatide, raloxifene or no active anti-resorptive agent for 12 months. Substudy 2 included only patients who were inadequate responders to prior anti-resorptive agents and were continued on teriparatide for 12 months. A total of 503 patients received teriparatide for 24 months. The study found statistically significant improvements in BMD of the lumbar spine, BMD of the total hip and BMD of the femoral neck with extending treatment from 18 months to 24 months.

Saag et al (n=214) was a randomised, double-blind, double-dummy, active comparator study in patients with glucocorticoid induced osteoporosis. Patients who used glucocorticoids for 90 days or more, with a BMD T-score of -2 or less at total hip, femoral neck or lumbar spine (or -1 if the patient had a previous fracture) were included. Patients were randomised to receive either teriparatide with a placebo tablet, or a subcutaneous placebo with alendronic acid 10mg once daily. The mean increase in BMD score from baseline to month 36 was significantly greater for teriparatide than alendronic acid (10.3% versus 5.5% [$p<0.001$]). The TBS score for teriparatide was significantly higher than alendronic acid from month 18 until month 36 [$p<0.05$].

The cost associated with an additional 6 months of treatment was likely to offset by using biosimilar teriparatide (see item 10.2), and given the additional treatment benefit, this strategy was considered cost-effective.

The Committee noted that the outcomes were limited to surrogates (i.e. BMD) and there was no data from these studies to confirm a reduction in fracture risk. A recent systemic review and meta-analysis

however identified teriparatide reduced hip fractures risk by 56% versus controls therefore the Committee accepted that improvements in surrogate endpoints would likely lead to improvement in clinically meaningful outcomes.

In summary, the Committee approved the 24-month treatment course of teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who meet NICE criteria.

10.2 Teriparatide biosimilar

Two biosimilar teriparatide products, Terrosa® and Movymia®, are available via Homecare providers. Whilst the products are equivalent in terms of safety and efficacy to the originator Forsteo®, the devices are different; Forsteo is formulated as a single-use disposable device whereas the biosimilars are formulated as a refillable pen with interchangeable cartridges.

Terrosa® was preferred to Movymia® as the homecare service proposal was approved by the National Homecare Medicines Committee (NHMC).

The Committee heard a testimonial from a BMD Specialist at RNOH, who supported the use of biosimilar teriparatide in new patients, however requested that existing patients are not switched due to the difference in pen device and the subsequent need for retraining.

The Committee considered two alternative approaches to implementation of biosimilar teriparatide; the first involved actively switching all patients and the second involved starting new patients on biosimilar teriparatide only. Based on annual usage by NCL Trusts, the difference between approaches was £44,000 in Year 1, £14,000 in Year 2 and £0 in Year 3. In conclusion, actively switching all patients might save an additional £58,000 over 2 years although savings would be lower if a decision was made not switch patients with only a few months of treatment remaining. It was unknown what proportion of the current spend is reimbursed by NCL CCGs.

Mr Purohit commented that RNOH would work with the homecare provider to determine if they will be able to help in training patients who could potentially switch to Terrosa®. RNOH and NEL CSU will discuss offline the potential strategy for patients currently using Forsteo® at RNOH.

In summary, the Committee added Terrosa® to the NCL Joint Formulary and removed Forsteo® for all new patients.

11. Biosimilar infliximab

11.1 Biosimilar infliximab (Zessly®)

The Committee added Zessly® to the NCL Joint Formulary as it represented the best-value infliximab on current contracts. It was not possible to predict if Zessly would remain the best-value infliximab in the long-term however it is better value than the existing biosimilar infliximab in use in NCL (Remsima®)

In summary, the Committee added Zessly® to the NCL Joint Formulary and removed Remsima® for all new patients.

11.2 Biosimilar to biosimilar switching

An active switch from Remsima® to Zessly® would yield significant NHS savings. The Committee heard it was not yet standard practice to switch between biosimilars and there were no randomised double-blinded controlled studies assessing the safety of this approach. The proposal was being considered as other UK hospitals (including GSTT, Lewisham, St Georges and Southampton) have already switched patients on biosimilar infliximab to a second biosimilar infliximab. The theoretical concern with multiple switches is the risk of developing anti-drug antibodies (ADA) and subsequent treatment failure.

One low quality observational study (abstract only) from a single-centre reported that patients treated successively with two biosimilar infliximabs were no more likely to develop ADAs than patients who received only one biosimilar infliximab.

An in-house meta-analysis of 8 studies; infliximab (n=566), adalimumab (n=2,655) and etanercept (n=408) pooled data for patients who remained on a single treatment (i.e. originator or biosimilar) and compared that to pooled data for patients who switched between originator and biosimilars. Results found no differences between the ‘no switch’ and ‘single switch’ groups in terms of emergent ADAs and clinical effectiveness.

The Committee concluded there was low quality evidence that switching twice was safe and there was high-quality evidence that a single switch has no impact on clinical response or development of ADAs. In light of this, there was no evidence to support a claim that switching was associated with an increased immune response therefore 'two switches' is also considered safe. The proposal should be discussed with clinical leads at each Trust to confirm clinical acceptability, identify any practical concerns and establish appropriate reimbursement mechanisms with CCGs for the costs associated with switching.

12. Guideline: High-cost drug therapy for Rheumatoid arthritis [update]

NEL CSU coordinated an update to the NCL Rheumatoid Arthritis pathway. The revised pathway includes three additional 'non-NICE' recommendations as below:

1. First-line biosimilar rituximab ± methotrexate (off-label) for patients with the following comorbidities:
    - History of a demyelinating disease
    - Interstitial lung disease (ILD)
    - Recent history of malignancy
    - Current diagnosis of malignancy
    - History of lymphoma or other B cell lymphoproliferative disease
    - Latent tuberculosis with a contraindication to the use of chemoprophylaxis
2. Second-line biosimilar anti-TNF monotherapy, after failure of first-line biosimilar anti-TNF monotherapy, for patients in whom rituximab monotherapy is not a preferred option (n.b. JFC approved rituximab monotherapy in this setting in July 2013).
3. Third-line, fourth-line and fifth-line rituximab ± methotrexate where rituximab has not been used in the first- or second-line setting.

The Committee heard that biosimilar anti-TNF is the preferred first-line agent for most patients however guidance from the British Society of Rheumatology (BSR) identify rituximab as the preferred agent for patients with a history of demyelinating disease, ILD and in patients with a past history of malignancy. For patients with a current history of malignancy and history of lymphoma or other B cell lymphoproliferative disease the data relating to anti-TNFs is inconclusive and whilst there is no direct evidence to support the safety of rituximab, most long-term data have not shown an increase risk. Patients with latent TB and contraindicated to chemoprophylaxis were not considered by BSR, however BSR describe an increased risk of reactivating TB with anti-TNF and that rituximab data appears reassuring. Professor Ehrenstein informed the Committee that the use of first-line rituximab is proposed for a small group of patients; the proposal to support the use of one agent over another is supported by clinician experience in limited numbers, registry data and guidelines.

There is no evidence to support the use of a second line anti-TNF following failure of first-line TNF over rituximab monotherapy; however it was noted that NICE TA415 recommends certolizumab monotherapy in this setting, and by extension other biosimilar anti-TNFs would be a cost-effective option.

The Committee acknowledged that evidence in these settings is limited and these recommendations are broadly consistent with pathways used by neighbouring STPs (Hertfordshire and South East London). Hertfordshire recommend only 3 lines of biologics in patients who cannot have methotrexate I.e. rituximab monotherapy is only recommended in the 1st, 2nd or 3rd line setting.

In summary, the Committee approved the elements of the NCL Rheumatoid Arthritis Pathway as presented. The NEL CSU is working on the final RA pathway.

13. Updated national guidance for liothyronine

This item was deferred to the November 2019 JFC meeting.

14. Epidyolex® update

Cannabidiol oral solution is now licensed for the adjunctive therapy of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, in conjunction with clobazam, for patients aged two years or older. The free-of-charge scheme approved by the Committee in January 2019 is now closed to new patients, though patients currently enrolled on the scheme will still be provided with free-of-charge medication until Epidyolex® has received a positive NICE TA or is funded by NHS England.

At the time of review, the Committee were informed that the medication would not be classified as a controlled drug. However, following EMA approval of the medicine, a small impurity of

tetrahydrocannabinol (THC) was identified, which was large enough to justify regulation of the licensed product as a Schedule 2 controlled drug in the UK. Therefore, any prescriptions and storage requirements for Epidyolex® should adhere to controlled drug regulations.

15. Ranitidine supply disruption alert

The Committee was informed of a supply disruption alert produced by the Department for Health & Social Care (DHSC) due to a recall of ranitidine. A manufacturer led recall has been conducted as a precautionary measure which has resulted in a shortage in supply. The DHSC alert recommends that patients should be reviewed as repeat prescriptions are requested and switched to a clinical alternative if ongoing treatment is required. The alert also suggests that where on-going acid suppression therapy is clinically warranted, the first-choice agent recommended was a proton pump inhibitor (PPI), specifically omeprazole, as there are sufficient supplies to manage the increase in demand. There is also a recommendation to avoid a switch to an alternative H_2-antagonist in the first instance as it may exacerbate a shortage of these products. Based on the current use of ranitidine in primary care, an NCL-wide switch to a PPI may be cost minimising, whilst an NCL-wide switch to an alternative H_2-antagonist would result in significant cost pressure.

The Committee heard from Prof Moore that many patients initiate acid suppression for short-term indications but erroneously remain on treatment life-long. It was noted that acid suppressants are 'drugs of dependence' and abrupt withdrawal could lead to rebound acid secretion; this may wrongly be interpreted as confirmation that long-term acid suppression is required however rebound acid secretion can be avoided with dose-tapering and prescribing supportive alginate on a 'when required' basis. Prof Moore recommended that NCL use the shortage as an opportunity to review all patients taking ranitidine with a view to gradually withdrawing treatment for patients without long-term indications. It would also give an opportunity to inform clinicians of the implications of long-term PPIs and H_2-antagonists use.

The Committee agreed patients should be reviewed and not automatically switch to an alternative agent, and saw benefit with NCL developing advice for GPs, patients and Trusts. Prof Moore agreed to draft the first version of the GP letter.

Actions:

i) RFL DTC colleagues to create a ranitidine shortage alert for GPs

ii) JFC Support to create a patient information letter informing of the disruption in ranitidine supply

iii) JFC Support to create a statement for Trusts on the disruption in ranitidine supply

16. JFC meeting dates 2020

The NCL JFC committee will continue to meet on the third Monday of the month throughout 2020.

17. Annual report 2018/19

This item was deferred to the November 2019 JFC meeting.

18. Next meeting

Monday 18th November 2019

19. Any other business

Nil