North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Monday 15 January 2018
G12 Council Room, South Wing, UCL, Gower Street, London WC1E 6BT

Present:	Dr R MacAllister	NCL JFC Chair	**(Chair)**
	Dr R Sofat	UCLH, DTC Chair	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Dr F Gishen	RFL, Palliative Medicine Consultant	
	Dr R Woolfson	RFL, DTC Chair	
	Dr M Dhavale	Enfield CCG, GP Clinical Lead Medicines Management	
	Mr S Richardson	WH, Chief Pharmacist	
	Mr S Semple	MEH, Chief Pharmacist	
	Ms L Reeves	C&I, Chief Pharmacist	
	Dr D Hughes	RFL, Consultant Haematologist	
	Dr A Sell	RNOH, DTC Chair	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr C Daff	Barnet CCG, Head of Medicines Management	
In attendance:	Mr A Barron	NCL JFC, Support Pharmacist	
	Mr J Minshull	NCL JFC, Support Pharmacist	
	Mr P Bodalia	UCLH, Principal Pharmacist	
	Ms M Kassam	MEH, Formulary Pharmacist	
	Mr B Mac Kenna	Islington CCG, Deputy Head of Medicines Management	
	Ms S Sanghvi	UCLH, Formulary Pharmacist	
	Mr K Paik	MEH, Clinical Pharmacist	
	Dr K Moore	RFL, Consultant Hepatologist	
	Ms E Yasmin	UCLH, Consultant in Reproductive Medicine	
	Mr V Talaulikar	UCLH, Consultant in Reproductive Medicine	
	Dr M Vilarino-Varela	RFL, Consultant Oncologist	
Apologies:	Mr G Kotey	NMUH, Chief Pharmacist	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Mr T Dean	Patient Partner	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Dr R Kapoor	UCLH, Consultant Neurologist	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	Mr B Sandhu	NEL CSU, Assistant Director Acute Services	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Dr M Kelsey	WH, Chair DTC	
	Dr A Mian	NMUH, Clinical Director for Specialty Medicine	
	Ms E Wassuna	Enfield Community Nurse, Bone Health	

2. Meeting observers

The Committee welcomed Mr Graham Hood, CPhO Pharmacist Clinical Fellow at Public Health England, as an observer.

Dr Fox (RNOH) has stepped down as Chair of the RNOH DTC and Dr Alexander Sell (RNOH) is the new Chair. Mr T James (MEH) has stepped down as Chief Pharmacist and Dr Stuart Semple (MEH) is the acting Chief Pharmacist. Dr MacAllister welcomed Dr Sell and Mr Semple as new members of the Committee and thanked Dr Fox and Mr James for their contributions.

The Committee received notification that Dr Raj Kapoor (Consultant Neurologist) is retiring in March 2018. Committee members were asked to nominate specialists from within their organisation to replace Dr Kapoor.

3. Minutes of the last meeting

Agenda item "7.5 Faster acting insulin degludec (Fiasp®)" was corrected to "7.5 Faster acting insulin aspart (Fiasp®)". The minutes and abbreviated minutes were otherwise accepted as accurate reflections of the November meeting.

4. Matters arising

4.1 APPEAL: Faster acting Insulin aspart (Fiasp) for diabetes in pregnancy

An appeal was received from Dr S Naik (UCLH), Dr E Karra (RFL) and Dr M Cohen (RFL) for the use of Fiasp in a revised population – women who require mealtime insulin during pre-natal optimisation and throughout pregnancy only.

The ground for appeal was the 'original decision was based on inaccurate or incomplete information'. The clinical experts clarified post-prandial glucose levels (PPG) are the target of insulin management in pregnancy, rather than HbA1c. Current practice is for pregnant women to take NovoRapid immediately pre-meal, however if they experience continued problematic PPG levels, the injection time would be moved back to 15-20 min pre-meal. It was anticipated that Fiasp, with a faster absorption profile would allow for better PPG control and would negate the need to push back injection time by ~15 minutes.

The Committee considered the evidence around three questions; (i) whether PPG targets are the most appropriate targets during pregnancy, (ii) the magnitude of improvement in PPG control required to be clinically meaningful in terms of maternal and foetal outcomes, (iii) the evidence supporting PPG level improvements with Fiasp during pregnancy.

NICE NG3 recommends a 1-hr PPG target of 7.8mmol/L and 2-hr PPG target of 6.4mmol/L. NICE formed this recommendation based on "very low quality" evidence from two separate studies (Rowan et al. 2010; Combs et al. 1992). The studies support a narrative that rates of adverse maternal and fetal outcomes (pre-eclampisa, large for gestational age babies) are higher/lower for patients with PPG lower/higher than the given thresholds. The narrative is supported by the HAPO study which found a linear relationship with 1-hr and 2-hr PPG and adverse outcomes in non-diabetic women. The Committee accepted PPG was the most appropriate target during pregnancy.

When assessing the magnitude of improvement in PPG required to be clinically meaningful, the Committee did not identify any relevant literature in patients with diabetes. The HAPO study reported the odds ratio for premature delivery (before 37 weeks) for an increase of 1.7mmol/L in 1-hr PPG level to be 1.18 (95% CI: 1.12-1.25). Similarly the OR for premature delivery for an increase of 1.3mmol/L in 2-hr PPG level to be 1.16 (95%CI: 1.10-1.23). The Committee accepted an improvement in PPG (either 1-hr or 2-hr PPG levels) in the magnitude of 1mmol/L was likely to result in a clinically meaningful reduction in the risk of adverse maternal or fetal outcomes.

The Committee noted an absence of pharmacokinetic, efficacy or safety data of Fiasp in pregnancy. This omission was considered particularly relevant as clinical experts had reported absorption of NovoRapid to be delayed during pregnancy therefore it remained entirely unknown whether Fiasp would offer any benefit in this population. The relevant data from non-pregnant adults in ONSET 1 study was re-reviewed; secondary endpoints included 1- & 2-hr PPG levels after a standard liquid meal test (80 g carbohydrate consumed within 12 min) after 26 weeks treatment. Results from this analysis showed Fiasp was associated with a lower PPG rise; between group difference from baseline was -1.18mmol/L (95% CI: -1.65 to -0.71) for 1-hr PPG levels and -0.67mmol (95% CI: -1.29 to -0.04) for 2-hr PPG levels. The Committee questioned the relevance of this outcome as 'standard liquid meal tests' are not applicable in the real world. The Committee explored other outcomes of interest and agreed SMBG measurements from 7-9-7-point profiles (pre- and postmeal, bedtime, and once at 4:00 A.M) on three consecutive days before the scheduled clinic visits at weeks 0 and 26 were more relevant. Results from these outcomes

found no significant difference in 7-9-7-points SMBG profiles (between group difference from baseline of -0.07mmol/L; 95% CI: -0.29 to 0.15) but most importantly, no significant difference in 2-hr PPG levels (between group difference from baseline of -0.15mmol/L; 95% CI: -0.43 to 0.12 [Supplementary Table 6]). Difference in 1-hr PPG levels (SMBG) was not reported.

In summary, the Committee agreed 1- & 2-hr PPG levels were relevant outcomes when managing diabetes in women who are pregnant. There were no data to support Fiasp in pregnancy, and if extrapolating data from non-pregnant adults, the non-statistically significant improvement in 2-hr PPG levels observed in ONSET 1 fell far below the clinically meaningful threshold. The Committee concluded there was evidence to support a claim of no benefit in this population, which provides stronger grounds for rejection than a lack of evidence to support benefit. No further appeals would be considered until comparative data of Fiasp and NovoRapid in pregnancy was available. The Committee upheld their original decision.

Decision: Not approved

4.2 APPEAL: Pembolizumab for treatment of urothelial cancer in patients ineligible for platinum-based chemotherapy

The Committee welcomed Dr Vilarino-Varela to the meeting to discuss the appeal to use pembrolizumab to treat urothelial cancer in patients who are ineligible to receive platinum-based chemotherapy. In November 2017, the JFC reviewed the evidence for use of pembrolizumab in this cohort of patients (KEYNOTE 52); pembrolizumab would be provided Free of Charge from the company. The Committee noted that atezolizumab, a PD-L1 binding agent, was already available for the same indication and funded via the Cancer Drug Fund, with NICE approval imminent at the time (a positive NICE TA was published later in November 2017), and therefore were of the view that pembrolizumab does not need to be added to the formulary for this indication. The Committee also noted the lack of head-to-head data to help direct choice between the two drugs.

Dr Vilarino-Varela requested that the committee reconsider its decision based on the precedent from NICE that multiple drugs be available for the same indication.

Dr Vilarino-Varela informed the Committee that she felt there was little difference between atezolizumab and pembrolizumab, and until phase 3 data are available it will be difficult to identify the difference between the two agents. Having both drugs available would provide clinicians with the option to select the agent based on preference or experience. She proposed a hypothesis that differences in the pharmacology between the two agents (pembrolizumab binds directly to PD-1, whereas atezolizumab binds to PD-L1 and PD-L2) may result in pembrolizumab being slightly more effective and in atezolizumab being slightly less immunogenic, however she acknowledged that there were no head-to-head data to confirm this hypothesis. Additionally, it is known that both drugs have the potential for autoimmune reactions. The Committee noted that a number of clinical trials are being set up in RFL for pembrolizumab, which will result in clinicians having more experience with this medicine.

The Committee discussed its role with regards to approving medicines for use ahead of alternatives with a positive NICE Technology Appraisal. As there was no way proposed to differentiate between patients who would receive atezolizumab or pembrolizumab, the Committee was of a view that to approve the pembrolizumab Free of Charge scheme would be inconsistent with its responsibility to ensure that a medicine without a positive TA not be recommended ahead of a medicine with a positive TA.

In summary, the Committee did not think that sufficient evidence had been provided to change its original decision. Additionally, it felt that to approve a medicine without a positive NICE TA ahead of atezolizumab would be inconsistent with its responsibilities with regards to NICE, therefore the Committee agreed that pembrolizumab should not be added to the joint formulary for this indication.

Decision: Not approved

5. Declarations of relevant conflicts of interest

There were no declarations of interest.

The Committee discussed whether payments made by Pharmaceutical companies to individuals were likely to influence that individual's decision making. The Committee agreed that payments were unlikely to have a significant impact for drugs with either a very large or no treatment effect; such decisions would be unambiguously 'yes' or 'no' respectively. However the Committee considered that payments may influence opinion on very marginal effects; supporters of a company (i.e. those who accept payments

from them) might perceive the overall risk-benefit more favourably than someone with no commercial interest. In the UK, the ABPI now discloses payments made to medical and other professionals on the ABPI website. Approximately 50% of medical professionals withhold permission to disclose their payments. The Committee agreed that applicants should be asked to make a detailed statement of their income from Pharmaceutical Companies, if it is not already disclosed to the ABPI. It was accepted that the JFC might need to amend its ToR to facilitate this disclosure.

6. Local DTC recommendations / minutes

6.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
RFL	Nov-17	Tolvaptan	SIADH if there is potential to cause a delay to the commencement of chemotherapy (NHS England: 16051/P)	Decision: Added to NCL Joint Formulary Tariff status: Excluded from tariff Funding: NHSE Fact sheet or shared care required: No
RFL	Nov-17	Vedolizumab	Ulcerative colitis and Crohn's disease in paediatric patients	Decision: Added to NCL Joint Formulary Tariff status: Excluded from tariff Funding: NHSE Fact sheet or shared care required: No
UCLH	Oct-17	Niraparib (compassionate access)	Relapsed platinum sensitive ovarian, fallopian tube or primary peritoneal cancer	Decision: UCLH only Tariff status: Excluded from tariff Funding: NA - FOC Fact sheet or shared care required: No

6.2 Approved under evaluation

DTC site	Month	Drug	Indication	JFC outcome
WH	Nov-17	Chloroprocaine (Ampres)	Spinal anaesthesia in adults where the planned surgical procedure should not exceed 40 minutes	Decision: Under evaluation at WH only

7. New Medicine Reviews

7.1 Terlipressin infusion for hepato-renal syndrome (Applicant: Dr K Moore, RFL)

The Committee considered an application to use terlipressin infusion (TERLI-INF) for hepato-renal syndrome (HRS). Current treatment of HRS uses terlipressin bolus (TERLI-BOL) which is consistent with the majority of the evidence base.

A meta-analysis by Cochrane found terlipressin to be effective at reducing mortality (RR = 0.85 [95% CI: 0.73 to 0.93], NNT to prevent one death = 10) and reversal of hepatorenal syndrome (RR for non-reversal of hepatorenal syndrome = 0.63 [95% CI: 0.48 to 0.82], NNT to reverse one case of hepatorenal syndrome = 4). There is no standardised dose schedule for terlipressin administration because of the lack of dose-finding studies, however the typical starting dose in the trials included within the Cochrane review was 1mg every 4-6 hours. Current practice at RFL is to use 0.5mg every 4-6 hours.

The Committee considered the evidence for TERLI-INF. Cavallin et al. (n=78) conducted an open-label, multicentre, non-inferiority randomised controlled trial comparing TERLI-INF to TERLI-BOL. Adult patients with liver cirrhosis and confirmed HRS were included. The starting dose of TERLI-INF was 2mg/day and 0.5mg every 4 hours for TERLI-BOL. Results found a lower proportion of patients developed a treatment-related AE with TERLI-INF compared to TERLI-BOL (35.29% vs. 62.16%; $p<0.025$). For the secondary endpoint of 'complete response' there was no significant difference between arms although data trended in the direction of favourable efficacy with TERLI-INF (55.88% vs. 45.95% [p=NS] for TERLI-INF and TERLI-

BOL respectively). Conflictingly, TERLI-INF was associated with a lower 90-day transplant-free survival (53% vs. 69%). In a separate analysis; 6 patients randomised TERLI-BOL experienced severe treatment-related AE at the lowest dose of 0.5mg every 4 hours and were started on TERLI-INF; all 6 patients tolerated treatment and developed a complete response. The study had a large number of methodological weaknesses; the principle concern was adverse effects (AEs) being the primary endpoint despite a lack of published evidence confirming the two interventions were equivalent in terms of efficacy (mortality and reversal of HRS).

The Committee heard from Dr Moore that he proposed to administer 0.5mg STAT followed by 2mg/24hr infusion. A patient would be reviewed for response after 8-12 hours; non-responders would be up-titrated. Patients with bleeding varices would still receive TERLI-BOL or emergency endoscopic treatment and would not be eligible for TERLI-INF. Terlipressin infusion is an unlicensed route of administration and the 24hrs stability is not documented in key reference sources. Work is underway to identify whether this method of administration can be supported.

The Committee were satisfied that TERLI-INF and TERLI-BOL were likely to be equivalent in terms of efficacy, and were reassured by the intensity of monitoring afforded to patients with HRS. The AE rate and serious AE rate were lower with TERLI-INF than for TERLI-BOL therefore the Committee approved the use of terlipressin infusion for hepato-renal syndrome. The approval was conditional on Pharmacy confirming 24hr stability of 2mg terlipressin in 50mL glucose 5%.

Post meeting note: Terlipressin is stable at a concentration of 2mg in 100mL glucose 5% when stored at room temperature for up to 24 hours in daylight/dark

Decision: Approved
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: No

7.2 Letrozole for ovulation induction (Applicant: Ms E Yasmin & Mr V Talaulikar, UCLH)

The Committee considered an application to use letrozole to induce ovulation in women with WHO Group II anovulation. It was proposed that letrozole would be used second line after failure of clomifene citrate, before use of gonadotrophin releasing hormone.

A meta-analysis of twenty-six RCTs (n=5,560 women) assessing the safety and efficacy of aromatase inhibitors (AIs) demonstrated that letrozole resulted in a higher live birth rate than other agents used in this indication (OR 1.64 [95% CI 1.32 to 2.01]. Pregnancy rate, a secondary outcome reported in 15 studies (n=2,816 women), was higher in for letrozole than it was for clomifene citrate (OR 1.4 [95% CI 1.18 to 1.65]). There was no statistically significant difference for miscarriage rate between AI and clomifene citrate (OR 1.32 [95% CI 0.92 to 1.88]). The rate of multiple pregnancies, which the committee discussed was a clinically meaningful outcome to consider, was lower for AI than for other agents (OR 0.38 [95% CI 0.17 to 0.84]); this difference was not sustained when only studies comparing AI to clomifene citrate were considered.

Additionally, the Committee consider the evidence from a UK-based DBRCT (n=159) comparing letrozole to clomifene citrate in adults with anovulatory infertility, which demonstrated that letrozole resulted in a higher pregnancy rate than clomifene citrate (rate ratio 1.4 [95% CI 1.1 to 2.0], p=0.022); rate difference for the two agents was slightly smaller than the minimally clinically important rate difference. A larger RCT (n=750) demonstrated a higher rate of live births with letrozole than with clomifene citrate (rate ratio 1.44 [95% CI 1.10 to 1.87), though the clinical importance of this was questionable. Notably, there were four congenital malformations reported in the letrozole arm, compared to zero in the clomifene citrate arm of this trial.

The Committee heard from Ms Yasmin, who highlighted a network meta-analysis (NMA) of fifty-seven trials (n=8,082 women) comparing treatment strategies for women with WHO group II anovulation. Specifically, this included twenty-one trials including letrozole (n=1,758), identifying that letrozole has a statistically significant superior pregnancy rate than clomifene citrate (OR 1.58 [95% CI 1.25 to 2.00]). The pregnancy rate for letrozole is superior to that for placebo (OR 5.35 [95% CI 2.63 to 10.87]). This NMA used live birth rate as a secondary outcome, demonstrating letrozole to be superior to clomifene (OR 1.67 [95% CI 1.11 to 2.49]). This study also confirmed that the rate of multiple pregnancies was lower for letrozole than for clomifene. It also reported the rate of congenital malformations from letrozole, which

ranged from 0% to 3.9% of trial participants; conversely the reported ranges for malformation following clomifene citrate were 0% to 4.8% in RCTs.

The Committee noted that there was inconsistency about the risk of malformation following treatment with letrozole to induce ovulation. Ms Yasmin acknowledged the concerns about the teratogenic potential of letrozole when used in this off-label manner, highlighting that the original study raising these concerns about letrozole was methodologically flawed and was no longer considered relevant. Ms Yasmin explained that women would only receive letrozole if they had a period or a negative pregnancy test to confirm that they were not pregnant. She expected that letrozole would no longer be in the system at the time of implantation. Additionally, the Committee was assured that women will be counselled on the risk of malformation arising from letrozole therapy, just as they currently are when treated with clomifene citrate. Ms Yasmin did not feel that the rate of malformations following treatment differed greatly from the background rate occurring following natural pregnancy.

Mr Minshull explained to the Committee that he had written to Novartis to ask them whether they still had concerns about the teratogenic potential of letrozole, but had so far not heard from them (see **Post-meeting notes** below).

The Committee considered the demonstrable benefits from treatment with letrozole, against the potential for foetal malformation that has been reported. The Committee were content that the applicant would ensure that patients are fully informed about the risks and benefits of using letrozole for ovulation induction; appropriate steps were being taken to ensure that women did not have letrozole administered when pregnant; and that potential malformations would be reported by the treating clinician to a national database to ensure shared learning. The Committee approved letrozole for use as a second-line option to induce ovulation in women with WHO group II infertility, following failure of treatment with clomifene citrate.

Post-meeting notes: Novartis has written confirming the letter it sent to healthcare professionals in 2005 to warn them about the risks associated with using letrozole outside its approved indications (specifically as a treatment for infertility). Novartis continues to draw attention to the fact that letrozole is contraindicated in pregnancy and in women with pre-menopausal endocrine status, and that it may cause congenital malformations and has been shown to cause reproductive toxicity in animals. Novartis has not indicated that it considers its original warning to be out of date.

Decision: Approved
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: No

7.3 Alectinib previously untreated ALK-positive advanced non-small-cell lung cancer (Applicants: Dr M Foster, UCLH)

The Committee considered an application to use alectinib first-line in the treatment of ALK-positive, advanced, non-small cell lung cancer. This application is for use in line with the licensed indication for the medicine. Alectinib was available for use as part of an approved EAMS scheme until it received its marketing authorisation in December 2017. Resultantly, the medicine is no longer available free of charge, but there are currently no funding arrangements in place; a NICE Technology Appraisal is anticipated in August 2018.

The Committee considered evidence from two, open-label, phase III, head-to-head trials comparing alectinib to crizotinib (a NICE-approved ALK-inhibitor) in adults with advance (stage IIIB/IV) NSCLC who had received no prior treatment. Peters *et al* (n=303) randomised patients to receive either alectinib 600 mg BD or crizotinib 250 mg BD. Progression free survival (primary efficacy outcome) favoured alectinib over crizotinib (HR 0.47 [95% CI 0.34 to 0.65], p<0.001). Time to CNS progression (a secondary outcome) was also longer with alectinib that with crizotinib (HR 0.16 [95% CI 0.10 to 0.28], p<0.001). It was notable that the overall survival data were immature so could not be used for decision making, though at data cut-off (maximum follow up 27 months for crizotinib and 29 months for alectinib) hazard ratio for death was not statistically different between the two treatment arms (0.76 [95% CI 0.48 to 1.20], p=0.24). Evidence from the second phase III trial (Hida *et al*, n=207) demonstrated similar findings in a Japanese population: PFS favoured alectinib (HR 0.34 [99.7% CI 0.17 to 0.71], p<0.0001). Objective response in patients with at least one measurable lesion was considered as a secondary outcome in this study, numerically favouring alectinib but with overlapping confidence intervals. Overall survival data were again immature.

The Committee noted that there are two alternative ALK-inhibitors available for the management of untreated, ALK-positive advanced NSCLC: crizotinib (recommended in NICE TA) and ceritinib (NICE TA expected January 2018; positive FAD). Although the head-to-head data comparing alectinib to crizotinib favoured alectinib in terms of progression free survival, the Committee was aware of its responsibilities with regards to NICE Technology Appraisals. Specifically, the Committee noted that approval of alectinib would position it ahead of crizotinib; to comply with the positive NICE TA for crizotinib the Committee must not recommend that a medicine without a positive NICE TA be used in preference to it. As a result, the Committee agreed that it was not in a position to recommend alectinib be used in this indication; this position will be reviewed when the NICE TA for alectinib first line in untreated, ALK-positive, advanced NSCLC is published.

Post-meeting notes: A positive NICE Technology Appraisal has now been published for ceritinib (untreated anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer in adults.

Decision: Not approved

8. Infliximab dose escalation in ulcerative colitis (UC) following a secondary loss of response to standard dose infliximab

The Committee considered a request from the Inflammatory Bowel Disease High Cost Drug working group to approve the use of dose-escalated infliximab following a secondary loss of response.

The Committee heard that dose-escalated infliximab and adalimumab are approved by NICE and considered best-practice in the management of Crohn's disease (CD), and similarly dose-escalated adalimumab is approved by NICE and is standard of care at UCLH for UC. Dose-escalated infliximab for UC is unlicensed therefore is not included within the relevant TA.

An LMEN evaluation identified three observational studies investigating the effects of dose-escalated infliximab in patients who developed a secondary loss of response to standard dose infliximab. All studies used infliximab dosed at either 10mg/kg every 8 weeks, or 5mg/kg every 4-6 weeks. Taxonera et al. (n=79) found dose-escalating infliximab resulted in 68.4% achieving a clinical response at 12 weeks and of those, 74.0% achieved sustained benefits (median follow-up was 15 months). Similarly, Cesarini et al. (n=41) found a clinical response rate of 90.2% at 4-8 weeks and of those, 68.3% maintained clinical remission at 12 months. Yamada et al. (n=17) reported 94.1% achieved and maintained clinical remission with dose-escalated infliximab.

It was unclear how many patients would require dose-escalated infliximab. The Inflammatory Bowel Disease High Cost Drug working group would estimate numbers and the CSU would include these in the pathway cost impact assessment which would be presented to CCGs.

The Committee provided clinical approval for dose-escalated infliximab (max. 10mg/Kg every 8 weeks, or 5mg/Kg every 6 weeks) following a secondary loss of response to standard dose infliximab. Funding approval was to be sought as part of the pathway cost impact assessment completed by the CSU.

Decision: Clinically approved, pending funding approval (through IBD HCD pathway which is under development)
Prescribing: Secondary care only
Tariff status: Excluded from tariff
Funding: CCG
Fact sheet or shared care required: No

9. Biosimilar intravenous trastuzumab patient information leaflets (PILs) and implementation plan

The first IV biosimilar trastuzumab is expected to be available from February 2018 with a further two available by June 2018. SC Herceptin remains patent protected.

NCL data shows a total Herceptin spend of approximately £3.5 million with approximately 30% being the intravenous product and 70% the subcutaneous product. The proportion of IV:SC is similar across all four Trusts (UCLH, RFL, NMUH and WH).

The proposal to switch patients from IV Herceptin to IV biosimilar trastuzumab has received a positive reception from clinical leads at RFL and UCLH. The process of switching is a relatively simple process and no significant barriers to implementation are expected. JFC Support will work with Trusts to share best practice and expedite the process.

SC and IV routes of trastuzumab are clinically equivalent therefore the availability of IV trastuzumab raises the possibility of transitioning patients from SC Herceptin to IV biosimilar trastuzumab. This proposal would have implications for the patient experience. The "go / don't go" decision was likely to be dependent on overall savings (drug savings net increase in production costs), production capacity and outpatient infusion clinic capacity amongst other factors.

The Committee agreed to proceed with IV biosimilar trastuzumab in two phases:

- Phase 1: All Trusts switch IV Herceptin to IV biosimilar trastuzumab as soon as practicably possible.
- Phase 2: All Trusts to develop a resource impact assessment of switching SC Herceptin to IV biosimilar trastuzumab. This should be reviewed at a board level for a decision on whether to conduct this switch.

Current practice across NCL is for SC Herceptin to be administered in clinic, rather than patients' homes. Dr Hughes reported that home administration of chemotherapy has been considered however the costs for home administration are similar to Day Unit administration, and patients with malignancies appear to prefer to come to clinic.

The Committee heard that treatment courses of trastuzumab (SC and IV) were approximately 3-6 months. ***Post meeting note: treatment courses are for 1 year [early breast cancer] or until treatment progression [metastatic breast cancer] which on average is 14 months (95%CI: 11 to 16 months).***

The Committee reviewed a draft patient information leaflet (PIL) for patients switching from IV Herceptin to IV biosimilar trastuzumab. The PIL was originally developed by the Cancer Vanguard and had been updated by The Royal Marsden and JFC Support. The Committee agreed to circulate the draft PIL to stakeholders within their organisation for comment. The updated PIL would be approved by Chair's Action outside the meeting and added to the NCL MON website.

10. Low Value Items

Mr Minshull informed the Committee that he had distributed drafts of the following NCL JFC "non-formulary" Position Statements following publication of NHS England guidance on "Items which should not routinely be prescribed in primary care":

- Co-proxamol tablets
- Glucosamine & chondroitin supplements
- Herbal supplements
- Homeopathy
- Lutein and antioxidants
- Omega-3 Fatty Acids
- Rubefacients

Mr Minshull requested that comments should be received before publication on 21 January.

11. Summary of MHRA Alerts for Bisphosphonates and Denosumab

Mr Minshull presented a summary of MHRA Alerts for Bisphosphonates and Denosumab. This was compiled following a recent study that highlighted that UK general practitioners have limited knowledge about bisphosphonate-related osteonecrosis of the jaw, and that MHRA recommendations were often not being followed when patients were initiated on bisphosphonates.

This summary has been compiled to aid in any local development of information for GPs or community pharmacists about the risks from these commonly used medicine. It can also be shared with other prescribers (e.g. rheumatology, care of the elderly, oncology) in NCL who initiate or review bisphosphonate treatment.

12. Glaucoma Guidelines (MEH)

The Committee noted that a minor amendment had been made to the previous version. Carteolol 1% and 2% eye drops previously appeared for restricted use only, but have been removed following discontinuation of this product.

Guideline approved.

13. **JFC Work plan**

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

14. **Next meeting**

Monday 19 February 2018, G12 Council Room, South Wing, UCL, Gower St. WC1E 6BT

15. **Any other business**

Amitriptyline – the marketing authorisation for some generic amitriptyline tablets have been updated to include neuropathic pain in adults as an indication. As these are now licensed, the line warning about "off-label" indication will be removed from related NCL documents about neuropathic pain.