North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Monday 16 April 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	
	Dr R Woolfson	RFL, DTC Chair	
	Dr M Kelsey	WH, DTC Chair	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Dr R Tahlil	Haringey CCG, GP Clinical Lead Medicines Management	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Mr S Richardson	WH, Chief Pharmacist	
	Ms K Davies	NEL CSU, Deputy Director Medicines Management	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Dr D Hughes	RFL, Consultant Haematologist	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Dr F Gishen	RFL, Palliative Care Consultant	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
In attendance:	Mr A Barron	NCL JFC, Support Pharmacist	
	Mr J Minshull	NCL JFC, Support Pharmacist	
	Dr P Bodalia	UCLH, Principal Pharmacist	
	Ms M Kassam	MEH, Formulary Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Ms S Sanghvi	UCLH, Formulary Pharmacist	
	Mr S O'Callaghan	UCLH, Formulary Pharmacist	
	Dr R McMillan	UCLH, Oral Medicine Consultant	
	Dr S Huq	UCLH, Clinical Pharmacology Consultant	
	Dr L Yew	NMUH, Oncology Consultant	
	Ms A Cummins	NMUH, Oncology Pharmacist	
	Mr S Cheesman	UCLH, Oncology Pharmacist	
Apologies:	Mr G Kotey	NMUH, Chief Pharmacist	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	M S Semple	MEH, Interim Chief Pharmacist	
	Dr A Sell	RNOH, DTC Chair	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr T Dean	Patient Partner	
	Ms L Reeves	C&I, Chief Pharmacist	
	Dr M Dhavale	Enfield CCG, GP Clinical Lead Medicines Management	
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr A Mian	NMUH, Clinical Director for Specialty Medicine	
	Mr C Daff	NHS Barnet, Head of Medicines Management	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	

2. Meeting observers

Dr Huq and Mr O'Callaghan were welcomed as observers to the meeting.

3. Minutes of the last meeting

The draft minutes had not been circulated sufficiently in advance to allow committee members to review. Members were asked to send any points of clarification to Mr Barron by 23 April 2018. The full and abbreviated minutes would be approved after this point if comments have not been received.

4. Abbreviated minutes of the February 2018 meeting

The abbreviated minutes from February 2018 were approved.

5. Matters arising

5.1 Freestyle Libre® - London implementation of the RMOC guidance for Type 1 diabetes

The Committee modified their recommendations from the February 2018 meeting to reflect that people living with diabetes who are unable to test (e.g. those living with physical or mental disabilities) could be candidates for a trial of Freestyle Libre. This was pragmatic view and was not based on published evidence. The February 2018 minutes would be updated to reflect this.

5.2 Alectinib in anaplastic lymphoma kinase (ALK) +'ve advanced non-small-cell lung cancer (NSCLC) [APPEAL]

In January 2018 the JFC had considered an application for alectinib to be added to the formulary for previously untreated ALK-positive advanced non-small-cell lung cancer. The Committee had considered the published clinical trial data from two open-label, phase III studies of alectinib compared with crizotinib, noting that progression free survival favoured alectinib and crizotinib, and time to CNS progression (a secondary outcome) was longer with alectinib than with crizotinib. In January 2018, the JFC noted that overall survival data were immature and therefore could not contribute this endpoint as part of the decision making process. Additionally, two alternative ALK-inhibitors were available for the management of the same condition and had NICE approval (crizotinib) or had imminent NICE approval (ceritinib); the Committee agreed that it was not in a position to recommend a medicine ahead of a NICE approved technology. Finally, at the time of discussion, alectinib had neither funding approval through the Cancer Drugs Fund, nor was there a Free of Charge scheme; therefore a significant cost-impact had to be taken into account.

Dr M Forster (Consultant Oncologist, UCLH) sent an appeal *in absenti*a based on the existence of a new Free of Charge Scheme. He also requested that the Committee reconsider the evidence of alectinib efficacy in CNS disease on the basis of new data showing a signal of superior activity. Furthermore, it was proposed that the tolerability of alectinib compared to crizotinib and ceritinib was also positive. On the basis of these two favourable points the Committee considered the proposal to make alectinib a first line option.

The Committee noted the alectinib Free of Charge Scheme in operation by Roche Pharmaceuticals, and were reassured that use of alectinib did not represent a cost-pressure to the local health economy. The Committee also discussed an update to NICE policy on local formularies recommending non-NICE approved medicines ahead of approved medicine. In contrast with the previous guidance, local formularies are permitted to indicate a preference for medicines without a positive NICE TA provided medicines with a NICE TA are available without additional restrictions. The Committee was satisfied that it would not be acting outside of its obligations if it were to approve alectinib in this indication.

Finally, the Committee reconsidered the evidence provided by Peters *et al* (2017) in the open-label RCT considered in January. The Committee noted that CNS metastases and prior treatment were well-balanced at baseline in a subset of the overall trial population (40%). The time to CNS progression (defined as time from randomisation to first radiographic evidence of CNS progression, including new or progressed baseline lesions) favoured alectinib over crizotinib (HR 0.16 [95% CI 0.10 to 0.28, $p<0.001$]); during the follow-up period, CNS progression rate was 12% in alectinib compared to 45% in crizotinib, with a twelve-month cumulative CNS progression of 9.4% (alectinib) vs. 41.4% (crizotinib). The Committee noted that it is important to be cautious when interpreting this surrogate outcome as tumour volume does not always correlate well with overall survival and patient experience.

Addressing comparative tolerability of alectinib, crizotinib and ceritinib, the Committee noted that clinical trial data were not available for alectinib versus ceritinib, therefore adverse event rates were compared

for crizotinib versus alectinib, and an indirect comparison was made using adverse event rates for ceritinib in a trial comparing it to chemotherapy in a similar patient cohort. The Committee noted that although the overall rate of grade 3 to 5 adverse events was slightly lower for alectinib than crizotinib (41% vs. 50%), the serious adverse event rate (28% vs. 29%) and fatal adverse event rate (3% vs. 5%) were similar for both drugs. However, adverse events likely to have a serious impact on a patient's experience of therapy were far more common for crizotinib than alectinib: nausea (48% vs. 14%), diarrhoea (45% vs. 12%) and vomiting (38% vs. 7%). Rates for these adverse events with ceritinib are 85% (diarrhoea), 69% (nausea) and 66% (vomiting).

In summary, the Committee was satisfied that alectinib was likely to be more effective than criztonib, and better tolerated than both crizotinib and ceritinib. It was satisfied that approval of a free of charge medicine first line ahead of NICE TA approved medicines would not be inconsistent with its duties with regards to the NICE approved medicines as long as no additional barriers were put in place to restrict access to the NICE approved medicine. The Committee therefore agreed to add alectinib for the first line treatment of previously untreated ALK positive advanced NSCLC to the NCL Joint Formulary, in line with the Free of Charge scheme provided by Roche. This position will be reviewed when the NICE TA for alectinib is published.

Decision: Approved
Prescribing: Secondary care only
Tariff status: Free of Charge scheme
Funding: Free of Charge scheme
Fact sheet or shared care required: No

Post-meeting note: It was clarified that the applicant's intention is to offer alectinib first line for all patients rather than just those who have CNS involvement at baseline.

6. JFC Work Plan & outstanding actions

6.1 Outstanding action: Oral ketamine for acute pain [August 2017]

In August 2017 Dr Ishaq offered to support RFL in the development of a data collection form for an evaluation of oral ketamine in acute pain. Data from this evaluation was requested for review at JFC. Ms Samuel had asked the RFL acute pain consultants to share their data collection form with Dr Ishaq however Dr Ishaq had not received the form. The RFL evaluation is already underway so this action was closed.

6.2 Outstanding action: Treatment pathways for oral mucosal inflammatory disease [June 2017]

The treatment pathway for the oral mucosal inflammatory disease had been reviewed at JFC in February 2018; JFC/UCLH DTC were undertaking a programme of work to review the non-formulary medicines listed on this pathway. This action was closed.

6.3 Outstanding action: Low-flow vascular malformations [January 2018]

The RFL approval of 'Sirolimus for arteriovascular malformation – low flow' is more accurately described as 'Sirolimus for low-flow vascular malformations in the head and neck' and minutes have been updated to reflect this. UCLH approved bleomycin sclerotherpy for the same indication in February 2018 (ratified at JFC in March 2018) however the Committee agreed the evidence base was insufficient to recommend one therapy over another. Both drugs would remain restricted to the respective sites. This action was closed.

6.4 Outstanding action: Catheter directed therapy for DVT, high risk PE and intermediate risk PE

Work was ongoing at UCLH to evaluate the role of catheter-directed therapy and a summary would be brought back to the Committee.

6.5 JFC Work Plan

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

7. Declarations of relevant conflicts of interest

There were no declarations of interest.

8. Local DTC recommendations / minutes

8.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Feb-18	Cinacalcet	Complex primary	Decision: Added to NCL Joint Formulary

			hyperparathyroidism in adults in line with NHSE clinical commissioning policy 16034/P	Prescribing: Secondary care only Tariff status: Included Funding: Trust Fact sheet or shared care required: No

9. New Medicine Reviews

9.1 Colchicine (off-label) for oral mucosal inflammatory disease (Applicant: Dr R McMillan, UCLH)

The Committee considered an application to use colchicine for 'Recurrent apthous stomatitis (RAS)' and 'Oral ulceration in Behcet's disease'; two types of oral mucosal inflammatory disease.

The Committee first considered the evidence for RAS. A Cochrane review concluded that no single treatment was found to be effective. A randomised, controlled, 'partially' blinded trial compared the efficacy of clofazimine, colchicine 0.5 mg TDS, and placebo for RAS (n=66). Results at 6 months showed that the percentage of individuals who had no further ulcerative episodes after beginning treatment with placebo and colchicine were not significantly different (p=1). The Committee considered that the negative result was potentially a consequence of the high rates of 'treatment interruption' due to intolerance with colchicine initiated at 0.5 mg TDS (61% by month 6). The study was not powered for a comparison of colchicine to placebo. A second randomised, controlled, active-comparator, double-blinded study compared the efficacy of colchicine 0.5 mg daily and prednisolone 5 mg daily for RAS (n=34). Results at 3 months showed both arms experienced significant improvements from baseline, however no significant differences were found between the two groups in degree of pain and burning sensation (p=0.209), number of RAS per each patient (p=0.673), size of lesions (p=0.947) and recurrence during treatment (p=0.171). All patients remained on treatment for the three month investigative period. Two retrospective observational analyses support the use of colchicine for RAS, the longest of which had a mean follow-up of 4.7 years revealed 31% had still improved with colchicine treatment.

The Committee then considered the evidence for oral ulceration in Behcet's disease. A Cochrane review concluded there was insufficient evidence to support or refute the use of any intervention for Behcet's disease. A 4+4 month, randomised, controlled, double-blind cross over study assessed the effectiveness of colchicine 1mg daily and placebo for Behcet's disease (n=169). The primary outcome was a comparison of a composite scoring system for the symptoms of Behcet's disease ('Iranian Behcet's disease dynamic activity measure'; IBDDAM). At baseline all patients had oral ulceration. Results after 4 months of each treatment showed IBDDAM scores for the colchicine arm improved from baseline (mean 3.55 to 2.75, p<0.001) and did not change with placebo (mean 3.17 to 3.63; p=NS); the between group difference was significant (p<0.001). The Committee heard the IBDDAM score was not used in clinical practice and may not be a validated measure of disease. A second 24-month, randomised, controlled, double-blinded study assessed the effectiveness of colchicine [dose adjusted for body weight; 0.5 mg BD to QDS] and placebo for Behcet's disease (n=56+60=116). At baseline, all patients had oral ulceration. Results at 24 months showed no difference in the 'time to complete resolution of oral ulceration' as almost all had ulceration within first 4 months of the study. There were also no differences in the mean number of oral lesion between colchicine and placebo that occurred over the whole study period; female patients (15.6 vs. 21.3 ulcers for colchicine and placebo respectively [p=0.136]), male patients (25.7 vs. 24.9 ulcers [p=0.492]).

Adverse effects reported in the clinical trials were predominantly gastrointestinal, however more serious adverse effects were listed in the SPC; renal damage, hepatic damage and bone marrow depression. The Committee heard colchicine is only licensed for short-term use, however it is routinely used long-term for familial Mediterranean fever (amyloidosis). Dr McMillan informed the Committee that long-term use of colchicine for RAS and oral Behcet's disease is established practice at UCLH and in his personal experience, approximately one third of patients respond to treatment. With regards to monitoring, the patient numbers fall below the threshold for development of a shared care guideline, therefore patient specific care plans communicated via clinic letters would be required. Dr McMillan reassured the Committee that responsibility for prescribing would not be transferred until patients are stable (approximately 3 months after initiating therapy) and the ongoing monitoring requirements were not onerous; FBC, U&E, LFTs at 3 months, 6 months and then annually. If any parameter fell out of range, his letters include a direct clinic phone number for GPs to obtain advice.

In camera, the Committee noted the inconsistent evidence-based however when considering the limited alternative therapeutic options, unpleasantness of the condition, limited patient numbers and low treatment costs, the Committee agreed the benefits outweighed the risks and agreed to add colchicine for oral mucosal inflammatory conditions to the NCL Joint Formulary.

Decision: Approved
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Primary and secondary care
Fact sheet or shared care required: No
Other notes: Starting dose 0.5mg OD, increase to 0.5mg TDS if tolerated. Transfer of care to GPs after stabilisation in secondary care. Monitoring requirements to be communicated to the GP via letter. Monitoring requirements are FBC, U&E and LFTs at 3 months, 6 months and then annually, CK only if myalgia.

Post meeting note: The National Amyloid Centre was contacted to establish their monitoring criteria for long-term colchicine when administered at doses 1-2 mg daily (max. 3 mg daily). They report "We have seen remarkably few problems with life-long use. We advise FBC, U&E and LFTs at 3 months, 6 months and then annually. We have stopped doing routine CK as it was not informative unless evidence of muscle aches. We've very rarely pulled the dose back for a transaminase rise but almost all dose limiting side effects are GI - mostly diarrhoea and less often nausea. We advise to be very careful with drugs that inhibit the efflux pump - especially clarithromycin and azoles, we are careful with CYA but use with renal transplants and favour statins with wider metabolism such as fluvastatin or pravastin (but lots of patients are on atorvastatin with no difficulties)". Dr R McMillan agreed to adhere to these recommendations and had amended his department protocols accordingly.

9.2 Dapsone (off-label) for oral mucosal inflammatory disease (Applicant: Dr R McMillan, UCLH)

The Committee considered an application to use dapsone in three oral mucosal inflammatory conditions: mucous membrane pemphigoid (MMP), recurrent aphthous stomatitis (RAS) and linear IgA bullous dermatosis. Dapsone is off-label in all these indications. The Committee noted the lack of high quality evidence to support dapsone use in any of these indications, though acknowledged this was due to the relative rarity of the conditions.

The Committee first considered the evidence for MMP. No randomised controlled trial evidence looking at impact of dapsone on oral ulceration in MMP was found. A Cochrane review from 2003 reported a number of case studies and series where dapsone has proved efficacious at inducing skin and lesion healing. The only RCT trial evidence identified by this review was for ocular MMP (as opposed to oral disease). In addition to the Cochrane review, a further structured review conducted in 2009 failed to identify any RCT evidence, but reported that in seven case series of patients treated with dapsone for MMP (n=202 patients), 84% showed clinical improvement on dapsone. The largest single series included 69 patients and showed a success rate of 45% with dapsone monotherapy and a further 42% success when cyclophosphamide or azathioprine combination was used. The extent of oral involvement was not reported in this study. One prospective, open-label, uncontrolled study (n=17 received dapsone) of patients with oral manifestation of MMP who did not respond adequately to topical treatment demonstrated that fifteen patients had a good response to dapsone (ten patients had total resolution, five had >75% improvement). A retrospective chart review of 20 patients with MMP who were seen at an Oral Medicines department was also considered. Eleven of these twenty patients didn't respond to initial topical steroid treatment and went on to receive dapsone in an increasing dose regimen, all of whom went on to benefit from dapsone treatment: 7 had total response, 4 had greater than 75% response. It was noted that two patients discontinued due to haemolytic anaemia and methemoglobinaemia.

The Committee considered the evidence for RAS. A Cochrane review (2012) failed to find any studies of suitable methodological quality for dapsone in this indication. The Committee considered the findings of a double-blind, unpowered, twelve-week, placebo controlled trial that demonstrated improvement in oral symptoms (using an unvalidated scale: "oral clinical manifestation index or "OCMI") from dapsone and zinc sulphate compared to a glucose-based placebo. After twelve weeks of treatment, zinc sulphate was associated with the numerically largest reduction in OCMI (11.93±1.39 to 0.93±2.46), followed by dapsone (10.87±1.41 to 2.80±4.18). Glucose had the smallest reduction in OCMI (10.80±1.42 to 8.67±4.20). This difference was statistically significant at week 12.

The Committee considered the evidence for Linear IgA Dermatitis. There were no clinical trial data available for dapsone in this indication. There were two retrospective reviews and a number of case studies considered by the Committee; outcomes from these studies were not reported in a standardised format, though show that the majority of patients included responded to dapsone therapy. In one large retrospective review (n=19), dapsone was found to be a largely effective intervention, though oral manifestations were only described in 2 cases. Lesions healed after mean 10 days of treatment in 11

cases and requiring adjunct with steroid in 8 cases. Eight cases required prolonged treatment (mean duration 38 months, range 2 to 5 years).

The Committee considered the monitoring requirements for dapsone, noting that there are a variety of regimens in use. It was noted that the monitoring regimen used for patients receiving dapsone for HIV opportunistic infections is likely to be unnecessary in this cohort of patients due to the fact that enhanced monitoring is used in HIV because of the increased likelihood of oxidative haemolysis caused by antiretroviral medication. Dr McMillan explained that the unit at the Eastman Dental Hospital already employs a monitoring regimen that could be used by GPs if prescribing is transferred to primary care following specialist initiation.

In camera, the Committee was satisfied that the available evidence was sufficient to justify prescribing dapsone for these three indications. Although studies were small (often single cases) and of poor quality, it was recognised that according to the Eastman Dental Hospital pathway, dapsone will be used in only a small number of patients with unpleasant conditions. The Committee agreed the benefits outweighed the risks and agreed to add dapsone for oral mucosal inflammatory conditions to the NCL Joint Formulary.

Post meeting note: Eastman Dental Hospital monitoring recommendations for dapsone are for FBC and reticulocyte count weekly for four weeks, monthly for 6 months, then every 3 months thereafter. LFTs should be monitored monthly for 3 months, then every 3 months thereafter for duration of therapy.

[UPDATE September 2020]
Post meeting note: Eastman Dental Hospital monitoring recommendations for dapsone are:

- ***Initially: FBC, LFTs and reticulocytes:***
    - ***weekly for four weeks***
    - ***monthly for 3 months***
    - ***then every 3 months thereafter***
- ***After a dose increase: FBC, LFTs and reticulocytes at weeks 2, 4 and 8***

Decision: Approved
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Primary and secondary care
Fact sheet or shared care required: No
Other notes: Typical dose 50mg to 200mg daily. Transfer of care to GPs after stabilisation in secondary care. Monitoring requirements to be communicated to the GP via letter. Monitoring requirements are detailed above.

10. Biosimilar trastuzumab (intravenous) for all indications where originator intravenous trastuzumab (Herceptin®) is commissioned

Biologic medicines are made in living cells therefore changes to the manufacturing method can lead to changes in the final molecule; regulators carefully monitor these changes to ensure a change does not impact on the way the drug works. The amount of supportive data required to retain approval, following a manufacturing change, varies with the level of risk. However following any change, the originator must prove it is equivalent to the molecule originally approved by regulators. There have been 23 moderate risk and 2 high risk changes to Herceptin since the original molecule was licensed.

The term 'biosimilar' is a regulatory term that describes how a biologic medicine obtains its license, which shares similarity to how the originator product *retains* rather than *obtained* its license. To obtain a license, the originator biologic needed to establish how safe and how effective it was, which required several large clinical trials. However for a biosimilar, the emphasis is on establishing how similar it is to the originator. By showing a biosimilar is essentially the same molecule as the originator, which is best done through analytical methods, the role of the clinical data becomes less important and is the 'final step' in the data gathering exercise. If the molecule is the same, it stands to reason that everything that applies to the originator, will apply to the biosimilar too. The final step in the biosimilar licensing process is known as 'extrapolation' which occurs after the regulator is confident similarity has been demonstrated and grants licenses in populations in which the biosimilar has not been studied. In the case of biosimilar trastuzumab, Phase III studies were carried out in Early Breast Ca, and the license was extrapolated to Metastatic Breast Ca and Metastatic Gastric Ca.

Three biosimilar intravenous trastuzumab medicines have received positive CHMP opinions; Ontruzant® (SB3; MSD), Herzuma® (CT-P6; Napp) and Kanjinti® (ABP 980; Amgen). The Committee considered which of these agents were preferred and when the switch should occur.

The Committee acknowledged that the majority of evidence supporting the claim of biosimilarity for the three biosimilar medicines was pre-clinical (analytical) and the Committee put trust in the EMA to evaluate this data. Phase I pharmacokinetic and pharmacokinetic studies for all three medicines were very similar and concluded bioequivalence.

The individual Phase III studies differed only slightly in study design; all recruited patients using trastuzumab + chemotherapy in the neoadjuvant setting and the primary endpoint was pathologic complete response. The chemotherapy regime used deviated from the UK standard in the Kanjinti study only. The study investigating Ontruzant included breast only in the primary endpoint, whereas the Herzuma and Kanjinti studies included patients with breast and lymph nodes (Ontruzant included breast and lymph nodes as a secondary endpoint). Similarity was considered demonstrated if the 95% CI of the absolute difference in the bpCR rate (a surrogate endpoint) between treatments was contained within the predefined margin of ± 13% (± 15% in the case of Herzuma).

- Ontruzant had upper 95% CI above the upper bound (i.e. trending towards superiority) however the EPAR identified a plausible reason for this finding and concluded Ontruzant was equivalent (and not superior). This is confirmed by very similar event-free survival data at 12 months.
- Herzuma fell within the predefined margins
- Kanjinti fell within the predefined margins for the 'central independent review' analysis

The Committee heard from Dr Yew that the differences in the studies would not have a meaningful impact on the within trial comparison of each biosimilar to Herceptin. The Committee agreed the small differences in the study designs and results did not alter the conclusion that biosimilarity had been demonstrated for all three biosimilars. Subsequently no one biosimilar was preferred over the others in terms of safety and efficacy. Dr Yew queried whether the biosimilars could be used in combination with pertuzumab; it was confirmed that pertuzumab is licensed "in combination with trastuzumab" not "in combination with Herceptin" and further, the EMA were satisfied there were no meaningful differences between each biosimilars and Herceptin, therefore the trial data for pertuzumab in combination with Herceptin may be extrapolated to pertuzumab in combination with biosimilar trastuzumab.

The Committee discussed other considerations; including time to availability of extended stability data, whether the regulators had concerns with manufacturing sites, vial sizes, whether the company had experience with biosimilars, whether NCL was over reliant on any one biosimilar manufacturer, costs and the opportunity-lost from choosing a product which was not yet available. The Committee agreed the opportunity-lost for waiting for the Kanjiniti could not be justified. The choice between Ontruzant and Herzuma was more marginal, however Herzuma was preferred overall.

In summary, the Committee approved Herzuma as the intravenous biosimilar trastuzumab of choice in NCL for all commissioned indications (early breast cancer, metastatic breast cancer and metastatic gastric cancer). NHSE MO CQUIN requires all Trusts to switch from intravenous Herceptin to intravenous biosimilar trastuzumab in 2018/19, however switching quickly will yield additional savings to the health-economy and was strongly encouraged.

11. Results from evaluation: Brivaracetam for partial epilepsy

This item was deferred.

12. Guideline for approval: Gender Dysphoria Shared Care - triptorelin

The Committee was asked to ratify a Shared Care Guideline that has been produced by the UCLH Gender Identity Service, which forms part of the Paediatric and Adolescent Endocrinology Service. The Committee was informed that this shared care guideline had been produced to support this highly specialised service to comply with the commissioning policy published by NHS England [E13/2(HSS)/e *Gender Identity Development Service (GIDS) for Children and Adolescents*], specifically:

"*GPs [to] prescribe and monitor any physical treatments; Paediatric Endocrine Liaison Clinic will supply a shared care agreement and respond to any queries or concerns around this."*

Only two specialist centres in England are commissioned to provide this service (UCLH and Leeds). The UCLH Paediatric and Adolescent Endocrinology Service has to date been working against a shared care guideline for gonadotrophin-releasing hormone analogue (GnRHa, triptorelin) they had developed to meet this requirement, however, the NCL Shared Care and Fact Sheet Group had been asked by the NCL

Heads of Medicines Management to take the guideline through the local approval process to formalise the process.

The Committee noted that use of triptorelin to suppress puberty in adolescents who meet the diagnostic criteria for gender dysphoria / incongruence is supported by an international, evidence-based, clinical practice guideline published by The Endocrine Society (Hembree *et al*. *J Clin Endocrinol Metab* 2017; 102(11)). A recent systematic review (Chew *et al*, *Paediatrics* 2018; 141(4)) of hormonal treatment used in young people with gender dysphoria identified few studies of GnRHa used in this indication (n=9), all of which are observational, and suffered from significant loss to follow-up due to their retrospective nature. GnRHa were effective at decreasing testicular volume in natal males and stopping menses, decreasing LH and FSH in natal females. They are associated with significant improvements to psychological measures, though impact on anger and anxiety are unclear and conflicting. GnRHa does not affect symptoms of gender dysphoria.

The Committee recognised that prescribers have a concern about the long-term risks associated with administering GnRHa to adolescents. The Committee considered the findings of Chew *et al* (2018) with regards to impact on bone mineral density (statistically significant decrease in lumbar spine BMD z-score, non-significant reduction in hip and femoral region absolute and z-score BMD); and impact on growth and body composition (velocity of growth decreased compared to pubertal peers, with more impact on younger children). No changes to carbohydrate or lipid metabolism were seen after one year of treatment, ALP reduction was seen in one study (likely due to reduced bone turnover) and a small number of patients (n=8 natal males) had deterioration in mental functioning.

The Committee was sympathetic that this NHS England commissioned service includes a requirement that GPs prescribe treatment as part of this highly specialised service. Individual GPs will rarely be asked to take on prescribing under this shared care due to the rarity of the condition, therefore it was requested that the guideline move from an "assumed acceptance" by the GP to an "active acceptance" to give them sufficient time to consider how they will support patients. Practice nurses are likely to be asked to administer this treatment, therefore it was requested that time is given to consult the CCG Practice Nurse leads about this guideline.

The Committee contemplated the proposal that prescribing could be undertaken by the hospital, with practices asked only to administer the medicine. The Committee agreed that this did not represent good medicines governance as the person administering would not be able to guarantee adequate storage of the medicine; this is compounded by the difficulty that arises from the UCLH service seeing patients from across England. It was acknowledged that the team at UCLH is currently operating a system like this, but the new version of the guideline is moving away from that approach.

There was a request that the Paediatric Endocrinology Liaison Service keeps hold of prescribing responsibility of the GnRHa for at least three months to allow side effects from treatment to manifest. Mr Minshull explained that this would put a significant burden on the clinic that they do not have the capacity to meet; currently GPs are often taking over prescribing of the initial injection. Additionally, it is expected that short-term adverse events are likely to manifest quickly after the first injection due to initial block of hormones.

The Committee agreed to allow time for the actions discussed above to be addressed before seeking approval of the guideline. The Committee agreed that they would raise the concerns about the need for this guideline with NHS England Specialised Commissioning as it felt that this kind of shared care guideline would be better developed by the commissioner of the service (NHS England) rather than by a local area prescribing committee.

Post-meeting notes: Camden CCG requested that additional information be included in the Shared Care Guideline to advise GPs of the steps that have been taken to ensure the person being treated has appropriate competence to make decisions about the therapeutic and inadvertent effects from GnRHa.

Actions: Mr Minshull to liaise with the UCLH Paediatric Endocrinology Service to find out how the Leeds service manages shared care. Amendments to be made to Shared Care Guideline to change to "Active Acceptance" by the GP rather than assumed acceptance; impact on the Endocrinology Service to be discussed. Line to be added to assure GPs that appropriate assessment of competence of the adolescent to make decisions has been carried out. JFC Support Pharmacists to write to NHS England on behalf of the Committee to highlight the challenge that the commissioning policy places on the Endocrinology Service, on GPs, and on the Area Prescribing Committee.

13. Guideline for approval: Perampanel Fact Sheet

Mr Minshull presented to the Committee an update to the Perampanel Fact Sheet that had been put together by UCLH. Ms Clark informed the Committee that there remained a question about how frequently neurologists are reviewing patients on perampanel and who is taking responsibility for stopping medication. Mr Minshull agreed to ascertain with the Fact Sheet authors that these points had been addressed.

The Committee approved this Fact Sheet pending resolution of these two outstanding questions.

Post meeting notes: Mr Minshull liaised with the guideline author and Camden CCG regarding these two points and it was agreed that the neurologist reviews patients every 4 to 6 months initially, but that this may reduce in frequency according to clinical need. GPs may be called upon to stop perampanel if required urgently, but should be able to discuss with a neurologist if they have any concerns. As this is a Fact Sheet rather than Shared Care Guideline, the information on frequency of monitoring is provided as an indication to the GP; if patients require support outside what is already planned for them, they should be reviewed/referred as appropriate. It was agreed that no further amendment to the Fact Sheet is required. The Fact Sheet has been finalised and uploaded to the NCL MON website.

14. **Guideline: Management and treatment of common infections in North Central London**
The Committee approved this guideline.

15. **JFC Annual Report for 2016/17**
The Committee approved the annual report.

16. **Next meeting**
Monday 21 May 2018, G12 Council Room, South Wing, UCL, Gower St. WC1E 6BT

17. **Any other business**

17.1 **NCL DOAC Prescribing Guidance: AF and VTE (monitoring schedule)**
Mr Minshull presented the Committee with a revised monitoring schedule proposal for DOACs. This was developed at the request of primary care, as it was recognised that the previous version represented an unmanageable burden for GPs continuing treatment. These recommendations bring the NCL guidance more into line with the European Heart Rhythm Association expert guidance from 2018.

The Committee agreed that this amendment represented a pragmatic approach to monitoring DOACs and were happy for this change to be made.

17.2 **Lidocaine 5% plasters for palliative care (off-label use)**
Dr Gishen advised the Committee an application for lidocaine 5% for palliative care was being written by the PallE8 regional reference group. The application was anticipated in July 2018.