North Central London
Joint Formulary Committee

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Thursday 27 July 2017
G12 Council Room, South Wing, UCL, Gower Street, London WC1E 6BT

Present:	Prof L Smeeth	NCL JFC Vice-Chair	**(Chair)**
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Dr M Kelsey	WH, Chair DTC	
	Mr T James	MEH, Chief Pharmacist	
	Dr V Thiagarasah	Enfield CCG, GP Clinical Lead Medicines Management	
	Dr R Fox	RNOH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr B Sandhu	NEL CSU, Assistant Director Acute Services	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Mr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Mr T Dean	Patient Partner	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
In attendance:	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr A Barron	NCL JFC, Support Pharmacist	
	Mr J Minshull	NCL JFC, Support Pharmacist	
	Dr S Eriksson	UCLH, Consultant Neurologist	
	Dr E Matthews	UCLH, Consultant Neurologist	
	Dr S McBride	Consultant Dermatologist, RFL	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
Apologies:	Mr C Daff	Barnet CCG, Head of Medicines Management	
	Dr R Sofat	UCLH, DTC Chair	
	Dr R MacAllister	NCL JFC Chair	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr G Kotey	NMUH, Chief Pharmacist	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Ms K Landeryou	Patient Partner	
	Ms L Reeves	C&I, Chief Pharmacist	
	Dr P Hyatt	NMUH, DTC Chair	
	Dr S Shaw	RFL, DTC Chair	
	Prof A Tufail	MEH, DTC Chair	
	Dr R Kapoor	UCLH, Consultant Neurologist	

2. Meeting observers

There were none.

3. Minutes of the last meeting

The minutes were corrected to indicate Ms Mortty's (Haringey CCG) attendance at the meeting in June 2017.

4. Matters arising

Mr Minshull informed the Committee that Mr Shah (Chief Pharmacist, RNOH) had highlighted a challenge for RNOH to send representation to the JFC when the meeting moves to a Monday afternoon. Mr Shah will discuss this change at the next RNOH DTC meeting. Mr Minshull confirmed that JFC meetings will still be changing to the afternoon of the 3rd Monday of the month from September 2017.

5. Declarations of relevant conflicts of interest

Mr A Barron declared that he has worked with Novartis on sacubitril valsartan (Entresto®); Novartis also manufacture secukinumab which is licensed for psoriasis considered under item 9.

6. Local DTC recommendations / minutes

6.1 Ixazomib in multiple myeloma (pre-NICE; zero-cost scheme)

The Committee considered a request to extend its approval for a pre-NICE zero-cost scheme for ixazomib, a first-in-class, oral proteasome inhibitor, to be used in the treatment of adults with multiple myeloma (MM). The Committee noted that in May 2016 it had ratified a UCLH UMC decision to approve free of charge access to ixazomib in combination with lenalidomide and dexamethasone for patients with MM who have received two or more prior therapies, and are not refractory to lenalidomide or proteasome inhibitor (PI).

The Committee noted that since May 2016, ixazomib has received a marketing authorisation for this indication, has been subject to a negative Appraisal Consultation Document (ACD) from NICE, and additional phase 3 data are available (TOURMALINE-MM1). The Committee agreed that the negative ACD may be a factor of drug cost rather than efficacy of the medicine, therefore proceeded to review the findings of the TOURMALINE-MM1 study.

TOURMALINE-MM1 (n=722) was a double-blind, placebo controlled RCT powered to detect a change in progression-free survival (PFS). Patients were randomised to receive either ixazomib or matched placebo, on top of lenalidomide and dexamethasone. Median PFS for all patients was 20.6 months in the ixazomib treated arm, compared to 14.7 months in the placebo treated arm (HR 0.74; 95% CI 0.59 – 0.94). On subgroup analysis, ixazomib demonstrates greater efficacy in patients with a high risk cytogenic abnormality (21.4 months vs. 9.7 months; HR=0.54 [95% CI: 0.32 to 0.92, p=0.02]), and showed a trend towards more efficacy the more previous lines of therapy a patient has undergone, with statistically significant superiority to placebo occurring in the ~30% of patients that have had three prior lines of therapy. The Committee noted the incidence of adverse events, including 33% incidence of thrombocytopenia and neutropenia, though it was noted that <1% of patients experienced the medical-emergency of febrile neutropenia. It was noted that data on overall survival are still unavailable, and therefore a decision has to be made based on interpretation of the benefits from PFS.

The Committee discussed the importance of equity of access to treatments across NCL. As patients currently treated at UCLH could potentially receive free of charge access to ixazomib, it would seem reasonable that patients treated at other hospitals should also have access where clinically appropriate. It was noted that in the event of a negative NICE Technology Appraisal, the scheme will continue to provide free of charge drug to patients already established on the scheme, until it is clinically appropriate for them to stop treatment. The Committee recognised that this decision applies only to the free of charge supply of the medicine, and will be superseded once NICE publishes its Technology Appraisal.

In summary, the Committee recommended that free-of-charge ixazomib be added to the NCL joint formulary for use at any hospital, for the treatment of adults with MM who have received two or more prior therapies and are not refractory to lenalidomide or PI (in line with the previous UCLH approval). The patient consent process agree by UCLH (including use of patient information leaflet) should be followed by all sites using ixazomib, as there is still uncertainty about the true benefit of this medicine, and use is likely to expose patients to adverse events. This decision will be reviewed on publication of the NICE Technology Appraisal.

Decision: Approved (zero cost drug only)

Prescribing: Secondary care only
Tariff status: Not applicable
Funding: Free of charge supply
Fact sheet or shared care required: No

Post meeting note: NHS England (London) has subsequently written to all Cancer Pharmacists in London explaining that they do not support this scheme due to uncertainty about the cost-effectiveness of this intervention and the budget impact of using additional lenalidomide where time to progression is extended. Resultantly, they have stated that no new patients may be commenced on ixazomib under this Free of Charge Scheme, and that patients already established on ixazomib under this scheme can continue to receive ixazomib until treatment is no longer required. NHS England will review this situation following publication of the NICE TA.

6.2 Approved by local DTC

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Mar-17	Venetoclax (compassionate access scheme)	Chronic lymphocytic leukaemia (CLL) in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B-cell receptor pathway inhibitor. CLL in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: NA Funding: FOC Fact sheet or shared care required: No
UCLH	Apr-11	Levosimendan	Acutely decompensated severe chronic heart failure who have failed to respond to conventional therapy and failed to respond to or did not tolerate inotropic agents (dobutamine or enoximone)	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: In-tariff Funding: Trust Fact sheet or shared care required: No
RFL	Aug-17 (in advance of minutes)	Alectinib (compassionate use)	ALK+ve advanced NSCLC for patients who have already progressed crizotinib and certinib	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: NA Funding: FOC Fact sheet or shared care required: No

7. New Medicine Reviews

7.1 Tofacitinib for rheumatoid arthritis (pre-NICE; zero-cost scheme; Applicant: Prof M Ehrenstein, UCLH)

The committee reviewed an application for the use of tofacitinib (free stock) in biologic experienced patients for rheumatoid arthritis. The committee noted that tofacitinib and baracitinib offer a novel mechanism of action in that they are JAK inhibitors, as well as being the first oral biological DMARD.

The committee reviewed a double-blinded, triple-dummy, head-to-head phase 3b/4 trial to investigate the efficacy and safety of tofacitinib monotherapy versus tofacitinib in combination with methotrexate, and adalimumab in combination with methotrexate. Inclusion criteria were individuals aged > 18 years with active RA despite treatment with weekly methotrexate. The primary end-point was the proportion of patients achieving and ACR50. Secondary end-points include proportion of patients achieving an ACR20,

ACR70, low disease activity, and disease remission. The results showed that at 6 months, the ACR50 response rate were 38% in the tofacitinib monotherapy arm compared to 46% in the tofacitinib and methotrexate arm and 44% in the adalimumab and methotrexate arm. Tofacitinib in combination with methotrexate was deemed non-inferior to adalimumab in combination with methotrexate as the difference in the proportion of patients achieving ACR50 response rates between the two groups was 2% (98.34% CI: -6 to 11%); thus within the pre-specified non-inferiority margin (-13%). Non-inferiority was not shown for tofacitinib monotherapy when compared to combination with methotrexate or when compared to adalimumab in combination with methotrexate. The committee noted that superiority was not shown for any of the comparisons. In terms of secondary end-points, the response rates followed a similar trend for that they were similar in the combination arms, but higher when compared to the monotherapy arm.

A second randomised, phase 3 trial investigated the efficacy of tofacitinib and adalimumab compared to placebo; all in combination with background methotrexate. The primary end-point were ACR20 response rates, secondary end-points were change in HAQ-DI, disease remission ACR50 and ACR70 response rates, and safety. The results showed the proportion of patients achieving ACR20 responses were 51.5% in the tofacitinib 5mg arm compared to 52.6% in the tofacitinib 10mg arm, 47.2% in the adalimumab 40mg arm, and 28.3% in placebo arm. Similarly, the change in HAQ-DI from baseline was -0.55 (tofacitinib 5mg), -0.61 (tofacitinib 10mg), 0.49 (adalimumab 40mg), and -0.24 (placebo) respectively. Results of ACR50, ACR 70, and DAS scores followed a similar trend.

The committee reviewed the evidence for a second JAK inhibitor called baracitinib. One randomised, double-blinded, placebo- and active-controlled, phase 3 trial investigated the efficacy and safety of baricitinib compared to placebo and adalimumab. Inclusion criteria were patients aged greater than 18 years with active RA. Patients were randomised to receive placebo, baricitinib 4mg once daily, and adalimumab 40mg every two weeks, in addition to existing background methotrexate. The primary end-point ACR20 response rates, with secondary end points of progression of joint damage, HAQ-DI, DAS-28 scores, disease remission, and safety. The results showed that the ACR20 response rate for baricitinib was 70% compared to 40% for placebo. Baracitinib was also non-inferior to adalimumab at week 12; ACR response rates of 70% for baricitinib compared to 61% for adalimumab (95% CI for the difference between 2% to 15%). According to the statistical analysis, baricitinib could therefore be considered as superior to adalimumab; however it should be noted that this was for ACR20 response rates and at 3 months only.

In terms of safety, the committee noted that no new or unexpected safety concerns were reported with either JAK inhibitors. The most common adverse reactions for tofacitinib were upper respiratory tract infections, alanine aminotransferase elevation, and urinary tract infections. The incidence of herpes zoster were similar in all groups; 1% versus 2% versus 2%, respectively.

The committee agreed that an indirect comparison between the two JAK inhibitors was not possible as trial design, inclusion criteria, and primary end-points were different. However, the committee were convinced that both JAK inhibitors were non-inferior to adalimumab, and that both will be approved by NICE.The committee noted that NICE are currently reviewing the use of tofacitinib and the final publication is due in December 2017. At present, there are no ACD or FADs published either. The Committee were also informed that NICE are also reviewing the use of baracitinib for RA and have published a FAD with the recommendations its use in biologic naïve and biologic experienced patients, as well as monotherapy. The final NICE TA is due to be published August 2017, however funding will only commence 90-days post publication.

In terms of cost, the committee heard that the average List price of baracitinib was £10,500 per annum, however NICE has agreed a PAS discount. Similarly, the List price for tofacitinib is £10,800 per annum, however it is currently being provided to the NHS at no cost until 90-days post NICE publication. In the unlikely event that NICE do not recommend tofacitinib, the company will continue to provide free stock to all patients already on the scheme until disease progression. In terms of convenience, baracitinib and tofacitinib are the first oral biologic DMARDs. All others are administered subcutaneously.

The committee questioned whether there is a clinical need for tofacitinib free-of-charge stock and whether it would be worth waiting for 90-days post baracitinib NICE TA publication when it would be funded. However, the committee were informed that there is currently a high unmet need in the treatment of patients that have failed, unable to tolerate or contra-indicated to four or more biologics. The committee discussed at length regarding the addition of fifth-line biologic onto the NCL pathway. Although the committee agreed that the addition of an agent with a different mechanism of action seems

sensible, there is still an absence of data supporting this. The committee questioned whether outcome data for fifth line biologic use can be presented to aid the committee make a decision.

In summary, the committee were satisfied that both JAK inhibitors were non-inferior to adalimumab however there was a need to establish whether fifth-line therapies were effective. To resolve this uncertainty, and to inform any future update to the NCL Rheumatology biologic pathway, the committee agreed that fifth-line free-of-charge tofacitinib was approved under evaluation and data from the evaluation should be reported back to JFC in April 2018. UCLH Rheumatologists should work with JFC to agree a data collection form for use across NCL. NHS funding of fifth-line tofacitinib was restricted to patients who started treatment under the terms of the free-of-charge scheme (as part of the evaluation) and who meet the NICE continuation criteria at 6 months. Tofacitinib and baricitinib would also be added to the NCL Rheumatology biologic pathway as possible first-, second-, third- or fourth-line therapies within 90 days of the respective NICE TAs. Funding for fifth-line therapy outside of the free-of-charge tofacitinib evaluation should continue to be applied for via IFR.

Decision: Approved (FOC) under evaluation
Prescribing: Secondary care only
Tariff status: NA
Funding: Free of charge
Fact sheet or shared care required: No

7.2 Palbociclib in locally advanced of metastatic breast cancer (pre-NICE; zero-cost scheme; Applicant: Dr Emma Spurrell, WH)

The Committee heard an application to use palbociclib, a CDK4 and CDK6 inhibitor, as a first line addition to aromatase inhibitor for patients with previously untreated, locally advanced metastatic breast cancer. The Committee noted that addition of palbociclib to aromatase inhibitor as first line therapy is a significant change to practice; according to the London Cancer Breast Cancer Treatment Guideline patients would be considered for tamoxifen, fulvestrant, exemestane (+/- everolimus) and megesterol acetate/medroxyprogesterone acetate, before proceeding to chemotherapy.

It was noted that NICE is currently conducting a technology appraisal for palbociclib used in combination with letrozole in this cohort of patients, with a FAD anticipated soon. The Committee was interested to note that the NICE ACD is currently negative because all plausible ICERs were considerably above the threshold considered by NICE to be cost-effective. It was acknowledged that this situation may change if the company provides additional data, or if a Patient Access Scheme is negotiated.

The Committee discussed the findings of the PALOMA-1 and PALOMA-2 studies. The Committee noted that the only overall survival data available were from PALOMA-1, a small (n=165), phase 2, open-label study, which showed a non-statistically significant difference of 37.5 months (95% CI: 28.4 to not estimable) in the palbociclib arm vs. 33.3 months (95% CI: 26.4 to not estimable) in the placebo arm (HR 0.813 [95% CI 0.492-1.345, p=0.42). PALOMA-1 found a statistically significant improvement to progression free survival (PFS) for palbociclib treated patients (20.2 months [95% CI 13.8 to 27.5]) vs. the placebo arm (10.2 months [95% CI 5.7 to 12.6]). This gave a progression free survival HR of 0.488 (95% CI 0.319 to 0.748, p=0.0004) in favour of palbociclib. At cut off, the median follow up was 29.6 months in the palbociclib arm, vs. 27.9 months in the placebo arm.

The Committee was disappointed to note that the larger, double-blind study (PALOMA-2, n=666) does not yet have overall survival data available. The Committee discussed how PFS is not a perfect surrogate for overall survival in the cohort of patients that would be identified for treatment with palbociclib, because there are so many other available lines of therapy that could be used. However, it was agreed that the large improvement in PFS demonstrated in PALOMA-2 was indicative that there were potential benefits from using palbociclib, but any decision should be reviewed once PALOMA-2 overall survival data are available if NICE has not already evaluated the drug. PFS increased from 14.5 months (95% CI 12.9 to 17.1) in the placebo arm to 24.8 months (95% CI 22.1 to not estimable) in the palbociclib arm, resulting in a HR radiologically confirmed progression or death of 0.58 (95% CI 0.46 to 0.72, p<0.001). To put these PFS data into perspective, Dr Spurrell had provided some examples of the types of PFS that can be expected from other therapies often used in patients with locally advanced metastatic breast cancer; for example anastrazole (PFS 11.1 months) vs. tamoxifen (5.6 months); letrozole (9.4 months) vs. tamoxifen (6 months); exemestane (10.9 months) vs. tamoxifen (6.7 months), thus it is the opinion of Dr Spurrell that the additional mean 10 months of PFS achieved by adding palbociclib to letrozole is clinically significant compared to the gains achieved from other therapies.

The noted the large rate of neutropenia (80.6%; 2.1% febrile neutropenia when palbociclib combined with letrozole) and of infections (54.7%) experienced by patients treated with palbociclib. Mr Minshull reported that Dr Spurrell was satisfied that the rate of febrile neutropenia experienced with palbociclib was low compared to that experienced with most chemotherapy regimens, and that patients would be adequately advised on how to recognise symptoms and what action to take.

The Committee discussed the risks associated with the terms of the free of charge scheme, noting that it would only allow new patients to register until 6 weeks following publication of the NICE FAD or until 30th September 2017 (whichever is sooner), thus there is a risk that the scheme will close to new patients before palbociclib is routinely commissioned following a positive NICE determination. Mr Minshull was asked to seek clarification from Pfizer that patients enrolled on the scheme will not have treatment withdrawn if there is a gap between the scheme closing and routine commissioning starting, or if NICE does not issues a positive technology appraisal. The Committee noted that UCLH is currently running a clinical trial for a similar medicine to palbociclib; the Committee agreed that appropriate patients should be encouraged to participate in a clinical trial, but that patients are free to choose not to participate and therefore access to palbociclib may be beneficial. Some patients may not be eligible for inclusion in clinical trials, therefore treatment options are needed for these patients.

In summary, the Committee agreed that it was early to be considering the benefit of palbociclib without overall survival data being available. However, the potential benefit in PFS and manageable tolerability profile, palbociclib may be useful for some patients. The Committee therefore approved palbociclib under the free of charge scheme. Approval is under the free of charge scheme only and formulary status will be reviewed once the free of charge supply ceases, or when NICE publishes it technology appraisal.

Post-meeting note: Mr Minshull has confirmed with Pfizer that patients already established on the FOC scheme at the point it closes will continue to receive free of charge palbociclib until the treating physician decides treatment is no longer clinically appropriate.

Decision: Approved (FOC)
Prescribing: Secondary care only
Tariff status: NA
Funding: Free of charge
Fact sheet or shared care required: No

7.3 Idebenone for Duchenne Muscular Dystrophy (EAMS; Applicant: Dr Ros Quinlivan, NHNN)

The Committee reviewed an application for idebenone to slow the loss of respiratory function in patients with Duchenne muscular dystrophy. Idebenone is a synthetic analogue of ubiquinone (coenzyme Q10) which may function as an electron carrier in the mitochondrial electron transport chain, to inhibit lipid peroxidation and protect cell membranes and mitochondria from oxidative damage. Idebenone is available as a short-term free-of-charge Early Access to Medicines Scheme (EAMS) in advance of product licensing and long-term funding approval.

The Committee heard evidence from DELOS, the single relevant Phase III, multinational, double-blind, randomised, placebo controlled trial to establish the efficacy of idebenone in DMD (n=64). Children and adolescents aged 10-18 years, able to provide reliable and reproducible repeat peak expiratory flow (PEF) within 15% of baseline of the first assessment, were included. Exclusion criteria were assisted ventilation and other symptoms of more severe disease. Patients were randomised 1:1 to idebenone or placebo. The primary objective was a reduction in loss of respiratory function as measured by spirometer-measured PEF%p from baseline to week 52. Secondary endpoints included forced vital capacity (FVC), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP) and peak cough flow. Baseline characteristics were balanced in terms of PEF%p although patients in the idebenone group were younger (13.5 years vs. 15.0 years for placebo) and had better FVC%p (55.3%p vs. 50.4%p for placebo) suggesting less progressed disease which might be expected to bias in favour of placebo (respiratory decline occurs maximally between the ages of 10 to 18 with the slope of decline flattening with age). For the primary endpoint, there was a reduction in PEF%p decline from baseline with idebenone; estimated treatment difference of +5.96%p (0.16 to 11.76; p=0.044). FVC%p showed only a non-significant trend towards a reduction in decline; estimated treatment difference of +3.27%p (-0.43 to 6.97; p=0.082). No significant differences were observed for MIP, MEP, peak cough flow or Paediatric Quality of Life Inventory. A post-hoc analysis suggested patients using idebenone were less likely to experience bronchopulmonary adverse events (including URTI, bronchitis, pneumonia, cough, influenza).

The adverse effect profile was acceptable with mild to moderate diarrhoea (usually not requiring the discontinuation of the treatment), nasopharyngitis, cough and back pain being most commonly reported. Idebenone is available as a zero-cost scheme for a maximum period of 12 months, or until the drug is routinely commissioned by NHSE. The UK list price is £77,428 per patient per annum however it is thought the company will be providing a patient access scheme for DMD.

The Committee heard from Dr Quinlivan that patients and patient organisations were aware the EAMS was limited to 12 months of treatment, and ongoing therapy was not guaranteed after this date. Patients would consent to these terms thereby mitigating financial risk to the Trust. There was no available data on idebenone having positive outcomes on skeletal muscle function.

In camera, the Committee discussed whether idebenone had a meaningful impact on respiratory function; the confidence interval for PVC%p, the respiratory measure used in clinical practice, was wide and spanned 'no difference' and furthermore, the FVC%p plots appeared to converge towards placebo at 52 weeks. There were no data beyond 52 weeks to support a claim of lasting or cumulative benefit, or time to non-invasive ventilation. The Committee has concerns over the generalisability of this paper to the population treated at NHNN; the study recruited patients aged 10 to 18, with a mean age of 14 years however the UCLH application was specifically for an adult service with advanced disease. Ventilator treatment was a specific exclusion criterion however many of the patients treated at NHNN required night-time ventilation. The overall exclusion [27%], early discontinuation [17%] and 'exclusion from mITT analysis' rates [11%] were high which raised doubts over generalisability of the data, even for younger patients. The Committee also raised concerns about the unbalanced baseline characteristics (age and FVC%p) which could introduce bias.

In summary, the Committee were sensitive to the severity of the condition and acknowledged the willingness to pay for Highly Specialised Technologies was higher than for more prevalent conditions. The Committee were not satisfied the evidence supported the use of idebenone for adults with Duchenne's who had already experienced a substantial decline in respiratory function. Despite the drug being available at zero-cost, the Committee felt they were unable to recommend treatment given doubts over efficacy, the risk of falsely raising patient expectation and making Commissioning decisions more challenging in the future. The Committee agreed to contact GOSH and NHSE to establish their approach to the EAMS and discuss the responses at the August 2017 meeting.

Decision: Deferred

Post meeting note: NHSE wrote to Provider Trusts (27 July 2017) to ensure Trusts were aware of the idebenone EAMS; UCLH and GOSH were the only Trusts in NCL eligible to apply. NHSE had not evaluated idebenone and asked NICE to review through their Highly Specialised Technology Evaluation process (currently 'Draft scope [pre-referral]'). The NCL JFC cannot register as a HST stakeholder therefore will contact the assigned stakeholders to ensure the evidence gaps for adults are formally considered. The Neuromuscular team at GOSH would like to use idebenone under the EAMS, but have not submitted anything formal to their DTC.

A Senior Medical Assessor from the MHRA clarified the target population in DMD is from the age of 10 years. Idebenone is indicated "to slow respiratory decline" and an upper age limit of 18 years was not imposed as the current restriction, by the requirement for patients to be in respiratory decline, was considered more meaningful clinically. The decline in patients respiratory function is known to reduce with increased age therefore patients whose respiratory function is no longer in decline, as might be expected in older patients, are not eligible for the idebenone EAMS. The MHRA share the JFC's concerns if idebenone is being administered to adults who have reached end stage respiratory deficit as there is no evidence of benefit in these patients and nor would one be anticipated from the drug's mechanism of action. The benefit-risk was concluded to be positive for the EAMS indication as specified. The MHRA would not endorse an extension of this to adult DMD patients who are no longer in a progressive phase of respiratory decline.

8. Biologics for psoriasis guideline: Preferential use of adalimumab (anticipating biosimilar adalimumab) – outcome from NCL consultation

In June 2017, the Committee considered a proposal to list adalimumab as the preferred first-line biologic for psoriasis, in anticipation of biosimilar adalimumab which would be available at a considerably lower acquisition cost than branded biologics. The proposal to improve the cost-effectiveness of first-line treatment follows a request from Acute Trusts to Commissioners to routinely fund biologics for a larger

cohort of patients (including patients with severe disease at high impact sites with significant functional impairment or distress) and additional sequential lines of biologic therapy (increasing from two to four). The proposal was submitted to NCL dermatologists for comment.

Feedback was received from specialists at RFL, UCLH and WH who broadly supported the proposal:

- Biosimilar adalimumab should be preferred for patients with some exceptions:
    - Those with contraindications to adalimumab e.g. heart failure, TB
    - When clinicians have significant concerns with adherence e.g. MH issues, frequent travellers
- Secukinumab should be reserved for patients where PASI-90 "is of paramount importance"
- Pathway should be reviewed in a year when more data is available (further data from the BADBIR database and dose escalation adalimumab)

One reviewer proposed that adalimumab would not be preferred for patients with a high body weight. The Committee acknowledged biologics were less effective for patients with a high body weight, and that ustekinumab was available at a higher dose for patients >100Kg; however the Committee did not know whether ustekinumab was superior to adalimumab in this cohort. A request to preferentially use ustekinumab for patients with a high body weight would therefore be subject to a therapeutic review at JFC.

Another reviewer proposed that all patients prescribed biologics be enrolled on a weight reduction programme. The Committee agreed this would be beneficial however commissioning such services was outside of the Committee's remit.

The Committee explored areas of potential uncertainty as part of this consultation:

Does recommending first-line adalimumab in NCL create inequitable access to treatment compared to other regions in England?

Inequitable access to treatment relates to patients in one area being refused care that is available in other regions. Adalimumab is a highly effective agent, with PASI-75 and PASI-90 responses superior to etanercept and similar to ustekinumab therefore preferentially using adalimumab as a first-line agent is not synonymous with inferior patient care. Furthermore, this proposal emerges from a draft pathway which recommends access to biologic medicines to more patients than currently available / routinely commissioned. If the pathway is approved, NCL might be expected to have superior access to treatment compared to other regions.

Does recommending first-line adalimumab undermine NICE guidance?

NICE has issued positive TAs for adalimumab, etanercept, ustekinumab, secukinumab and ixekizumab for patients with a PASI ≥10 and DLQI ≥10 who have failed to respond to standard systemic therapies. Importantly the TAs relate to first-line biologic use and do not mandate treatment beyond first-line therapy (see ustekinumab FAD section 4.9). NICE CG153 recommends second-line treatment however this is not mandated. If CCGs only fund newer agents as second- or third-line therapies, this precludes each of them as first-line agents *if* >1 line of therapy over a patient's lifetime is anticipated advantageous. NICE requires all drugs to be available as options for first-line use, however NCL recommends adalimumab as the first-line agent (unless contraindicated or significant concerns with adherence). Medical conditions with multiple TAs are usually updated as part of a multiple technology appraisal (MTA) and in such cases, state "start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose)". These documents take time to develop and are often not published in tandem with updates in practice, as seen with TA188 (somatropin; human growth hormone) which states "if more than one product is suitable, the least costly product should be chosen", published May 2010, two years after availability of biosimilar somatropin. NICE therefore has a track record of advising providers to use the cheapest (or most cost-effective) agent in cases where efficacy is considered equivalent. The use of biosimilar adalimumab first-line as the most cost-effective intervention would therefore not be outwith of their general guidance with the discrepancy likely to be a time-limited issue.

Does recommending first-line adalimumab undermine British Association of Dermatologist (BAD) guidance?

The proposal to use first-line adalimumab was based on evidence from the BAD systematic literature review and network meta-analysis. BAD stated "any differences in costs were not considered relevant to the recommendations on choice of which biologic to use at present" which NCL JFC consider ill-advised given the imminent availability of biosimilar adalimumab. BAD recommend adalimumab as a first-line therapeutic option, therefore NCL only propose a minor deviation by making adalimumab, not

ustekinumab, the preferred agent. Importantly, the NHS has no statutory requirement to adhere to BAD recommendations although should consider their recommendations carefully.

Using first-line adalimumab may be challenged by patients, patient groups and Pharmaceutical companies

The proposal to use first-line adalimumab is being considered alongside a proposal to increase the number of patients eligible for treatment (i.e. newly including patients with severe disease at high impact sites with significant functional impairment or distress) and funding additional lines of sequential biologic therapy. Clinical stakeholder engagement (described above) supports the recommendation to use the most cost-effective agent first-line, thereby freeing up funds to reinvest in the pathway and improve the overall health of the population. The NCL Patient Partners support the initiative.

Issuing a statement recommending first-line biosimilars might set a precedent for other pathways

Rheumatologists already use biosimilar etanercept as their first-line anti-TNF therefore a precedent to preferentially use biosimilars has already been established. The Committee will continue to support pathways that recommend the preferential use of biosimilar agents where a proprietary agent has not demonstrated superiority over the biosimilar comparator (e.g. golimumab / certolizumab vs biosimilar etanercept in RA, or ustekinumab vs. biosimilar adalimumab in psoriasis). The Committee intends to review the following pathways over the next 12 months to ensure appropriate use of biosimilars: Crohn's disease; ulcerative colitis; ankylosing spondylitis; psoriatic arthritis; and rheumatoid arthritis.

In summary, the Committee were satisfied that the proposal to use first-line adalimumab should be implemented regionally as it had the support from the majority of respondents and it made logical sense to implement. It was agreed that the draft pathway should be updated (in accordance with the above) and be submitted to NCL CSU for commissioning approval on behalf of the NCL CCGs.

9. Strontium ranelate discontinuation

Mr Minshull informed the Committee that strontium ranelate, a treatment for severe osteoporosis, will be discontinued in August 2017. Patients currently receiving strontium ranelate will need to have their treatment reviewed and an alternative agent found. UKMI has produced a memo that may be helpful for organisations to adapt for local use.

10. Denosumab in osteoporosis Fact Sheet (ratification following updates)

Mr Minshull informed the Committee that the authors had made a minor update of the fact sheet following the MHRA warning that denosumab increases the risk of osteonecrosis of the external auditory canal.

The Committee approved this minor update.

11. Committee membership

Mr Minshull informed the Committee that a request had been sent to NCL DTC Chairs, Chief Pharmacists and Heads of Medicines Management to identify clinicians interested in becoming part of the JFC. Specifically, there is a need to identify an oncologist following Dr Boleti stepping down from the Committee, and a General Medicine/Respiratory. The Chair thanked Dr Boleti for her contribution to the JFC over the years.

12. Pregabalin prescribing and dispensing guidance from NHS England

Mr Minshull informed the Committee that as of 17 July, NHS England has reversed its 2015 guidance that pregabalin for neuropathic pain conditions should be prescribed as the Lyrica brand only. This advice was issued following a patent dispute between Warner-Lambert Company LLC and a number of generic pharmaceutical suppliers. As of 17 July, NHS organisations are encouraged to support prescribing of pregabalin in line with normal practices; therefore generic pregabalin can be prescribed and dispensed for neuropathic pain conditions. Pregabalin has entered "Category M" of the Drug Tariff and will cost approximately 94-98% less than the Lyrica® brand.

Ms Taylor advised the Committee that although generic prescribing will represent a significant cost saving to the NHS, NHS England has indicated that it may claw-back these savings; therefore this won't necessarily represent a saving to the local health economy.

Mr Minshull advised the Committee that lower cost pregabalin should not distract attention away from the Public Health England request that prescribers minimise the risk of misuse of pregabalin by continuing to review patients and balance the risks and benefits of continued treatment.

13. JFC Work plan

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

14. Next meeting

Thursday 31 August 2017, Suite A (1st Floor) Maple House, 149 Tottenham Court Road, W1T 7BN

15. Any Other Business

Fluphenazine decanoate, a depot typical antipsychotic, will be withdrawn from the market in 2018.