North Central London
Joint Formulary Committee

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Monday 18 September 2017
G12 Council Room, South Wing, UCL, Gower Street, London WC1E 6BT

Present:	Dr R MacAllister	NCL JFC Chair	**(Chair)**
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	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 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	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Dr M Kelsey	WH, Chair DTC	
	Ms L Reeves	C&I, Chief Pharmacist	
	Mr T James	MEH, Chief Pharmacist	
	Ms EY Cheung	Camden CCG, Deputy 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	
	Mr B MacKenna	Islington CCG, Deputy Head of Medicines Management	
	Ms I Shaban	Islington CCG, Prescribing Adviser	
	Ms S Aggarwal	NMUH, Lead Pharmacist	
	Dr A Mian	NMUH, Consultant Rheumatologist	
Apologies:	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr C Daff	Barnet CCG, Head of Medicines Management	
	Dr R Sofat	UCLH, DTC Chair	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Mr G Kotey	NMUH, Chief Pharmacist	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Dr P Hyatt	NMUH, DTC Chair	
	Dr S Shaw	RFL, DTC Chair	
	Prof A Tufail	MEH, DTC Chair	
	Dr V Thiagarasah	Enfield CCG, GP Clinical Lead Medicines Management	
	Dr R Fox	RNOH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Dr R Kapoor	UCLH, Consultant Neurologist	

2. Meeting observers

The Chair welcomed Dr Faye Gishen and Dr Derralynn Hughes as new members and explained the role of the JFC.

The Chair informed the Committee that Ms Kelly Landeryou (Patient Partner) has stepped down from the JFC. *In absentia*, the Chair thanked Kelly for her contribution in what was a new role.

Brian MacKenna (Deputy Head of Medicines Management, Islington CCG) and Iman Shaban (Prescribing Adviser, Islington CCG) were welcomed as meeting observers.

3. Minutes of the last meeting

The minutes and abbreviated minutes were accepted as an accurate reflection of the August meeting.

4. Matters arising

4.1 Idebenone for Duchenne Muscular Dystrophy (EAMS)

In July 2017 the JFC deferred their decision on idebenone for Duchenne Muscular Dystrophy (DMD) subject to establishing GOSH and NHSE approach to the EAMS.

GOSH intend to review the application at their October 2017 DTC meeting.

NHSE wrote to Provider Trusts (27 July 2017) to ensure Trusts were aware of the idebenone EAMS however NHSE had not independently evaluated idebenone and instead asked NICE to review through their Highly Specialised Technology Evaluation process (currently 'Draft scope [pre-referral]'). NHSE included UCLH as an eligible centre for the EAMS.

JFC Support sought advice from the unit at MHRA who undertook the EAMS evaluation. A Senior Medical Assessor clarified the target population in DMD is from the age of 10 years. Idebenone is indicated "to slow respiratory decline" without any upper age limit. The inclusion requirement was that patients were experiencing respiratory decline The rate of decline in patients' respiratory function is known to diminish 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 Senior Medical Assessor also clarified, "The benefit-risk was concluded to be positive for the EAMS indication as specified. We would not endorse an extension of this to adult DMD patients who are no longer in a progressive phase of respiratory decline. The EAMS indication does not encompass these patients."

The MHRA further clarified that their expert advisors took the pragmatic view that clinician judgement would ultimatel determine whether a patient was in active respiratory decline although there was also a strong sense that once a patient had reached the stage of needing assisted there would be little to be gained from idebenone. A working definition of 'active respiratory decline' may therefore be to consider this to be 'before a patient has reached the stage of needing assisted ventilation'. Overall the JFC thought these criteria were somewhat ambiguous and that the decision by the MHRA to allow the use of this agent via the EAMS was unhelpful and that the MHRA had strayed beyond the evidence base.

Dr Quinlivan responded to the MHRA statement: (i) disease progression continues even when a patient starts night-time non-invasive ventilation (NIV) as the pressures need to be increased over time; some patients begin day-time use only, and progress to require 24 hours ventilation; and (ii) there is a very wide range of DMD severity, with only 25% of the current UCLH cohort requiring NIV. Furthermore, whilst observational data suggest the rate of decline of PEF reduces after approximately 18 years of life, it is not clear how this corresponds to decline in respiratory function – it is plausible that the PEF is an inadequate marker of respiratory function at extreme low values.

The Committee noted the treatment effect for idebenone observed in the DELOS study was small (estimated treatment difference of +5.96% predicted [95% CI: 0.16 to 11.76] at 52 weeks) even for patients whose respiratory decline is progressing at a high rate (DELOS inclusion criteria 10 to 18 years; mean age 13.5 years). Given the small benefit in a population most likely to benefit, the benefit of treatment was considered uncertain in adults not requiring ventilation, and completely unknown in adults requiring ventilation (NIV was a specific exclusion criteria in DELOS). Idebenone appears to be well tolerated therefore potential risks to adult patients on treatment were considered low albeit unknown. Idebenone is supplied free-of-charge through the EAMS therefore provided an appropriate consent process is in place, risks to the health economy are low.

The Committee was unable to reconcile these uncertainties. Idebenone would be commissioned nationally for DMD (NHS England) rather than locally, it was agreed JFC should raise the uncertainty at a national level (with NHSE and the NICE HST team) rather than taking a local decision not to approve the

EAMS. The Committee confirmed that the uncertainty in treatment effect in adults not requiring NIV (25% of the UCLH population) and adults requiring NIV (75% of the population) was sufficiently large that any cost of treatment was considered unacceptable; the Committee therefore approved the EAMS scheme under the proviso that all the below conditions were met:

- GOSH DTC agree idebenone should be initiated in patients with NIV requirements
- Every patient is consented to the EAMS and explicitly agree to treatment withdrawal if idebenone is not commissioned by NHS England, or if they do not meet the eligibility criteria
- Patients provide consent to treatment during routine clinical appointments thereby not increasing outpatient activity and associated costs whilst initiating treatment
- All prescribing for adults remains within UCLH

Action: Mr Barron to contact NHSE and NICE Highly Specialised Technologies Evaluation stakeholders regarding the uncertainty in using idebenone in adults generally, and particularly in adults requiring NIV.

Action: Mr Barron to contact GOSH to establish whether they intend to initiate idebenone in paediatrics with NIV requirements and whether they would expect patients to continue idebenone when they transition from care at GOSH to UCLH.

5. Declarations of relevant conflicts of interest

There were no declarations of interest

6. Local DTC recommendations / minutes

There were no local DTC decisions to consider

7. New Medicine Reviews

7.1 Co-proxamol

Mr Minshull presented a summary of the evidence for co-proxamol tablets, which was based on an evidence evaluation written by PrescQIPP in May 2013. This evaluation was presented to the committee in the absence of a formal application, following the request of the Medicines Optimisation Committee. Mr Minshull highlighted that despite having its marketing authorisation withdrawn in 2007 due to concern over its safety profile, over £200,000 per annum is still spent on this medicine across NCL CCGs, though this is likely to be for just approximately 50 patients. Mr Minshull explained that this medicine has not previously been approved by the JFC, and that the Committee is being asked to formally identify this as a non-formulary medicine.

It was noted that co-proxamol tablets contain a combination of paracetamol with a weak opioid. The paracetamol dose is widely considered to be sub-therapeutic and the weak opioid (dextropropoxyphene) is associated with cardiac side effects. The lack of evidence for improved efficacy of co-proxamol over paracetamol in single dose studies was noted by the Committee. No data were provided on the relative efficacy of paracetamol versus co-proxamol in the management of chronic pain, which is the more likely indication.

The safety risks that led to the marketing authorisation withdrawal were emphasised. These included the risk of fatal toxicity from doses at a small multiple of the normal therapeutic dose, risk of fatality from inadvertent overdose, and PK and PD interactions with alcohol reducing the threshold for fatal toxicity. A case report of a severe withdrawal syndrome in an elderly patient stopping co-proxamol abruptly was noted.

The Committee recognised that only a small number of patients remain on co-proxamol following the 2007 marketing authorisation withdrawal. It was noted that any patients remaining on co-proxamol are likely already to have discussed and rejected switching analgesics with their GP. However, the Committee was of the opinion that there are safer, effective alternatives to co-proxamol, and therefore there is no justification for its continued use. Patients who have been on co-proxamol for a long period may require a gradual withdrawal of co-proxamol due to the risk of severe withdrawal syndrome. The Committee agreed that co-proxamol should be considered non-formulary in North Central London and patients currently receiving this medicine actively reviewed.

Action: Mr Minshull to produce a position statement highlighting the formulary status of co-proxamol.

8. & 9 Ankylosing spondylitis and psoriatic arthritis pathways

The Committee welcomed Dr Aneela Mian (Rheumatology Consultant, NMUH) and Ms Sunita Aggarwal to the meeting. Dr MacAllister thanked Dr Mian for starting work on a pathway to guide prescribing of biologic medicines in ankylosing spondylitis. The Committee noted that there was a need for a pathway to be progressed in psoriatic arthritis. Dr Mian and the Committee were in agreement that a working group was required to be established across NCL to ensure these pathways had input from all specialists involved in the care of these patients, and to identify aspects of treatment that require an evidence evaluation. The working group would have secretarial support from the JFC.

The Committee noted the following points that the working group should address:

- Ankylosing spondylitis (AS)
    - What biologic will routinely be selected first line?
    - What criteria would be used to select between the biologic agents in AS (other than NICE recommendation that least expensive should be selected if more than one is suitable)?
    - After two biologics have failed, what do you do next?
    - If a patient enters remission, what would you do with their treatment?
- Psoriatic arthritis (PsA)
    - Following failure of DMARDs, what considerations go into picking between apremilast and a biological agent?
    - What biologic will routinely be selected first line?
    - What criteria would be used to select between the biologic agents in PsA (other than NICE recommendation that least expensive should be selected if more than one is suitable)?
    - After two biologics have failed, what do you do next?
    - If a patient enters remission, what would you do with their treatment?
    - If two DMARDs are not effective, and patient doesn't meet criteria for a biologic, is there anything other than symptomatic treatment that can be tried?

10. Low Value Prescription Items position statements

10.1 Lidocaine 5% plasters

Mr Minshull presented a Position Statement highlighting the non-formulary status of lidocaine 5% plasters. It was noted that in November 2012 the JFC had considered the evidence for lidocaine 5% plasters in neuropathic pain and had determined that they should not be added to the Joint Formulary.

Dr Gishen informed the Committee that there is some use of lidocaine 5% plasters in palliative care pain, for example in the management of painful scars. The Committee requested that Dr Gishen liaise with her palliative care colleagues across NCL to identify all the indications in which they wish to use lidocaine 5% plasters to enable a robust formulary application to be submitted. The Committee requested that Mr Minshull work with Dr Gishen to generate the formulary application.

The Committee agreed that the Position Statement reflects the current status of the medicine on the NCL Joint Formulary and approved the document.

10.2 Daily tadalafil tablets

Mr Minshull presented a Position Statement highlighting the non-formulary status of daily tadalafil tablets. Three indications were highlighted for which these should not be used: erectile dysfunction, nerve-sparing radical prostatectomy (NSRP), and benign prostatic hyperplasia. It was noted that the Committee had agreed in November 2014 and January 2015 that the only PDE5 inhibitors to be available on the Joint Formulary were PRN sildenafil and PRN tadalafil. At the same time, the JFC agreed that PDE5i for NSRP should be limited to regular sildenafil provided by the specialist. It was noted that the JFC has not discussed the evidence base supporting the use of tadalafil in benign prostatic hyperplasia.

The Committee noted that the patent for daily tadalafil will not expire until 2021, therefore there is financial benefit to the STP from ensuring this Position Statement is followed. The Committee requested that JFC members ensure this Position Statement is shared with GPs, urologists and specialist nurses.

The Committee agreed that the Position Statement reflects the current status of the medicine on the NCL Joint Formulary and approved the document.

10.3 Fentanyl immediate release preparations

Mr Minshull presented a Position Statement for immediate-release transmucosal fentanyl preparations. Although the JFC has not directly reviewed the evidence base for this specific preparation of this medicine, it has been assessed at various Acute Trust DTCs. This document notes that immediate-release oral morphine is the first-line opioid for breakthrough pain in NCL, therefore immediate-release fentanyl should not be used first-line. Immediate-release fentanyl preparations are only licenced as breakthrough pain in adults with cancer, who are already receiving maintenance opioid therapy. Dr Urquhart noted that the UCLH UMC had approved immediate-release fentanyl products for post-operative patients with moderate or severe breakthrough pain and have malabsorption syndrome (an off-label indication); these are likely only to be used for acute pain management.

Dr Gishen informed the Committee that it was unlikely that immediate-release fentanyl would ever be used first-line for pain, although there is definitely a cohort of patients for whom oral morphine is no longer suitable but are not ready to move on to injectable pain relief. The Committee were of the opinion that it is unlikely that fentanyl preparations would ever be used first-line in palliative care.

The Committee agreed that the Position Statement reflects the current status of the medicine in NCL and approved the document.

10.4 Liothyronine in Primary Hypothyroidism

Mr Minshull reminded the Committee about the position statement for liothyronine that has already been approved.

The Committee discussed some barriers to implementing this formulary decision. It was highlighted that, although GPs will be requested to switch patients from liothyronine to levothyroxine, these prescriptions have often been started by an endocrinologist either in secondary care or in the private sector. The Committee noted that there is already a switch tool produced by PrescQIPP that should be used to empower GPs to make this switch. Secondary care formulary pharmacists should ensure the position statement has been disseminated to endocrinologists within their Trusts so they are aware of the formulary status.

11. Eslicarbazepine evaluation proposal (Prof M Koepp)

The Committee welcomed Prof Koepp to discuss his proposal to run a prospective switching evaluation of eslicarbazepine for patients who experience adverse side effects from oxcarbazepine. Prof Koepp explained that he intends to test the hypothesis that eslicarbazepine will be better tolerated than oxcarbazepine due to the differences in pharmacokinetics between the two agents.

The Committee highlighted that there is no clinical evidence of superiority of eslicarbazepine compared to oxcarbazepine although was willing to explore the hypothesis of improved tolerability of eslicarbazepine versus oxcarbazepine through a structured evaluation. It was felt that a non-blinded evaluation would not be suitable to test this hypothesis as there would be considerable risk of bias from a subjective endpoint. The Committee therefore suggested that a blinded 'n-of-1 study' would be a suitable methodology to answer the uncertainty. Prof Koepp highlighted his belief that patients will immediately notice the difference in effect between oxcarbazepine and eslicarbazepine because it will be so profound. The Committee remained of the opinion that it is still important to test this hypothesis rigorously. As the manufacturer of eslicarbazepine had indicated an offer of unrestricted support for funding an evaluation, it was proposed that they should be approached to fund a blinded evaluation.

In summary, the Committee were supportive of Prof Koepp running an evaluation comparing the tolerability of eslicarbazepine and oxcarbazepine for patients who had reported intolerance to oxcarbazepine, but demonstrated a clinically meaningful effect. It was suggested that Prof Koepp liaise with the manufacturer of eslicarbazepine to provide funding required to conduct a blinded "n of 1" study. The JFC will provide support to Prof Koepp to set up the evaluation. The evaluation plan should be brought back to a JFC meeting for agreement; should it be approved, prescribing will remain in secondary care until the results of the evaluation have been analysed.

Action: Mr Minshull to liaise with Prof Koepp about establishing an 'n-of-1' evaluation of eslicarbazepine

12. Annual report

A draft of the Year 4 JFC Annual Report was circulated for information. The Committee agreed that the final version need not be brought back, but emailed to the members and relevant Stakeholders.

13. JFC Work plan

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

14. Next meeting

Monday 16 October 2017, G12 Council Room, South Wing, UCL, Gower St. WC1E 6BT

15. Any other business

Terms of Reference

Mr Minshull presented a version of the Terms of Reference with amendments highlighted. It was noted that amendments had been made to clarify the Committee's status with regards to remit, accountability, key relationships, the vice-Chairs and the appeals process.

The Committee requested that a line making reference to production of abbreviated minutes be added to the Terms of Reference.

The Committee approved the Terms of Reference pending the amendment noted.