North Central London
Medicines Optimisation Network

Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 15th September 2022

		Present	Apologies
Prof A Hingorani	NCL JFC Chair	✓	
Dr B Subel	NCL JFC Vice Chair		✓
Ms W Spicer	RFL, Chief Pharmacist	✓	
Ms G Smith	RFL, DTC Chair		✓
Dr A Scourfield	UCLH, DTC Chair	✓	
Mr J Harchowal	UCLH, Chief Pharmacist	✓	
Dr R Urquhart	UCLH, Divisional Clinical Director	✓	
Dr K Tasopoulos	NMUH, DTC Chair	✓	
Ms S Stern	NMUH, Chief Pharmacist		✓
Dr M Kelsey	WH, DTC Chair	✓	
Mr S Richardson	WH, Chief Pharmacist	✓	
Dr S Ishaq	WH, Consultant Anaesthetist	✓	
Dr A Worth	GOSH, DTC Chair		✓
Mr S Semple	NCL ICS, Interim Chief Pharmacist; GOSH, Interim Chief Pharmacist		✓
Mr A Sell	RNOH, DTC Chair		✓
Mr A Shah	RNOH, Chief Pharmacist	✓	
Prof A Tufail	MEH, DTC Chair		✓
Ms N Phul	MEH, Chief Pharmacist		✓
Ms K Delargy	BEH, Chief Pharmacist	✓	
Ms L Reeves	C&I, Chief Pharmacist		✓
Dr L Waters	CNWL, Consultant Physician in HIV	✓	
Ms R Clark	NCL ICB, Head of Medicines Management (Camden)		✓
Mr P Gouldstone	NCL ICB, Head of Medicines Management (Enfield)	✓	
Ms E Mortty	NCL ICB, Interim Head of Medicines Management (Haringey)	✓	
Ms M Singh	NCL ICB, Head of Medicines Management (Barnet)	✓	
Mr A Dutt	NCL ICB, Head of Medicines Management (Islington)	✓	
Dr D Roberts	NCL ICB, Clinical Director (Islington)		✓
Mr T Dean	Patient partner		✓
Ms S Amin	IPMO Programme Team, JFC Principal Pharmacist	✓	
Mr G Grewal	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Mr H Shahbakhti	RFL, Formulary Pharmacist	✓	
Mr A Barron	UCLH, Principal Pharmacist	✓	
Mr S O'Callaghan	UCLH, Formulary Pharmacist	✓	
Ms A Sehmi	NMUH, Formulary Pharmacist	✓	
Ms H Thoong	GOSH, Formulary Pharmacist	✓	
Mr D Sergian	MEH, Formulary Pharmacist	✓	
Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	✓	
Ms A Fakoya	NCL ICB, Contracts & Commissioning Pharmacist	✓	
Dr A Hosin	UCLH, Clinical Pharmacology Registrar	✓	
Dr A Drebes	RFL, Consultant Haematologist	✓	

Prof D Williams	UCLH, Consultant Obstetrician	✓	
Ms A Hussain	UCLH, Specialist Pharmacist	✓	
Ms D Waterton	WH, Medicines management nurse	✓	
Ms EY Cheung	NCL ICB, Deputy Head of Medicines Management (Camden)	✓	

2. Meeting observers

Prof Hingorani welcomed observers to the meeting.

3. Members' declaration of interests

Declarations of interests register included for information. No interests relevant to the agenda were declared, and no further declarations were raised by members or attendees.

4. Minutes of the last meeting

The minutes and abbreviated minutes of the August 2022 meeting will be circulated to the Committee for comment for an additional week and will be subsequently approved via Chair's action.

5. Matters arising

Nil.

6. Review of action tracker

Action tracker included for information.

6.1 Review of potassium permanganate

Discussions at the RFL dermatology specialists' group has resulted in interest to retain potassium permanganate on their local formulary as there is no direct alternative for certain indications. RFL aim to mitigate risks through a series of governance steps (e.g., a local SOP, EPMA alerts etc). Similar interest has been shown at UCLH.

The Committee upheld their decision to remove potassium permanganate from the NCL Joint Formulary but appreciated there may be specific local reasons to retain on local formularies in exceptional circumstances. Any use in NCL Trusts should ensure appropriate risk mitigation strategies (using approved procedures, guidelines and electronic system updates) are in place. Finally, the Committee agreed that potassium permanganate should be hospital only (no prescribing in primary care). JFC will communicate this decision to NCL Trust Formulary Pharmacists, Commissioners and Medicines Safety Officers to aid their response to the safety alert.

Medication: Potassium Permanganate
Decision: Removed from the NCL Joint Formulary; Individual NCL Trust DTCs to review and consider use in exceptional circumstances only
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Factsheet or shared care required: N/A
Additional information: If used within NCL Trusts, Trust DTCs to ensure appropriate risk mitigation measures are in place (e.g., approved procedures, guidelines, and electronic system updates)

Post-meeting note: JFC Support were informed that a small number of patients in NCL primary care have potassium permanganate on their repeat prescription list. Primary care clinicians are encouraged to review these patients, in consultation with the initiating clinician, to determine whether treatment is still required; if so, duration of treatment and risk mitigation measures should be established. If treatment is no longer required, potassium permanganate should be stopped.

7. JFC Outstanding Items & Work Plan

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

8. Local DTC recommendations / minutes

DTC site	Month	Drug	Indication	JFC outcome
JFC	Aug 2021	MHRA EAMS: Lutetium-177-PSMA-617†	PSMA-positive metastatic castrate resistant prostate cancer	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** N/A – Free of charge **Funding:** N/A – Free of charge **Factsheet or shared care required:** N/A
UMC	Nov 2020	Monofer (Iron isolmaltoside)	Gastroenterology patients at risk of hypophosphataemia with Ferinject	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A
MEH	Pre-dates DTC	Indocyanine green	Retinal angiography in paediatrics	**Decision:** MEH and GOSH only **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A **Additional information:** Subject to appropriate risk mitigation measures through Trust guidance

† The relevant commissioner should be notified in line with NCL Free of Charge scheme guidance. Approval is conditional on the provision of a free of charge scheme agreement and funding statement.

9. New Medicine Reviews

9.1 Rapid reviews for DMARDs used for autoimmune hepatitis

This item was deferred to the October 2022 meeting.

9.2 Xonvea (doxylamine and pyridoxine) for hyperemesis gravidarum

The Committee considered an application for doxylamine 10mg and pyridoxine 10mg (Xonvea®), a combination of a first-generation antihistamine and vitamin B6 respectively, licensed for nausea and vomiting in pregnancy for women who do not respond to conservative management, at an initial starting dose of 2 tablets at bedtime.

Koren et al was a randomised multi-centre, Phase III, placebo-controlled, double-blind study to assess the safety and efficacy of doxylamine-pyridoxine (10mg-10mg) delayed-release for the management of nausea and vomiting in women with a single pregnancy between 7-14 weeks gestation (n=256). Patients were randomised to receive either doxylamine-pyridoxine (n=131) or placebo (n=125). The primary endpoint, symptoms of nausea and vomiting as measured on the validated PUQE score, was improved with doxylamine-pyridoxine compared to placebo (a reduction in 4.8 points ± 2.7 vs. a reduction in 3.9 points ± 2.6; p=0.006). Another important outcome was patient request to continue compassionate use of their medication which was improved compared to placebo (48.9% vs. 32.8%; p=0.009). A key limitation of the study was the short duration of the study (15 days).

Zhang et al reported on the DESI study which was undertaken in 1975. This was a randomised, multi-centre (USA based), placebo-controlled, double-blind FDA regulatory study to assess the safety and efficacy of 8 interventions for the management of nausea and vomiting in pregnancy in the first 12 weeks of gestation (n=1599). Patients were randomised to receive doxylamine-pyridoxine (10mg-10mg) (n=213) or placebo (n=181). Outcome data collated via questionnaires completed by the study participants reported an improvement in symptoms. Key limitations of the study include the lack of prespecified outcomes or analyses by the authors, limited availability of baseline data and a high-risk of bias via the data collection method specified.

Oliveira et al was a randomised, active-comparator, double-blind study to assess the safety and efficacy of doxylamine-pyridoxine (10mg-25mg) for the management of nausea and vomiting in pregnancy (up to 16 weeks pregnant). Patients were randomised to receive either doxylamine-pyridoxine (n=18) or ondansetron-placebo (n=18). The primary endpoint, improvement in nausea as reported on a 100mm VAS score, was improved compared to the comparator (median VAS score decreased -51mm [interquartile range 37-64] compared to 20mm [interquartile range 8-51]; p=0.019). Other important outcomes were reduction in

vomiting on VAS which was improved compared to the comparator (median VAS decreased 41mm [interquartile range 17-57] compared to 17 [17-57]; p=0.049), and proportion of patients reporting sedation or constipation which reported no significant difference compared to the comparator. Key limitations of the study included a small sample size, use of the unvalidated VAS score, short duration (5 days) and a differing dose of pyridoxine as compared to Xonvea® (25mg vs. 10mg).

In terms of safety, doxylamine-pyridoxine had a similar risk of adverse effects as compared to other antihistamines and was reported to be well-tolerated in clinical trials. It was highlighted that Xonvea® is the only licensed anti-sickness medicine available in the UK for pregnancy induced nausea and vomiting. Doxylamine-pyridoxine was previously available under the brand name of Debendox® but was voluntarily withdrawn from the UK market in the 1970s due to concerns over increased risk of foetal abnormalities. Epidemiological studies examined by the Committee on Safety of Medicines concluded that there was no causal relationship between Debendox® and congenital abnormalities. A review conducted in 2014 by Madjunkova et al reported on a 1988 study by Einarson which examined outcomes of >200,000 women exposed to doxylamine-pyridoxine in the first trimester and found no increased risk of congenital malformations or other adverse pregnancy outcomes.

In terms of budget impact, Xonvea® is expected to cost an additional £39,021 up to £80,469 per annum, as compared to other agents.

The Committee heard from Professor David Williams that hyperemesis is a heterogenous condition with an unknown cause, often requiring an inpatient admission for management and associated to high morbidity. Symptoms usually improve at 14-16 weeks gestation. Current management includes the use of off-label anti-emetics, steroids and IV hydration. The proposed place in therapy for Xonvea® in a first pregnancy is third line after cyclizine, metoclopramide and prochlorperazine, but prior to ondansetron and steroids. Dr Williams highlighted that many women are reluctant to use ondansetron due to the unproven perceived risk of cleft palate in the first trimester.

In camera, the Committee noted that there was little or no evidence of superiority of Xonvea® over other agents, or direct evidence of benefit in patients failing to respond to other agents, including a lack of evidence of reduced hospital admissions. The committee also noted a relatively large budget impact. It was however noted that Xonvea® has a good safety profile and is the only licensed product for this indication in pregnancy.

In summary, the Committee agreed in principle to add Xonvea® to the NCL Joint Formulary for pregnancy associated nausea and vomiting as a treatment option after ondansetron, noting that patient choice should be considered if there were concerns over the use of ondansetron. The decision is subject to approval of a treatment hierarchy which should include clear prescribing and stopping criteria to aid primary care clinicians.

Decision: Deferred pending treatment hierarchy

10. Licensed metolazone 5mg tablets – unlicensed formulation request letter

The Committee was informed that a review of Xaqua® would be brought to the next meeting. As previously discussed, Xaqua® is a new licensed formulation of metolazone 5mg tablets which the manufacturer states has up to a two-fold difference in bioavailability compared to other (unlicensed and imported) metolazone preparations that are currently in use. In the interim, NCL JFC have informed clinicians to ensure patients who are stable on an unlicensed metolazone preparation be continued on therapy until Xaqua® is formally reviewed.

Wholesalers of unlicensed products have requested that clinicians provide a letter from the prescribing clinician to outline the rationale for ordering the unlicensed product when a licensed version exists. A standardised letter was presented to the Committee to ensure a consistent message. The letter was approved pending minor amends.

11. Anti-hyperglycaemic agents for type 2 diabetes guideline

The Committee was presented with an updated guideline for antihyperglycaemic agents used in type 2 diabetes. The guideline was produced as NICE have issued partial updates to existing guidance following studies conducted on SGLT2 and GLP-1 mimetics. The guideline has been updated and approved via the NCL Diabetes and Weight Management Network and has had NCL-wide consultation. The Committee approved the guideline.

12. NCL DOAC prescribing guideline

The Committee was presented with an updated guideline for DOAC prescribing in NCL. The guideline was produced to update the existing guideline and support other related DOAC initiatives in NCL. The Committee approved the guideline.

13. DOACs in non-valvular atrial fibrillation position statement

The Committee ratified the updated NCL position statement for choice of DOACs in non-valvular atrial fibrillation.

14. Updated high-cost drug pathways for inflammatory bowel disease

The Committee were presented with an updated high-cost drug pathway for inflammatory bowel disease. The pathway had a minor update following approval to use subcutaneous infliximab in patients initiated and stabilised on infliximab in secondary care (which was approved by NCL JFC in October 2021). A concern was raised regarding the use of high-cost drugs in paediatric IBD, which is of particular concern to paediatric patients approaching their 18th birthday and who have expressed a desire to transition to adult services at Whittington Health; this was outside the scope of the current document which focuses on ICB-commissioned therapies and will be escalated to NHSE specialised commissioning. The Committee approved the pathway.

15. Next meeting

Thursday 20th October 2022

16. Any other business

Dapagliflozin and empagliflozin for Heart Failure with Preserved Ejection Fraction (HFpEF) or Heart Failure with Moderately Reduced Ejection Fraction (HFmrEF)

The Committee was informed of requests to consider an application to use dapagliflozin or empagliflozin for HFpEF and HFmrEF. NICE have already approved use in heart failure with reduced ejection fraction (HFrEF) and are scoping for the two new indications. The initial NICE review meeting is expected to be held in January 2023, and due to the length of the consultation period and implementation process it is not expected that a decision be made prior to mid-to-late Q2 2023. The Committee discussed the possible risks involved with patient equity if NICE does not consider the treatments to be cost-effective. This was weighed against the benefits that treatment could provide to a difficult to treat population, therefore delaying a formulary review could deny patients access to a potentially effective treatment. The Committee agreed that an application can be made for consideration at JFC ahead of a NICE review.

Membership

The Committee thanked Stuart Semple (Interim Chief Pharmacist at GOSH and Interim Chief Pharmacist for NCL ICS) for his contributions and leadership across the sector. The new GOSH Chief Pharmacist (Jayne Ballinger) will be invited from the next meeting.