North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 21 May 2020

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Ms W Spicer	RFL, Chief Pharmacist	
	Prof A Tufail	MEH, DTC Chair	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Ms K Delargy	BEH, Deputy Chief Pharmacist*	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Dr M Kelsey	WH, DTC Chair	
	Dr A Sell	RNOH, DTC Chair	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Mr S Richardson	WH, Chief Pharmacist	
	Prof K Moore	RFL, Professor of Hepatology*	
In attendance:	Mr A Barron	NCL MEP, Project Lead	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Mr P Bodalia	UCLH, Principal Pharmacist	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Mr F Master	RFL, Formulary Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr F Ismail	NEL CSU, Contracting and Commissioning Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Mr J Flor	WH, Formulary Pharmacist	
	Ms S Amin	UCLH, Lead Medicines Optimisation Pharmacist	
	Dr P Taylor	NCL CCG, GP Clinical Lead for Evidence-Based Interventions	
	Ms S Y Tan	NEL CSU, Commissioning and Contracting Pharmacist	
	Mr J Dick	UCLH, Consultant Anaesthetist	
	Dr S Parker	UCLH, Surgical Registrar	
	Dr A Patel	RFL, Respiratory Consultant	
Apologies:	Mr C Daff	Barnet CCG, Head of Medicines Management	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Mr S Semple	MEH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr T Dean	Patient Partner	
	Ms G Smith	RFL, DTC Chair	
	Ms L Reeves	C&I, Chief Pharmacist	
	Dr A Stuart	NHS Camden, GP Clinical Lead Medicines Management	

**Deputising for Committee member*

2. Meeting observers

The Committee welcomed Dr Taylor (NCL CCGs GP Clinical Lead for Evidence-based Interventions) as an observer of the meeting.

3. Minutes of the last meeting

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

4. Matters arising

4.1 Nebulised prostacyclin (iloprost or epoprostenol) for respiratory failure

NHS England's 'Clinical guide for the management of critical care for adults with COVID-19 during the coronavirus pandemic' states the pulmonary vasodilators (e.g. inhaled nitric oxide and nebulised epoprostenol) can be considered to improve V/Q mismatching where available. The JFC interim position statement (approved April 2020) discouraged the use of medicines being used for an unapproved off-label indication for the purpose of treating the COVID19 infection outside of a registered clinical trial. This position was made following advice to Chief Pharmacists from NHSE Specialised Commissioning. Owing to the seemingly contradictory advice from NHSE, a request for clarification was sought.

Correspondence from NHSE indicated that the ITU guidance supersedes the NHSE Specialising Commissioning letter. The Committee therefore recommended that Trusts access prostacyclin in line with the NHSE guidance and the position statement should be updated to reflect this. Results from the RFL pilot trial will be presented at the next JFC.

5. Declarations of relevant conflicts of interest

No additional declarations were noted for the new medicine applications.

6. Local DTC recommendations / minutes

6.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Feb 20	Sildenafil	Persistent pulmonary hypertension of the newborn	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
Camden CCG	Feb 2015	Amitriptyline	Second-line pharmacological management of irritable bowel syndrome in patients who remain symptomatic despite use of an antispasmodic	Decision: Added to the NCL Joint formulary Prescribing: Primary and secondary care Tariff status: In tariff Funding: CCG/Trust Fact sheet or shared care required: No
UCLH	Pre 2012	Pancrex V powder	To unblock enteral feeding tubes	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

UCLH	Pre 2012	Pancrex V powder	Pancreatic enzymes deficiency in patients with NG or PEG tubes	Decision: Added to the NCL Joint formulary Prescribing: Secondary care initiation, primary care continuation Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
UCLH	Pre 2012	Pancrex V powder	Pancreatic enzymes deficiency in patients with swallowing difficulties who are unable to take Creon due to administration difficulties or oral irritation	Decision: Added to the NCL Joint formulary Prescribing: Secondary care initiation, primary care continuation Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

6.2 Approved under evaluation

DTC site	Month	Drug	Indication	JFC outcome
MEH	Oct 19	Atropine eye drops	Slow myopia progression in children and young adults	Decision: MEH only Prescribing: Tertiary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

7. New Medicine Reviews

7.1 Olaparib for pancreatic cancer [Pre-NICE FoC Scheme] (Dr Gillmore, RFL)

As the applicants were unable to attend, this item was deferred.

7.2 Botulinum toxin A to aid the repair of complex abdominal hernia

The Committee considered an application to administer botulinum toxin A (BTA) to the lateral abdominal wall muscles in order to aid the repair of complex abdominal hernia. The pharmacological basis for administering BTA is to relax and elongate the muscles which in turn ensures the hernia defect can be successfully repaired; this requires an additional day case admission in the care pathway in order to inject BTA two to four weeks prior to the operation.

A systematic review and meta-analysis (n=56) comparing pre-BTA and post-BTA changes found a significant reduction in defect width (-2.61cm [95% CI -3.37 to -1.86]) and significant elongation of both the left (0.95cm [95% CI 0.51 to 1.40]) and right (1.03cm [95% CI 0.58 to 1.47]) abdominal muscles. The meta-analysis had major limitations including the absence of a control arm in the component studies, the variety of administration techniques and variable BTA doses.

A literature search for studies conducted after the meta-analysis identified four relevant publications; these studies used a range of BTA doses and administration techniques. Each study was uncontrolled (the only comparison made was against different doses of BTA, different administration sites or pre-operative progressive pneumoperitoneum) and found an improvement in muscle elongation following BTA administration. Data from an unpublished study, identified by clinicaltrials.gov (NCT04131348) was presented (n=80), comparing patients with a large midline hernia who were treated either with anterior component separation (ACS) or BTA. Complete fascial closure was possible in all participants, although at a median follow up of 19.6 months two participants in the ACS group suffered recurrence (8.9%) compared to none in the BTA group.

BTA has been used off-label for a number of years at UCLH and data were presented on 16 patients treated between January 2018 and March 2019. Five patients had a previous unsuccessful repair and six

records did not note BTA administration information. The most common dose and administration technique was 300 units administered across six different sites. 13 patients had a successful repair (one patient did not attend surgery; one patient could not be closed fully and had mesh bridging; one patient could not be closed and was referred to another specialist centre).

General adverse effects noted from the above studies from BTA administration were a feeling of bloatedness and weaker coughing or sneezing. Patients in studies and UCLH patients suffered seroma which can require drainage (though this may be a result of the surgery and not BTA). Other common adverse effects from BTA included pain, injection site haemorrhage or reaction and hypersensitivity. This intervention is associated with additional costs due to the day case admission, with an estimated total cost of £1,086 per patient (£21,720 per annum).

Dr Parker and Mr Dick provided information on their clinical experience with BTA and hernia patients. It has been used at UCLH for the past four years in for complex patients. Although it is recognised that there is no formal definition of "complex hernia", patients who access the tertiary service generally have a complex presenting history, and those who have had a previous operation will have less muscle bulk to manipulate; patients have a CT-scan to identify if there is enough muscle bulk to administer BTA into. Whilst the dose used in the literature was variable, the applicants advised a regimen involving 300 units in total was typical. The recurrence rate of a hernia decreases significantly if the sheath can be surgically closed at the midline; the administration of BTA greatly increases the rate of successful closure. Although the treatment is more expensive in the short-term, there are long-term benefits in reducing recurrence, which later leads to further admissions and surgeries. From their experience, BTA administration does extend the muscle length by around 4cm from either side.

In camera, the Committee discussed the lack of reliable comparative published evidence available to confirm the effectiveness of this off-label intervention, however was satisfied that the treatment was likely to be safe. The Committee was also concerned by the lack of an agreed administration protocol or defined patient population, although there was support as it is to be utilised within a tertiary service and the cost of the medication were deemed trivial compared to the otherwise poor outcomes from failure of hernia closure. The Committee voted on the application in its current form:

Approve – 3
Not approve – 7
Abstention – 1

The Committee required the following information before considering an appeal:

1. A formal assessment of the feasibility of a randomised-controlled trial to resolve uncertainty in the efficacy, safety and effective dose for BTA
2. A protocol detailing the intended population, dose and administration technique
3. A clarification as to whether BTA will be internally funded or whether a business case will be submitted to NCL CCG

Decision: Not Approved

7.3 Varenicline in combination with nicotine replacement therapy for smoking cessation

The Committee considered an application for the use of varenicline in combination with nicotine replacement therapy (NRT) to aid smoking cessation for inpatients and outpatients as a first-line treatment. Varenicline has a NICE TA for its use as monotherapy to aid smoking cessation. It is licensed to be used alongside smoking until a target quit date (TQD) is reached, and then continued alone for up to 24 weeks. The proposal is to use varenicline alongside NRT with or without smoking prior to the TQD, representing an off-label use.

A systematic review and meta-analysis (n=904) compared the combination of varenicline and NRT versus varenicline alone. Three studies were included for analysis, which found significant improvements in abstinence in the combination group vs monotherapy in the early outcome with a follow-up period up to 12 weeks (OR = 1.50 [95% CI 1.14 to 1.97]) and in the late outcome with follow-up period up to 24 weeks (OR = 1.62 [95% CI 1.18 to 2.23]). The overall result of the study was heavily influenced by a single-RCT with a high drop-out rate. Further, this study was the only one which used an administration schedule similar to that proposed by the applicant (by initiating NRT two weeks prior to the TQD). The study found

the combination to cause more nausea, insomnia and abnormal dreams than monotherapy, though the combination therapy also caused less headache.

Safety studies were also presented. The EAGLES study (n=8,144) demonstrated that the primary endpoint (a composite of neuropsychiatric reactions) was reached in similar proportions amongst patients taking either varenicline, bupropion, NRT patches or placebo. The non-psychiatric cohort showed no difference in the varenicline vs NRT groups, and was significantly lower for varenicline vs placebo groups. In the psychiatric cohort, there were no significant pairwise treatment differences. A post-hoc analysis from the EAGLES study found no difference in time to major adverse cardiovascular events when comparing active treatment and placebo.

An MHRA alert in 2008 warned on the possible increased suicide risk with varenicline. However, this was updated with results from a UK nested cohort study (n=80,660) which stated no clear evidence to demonstrate an association between varenicline and non-fatal self-harm (HR = 1.12 [95% CI 0.67 to 1.88]). However, the MHRA concluded an increased risk could not be ruled out. The manufacturer advises that a rise in certain disorders (such as neuropsychiatric reactions) is associated with nicotine withdrawal rather than pharmacotherapy.

The Committee heard from Dr Patel that whilst varenicline is used alongside smoking until a target quit date for ambulatory patients, hospital inpatients cannot smoke therefore smoking is substituted with NRT. The Committee were reminded that smoking has a major impact on the quality and length of life therefore any pharmacological treatment is likely to be cost-effective.

In camera, the Committee agreed that the NICE TA for varenicline should be followed for ambulatory patients, in line with the product license. For inpatients, who are unable to smoke until the TQD, the Committee agreed varenicline in combination with NRT (rather than smoking) until the TQD should be available. In summary, varenicline was added to the NCL Joint Formulary, in combination with NRT until the TQD for hospitalised inpatients (who are unable to smoke) only.

Decision: Approved in combination with smoking until target quit date (NICE TA 123) and in combination with weaning dose of NRT for patients that cannot smoke during the smoking cessation period e.g. whilst hospitalised.
Prescribing: Initiation in Secondary care; NRT continued until the Target Quit Date and varenicline continued until the course is complete (by Primary, Secondary or Community health service)
Tariff status: In tariff
Funding: Hospital/CCG
Fact sheet or shared care required: No

8. RA pathway: Update during COVID-19 pandemic

A final RA pathway was presented for approval. The pathway permits broader access to oral drugs (JAKi) and low-cost anti-TNFs across 4 lines of therapy during COVID-19. The Committee approved the pathway.

9. Ranitidine

A summary of recent changes to the ranitidine shortage was presented to the Committee. The EMA have ordered the suspension in manufacture of all ranitidine products. The DHSC have now stated that all ranitidine (including intravenous formulations) will be out of stock from the end of May 2020. The drug tariff now includes a licensed omeprazole suspension at a higher cost than the price of the unlicensed formulation. JFC Support will work with Trust Specialist Pharmacists to update the ranitidine Trusts statement, and will update the Primary care statement in due course when more information is known about the use of unlicensed proton pump inhibitor liquids in NCL.

10. COVID-19 related guidelines

10.1 Position Statement: Use of investigational antiviral agents for COVID-19 in adults

The following items were presented for information. JFC Secretariat provides support to 'COVID-19 Therapeutics Advice & Support Group' who maintain position statements relating to the use of antivirals and immunomodulators for the treatment of COVID-19 in the hospital setting. NCL Trusts are encourages to follow the recommendations

10.2 Position Statement: Use of investigational immunomodulatory agents for COVID-19 in adults

As for item 10.1

10.3 Vitamin D: A rapid review of the evidence for treatment or prevention of COVID-19
For information only. The document was approved by the NCL COVID Pharmacy Cell.

10.4 Primary care recommendations for monitoring of ADHD medications during the COVID-19 pandemic
For information only. The document was approved by the NCL COVID Pharmacy Cell.

10.5 Managing medicines during the COVID-19 pandemic: Vitamin B12 injections (Maintenance)
For information only. The document was approved by Chair's Action.

11. Botox data collection form [Fowlers Syndrome]
Any comments to be sent to Ms Kassam by 28th May 2020. The data collection form was otherwise approved.

12. Next meeting
Thursday 18th June

13. Any other business
Nil