North Central London
Medicines Optimisation Network

NFC JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 19 August 2019
Boardroom 1st Floor, Maple House, London, W1T 7NF

Present:	Dr R Sofat	UCLH, DTC Chair (NCL JFC Vice Chair)	(Chair)
	Dr M Kelsey	WH, DTC Chair	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Dr A Sell	RNOH, DTC Chair	
	Mr S Semple	MEH, Chief Pharmacist	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Dr R MacAllister	NCL JFC Chair	(via telephone)
	Ms L Reeves	C&I, Chief Pharmacist	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
In attendance:	Mr A Barron	NCL MEP, Lead Pharmacist	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Dr P Bodalia	UCLH, Principal Pharmacist	
	Ms S Sanghvi	UCLH, Formulary Pharmacist	
	Ms H Mehta	NMUH, Formulary Pharmacist	
	Mr J Flor	WH, Formulary Pharmacist	
	Ms Y Al-Hayali	MEH, Formulary Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Mr F Master	RFL, Formulary Pharmacist	
	Ms M Thacker	RFL, Clinical Services Pharmacist	
	Ms D Joshi	UCLH, Lead Pharmacist Surgical Speciality	
	Dr J Sun	UCLH, Foundation Year 2 Doctor	
	Ms J Bloom	MEH, Associate Chief Pharmacist	
	Ms S Ahmed	WH, Rotational Pharmacist	
	Dr A Lamba	Barnet, GPwSI (Diabetes)	
Apologies:	Ms K Davies	NEL CSU, Deputy Director Medicines Management	
	Prof D Hughes	RFL, Consultant Haematologist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Mr S Richardson	WH, Chief Pharmacist	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Ms W Spicer	RFL, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Mr G Kotey	NMUH, Chief Pharmacist	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Dr S Yardley	CNWL, Consultant in Palliative Medicine	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	Mr C Daff	Barnet CCG, Head of Medicines Management	
	Mr T Dean	Patient Partner	

2. Meeting observers

Dr J Sun (UCLH, Foundation Year 2 Doctor) was welcomed as an observer to the meeting.

3. Minutes of the last meeting

The minutes were amended to reflect that ecilizumab for hyperhaemolysis should be made available to any Provider Trust with sickle cell service; it was noted that eciluzumab is a high-cost drug that is not routinely commissioned for this indication. UCLH have submitted a policy request to NHSE however in the interim, Provider Trusts need to secure internal funding approval before adding to local formularies.

It was clarified that the burosumab 'Post-NICE TA but pre-NHSE Commissioning' free of charge scheme for X-linked Hypophosphatemia in children and young people was now closed to recruitment.

4. Matters arising

4.1 VSL#3 update

Mr Dutt confirmed that following the removal of ACBS' endorsement of probiotics for pouchitis, VSL#3 was not blacklisted [in the Drug Tariff] and therefore can be prescribed in primary care. NHSE and NHS Clinical Commissioners recommend that probiotics are not routinely prescribed in primary care therefore CCG members proposed VSL#3 is retained in secondary care to minimise confusion and to prevent prescribing outside of the JFC approved indication of pouchitis. The overall spend on VSL#3 in NCL is low and the potential inconvenience as a result of limiting prescribing to secondary care was acknowledged. UCLH gastroenterology team are the only secondary care centre in NCL that recommends VSL#3 therefore it was agreed to defer this issue to UCLH UMC.

Action: UCLH UMC to review the potential resource pressure if patients are repatriated to secondary care to determine if this is appropriate.

4.2 Patiromer for hyperkalaemia - outstanding actions and update

A survey identified that Calcium Resonium® is not consistently used across NCL for the management of hyperkalaemia. Feedback suggests use is limited due to slow onset of action, limited efficacy and unfavourable side effect profile. The Committee reviewed an abstract from Royal London's renal unit outlining the retrospective use of patiromer in 105 patients for the treatment of hyperkalaemia in patients with AKI or on dialysis. Treatment success (defined as avoidance of emergency vascath insertion or emergency dialysis) was obtained in ≥75% of patients however it was unclear whether treatment success was due to patiromer administration, or concurrent potassium lowering treatment, or spontaneous resolution. Patiromer was well tolerated with only one patient discontinuing treatment due to nausea.

It was understood that the forthcoming European Renal Best Practice guideline (part of the European Renal Association) on hyperkalaemia does not recommend the use of patiromer for acute hyperkalaemia.

The Committee was informed that NICE have published a positive NICE FAD for a different potassium binder, sodium zirconium cycosilicate (Lokelma®), if used in emergency care for acute life-threatening hyperkalaemia (alongside standard of care) or in outpatient care for persistent hyperkalaemia secondary to CKD stage 3-5b or heart failure. The Committee heard that sodium zirconium cycosilicate has a faster onset of action compared to patiromer (1 hour vs. 4 – 7 hours) which was advantageous.

The Committee concluded the Royal London audit did not conclusively show patiromer to be clinically effective in the management of acute hyperkalaemia. Sodium zirconium cycosilicate was thought to have advantages over patiromer and the anticipated NICE TA would result in Provider Trusts being required to supply this to patient who meet the eligibility criteria. The Committee requested the applicant submit a new application for sodium zirconium cycosilicate for indications not covered by the NICE FAD.

Decision: Not approved

4.3 Andexanet for DOAC related bleeds - update

A survey of NCL Provider Trusts confirmed that the primary treatment for severe and uncontrolled DOAC related bleeds is Prothrombin Complex Concentrate (PCC); except for bleeds related to dabigatran, which is treated with Praxbind®. The use of PCC is known to be unlicensed but supported by international guidance, and requires Consultant Haematologist input before initiation at each site.

Neighbouring London Trusts were asked if they were considering the use of andexanet alfa in their respective organisations; none of those who responded planned to review this medicine in advance of guidance from NICE.

The Committee agreed it was inappropriate to review andexanet in advance of NICE owing to (i) the very high cost of the intervention which would be associated with a large opportunity-cost for hospitals as andexanet is currently 'in tariff', (ii) the prevention of duplication of effort with a national Committee, and (iii) the limited clinical trial data which used surrogate endpoints. JFC Support were asked to send the information obtained from NCL Trusts to NICE during their consultation process to aid their decision.

Action: JFC Support to register as a stakeholder for andexanet alfa NICE TA.

5. JFC Work Plan & outstanding actions

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

6. Declarations of relevant conflicts of interest

No additional declarations were noted for the new medicine applications.

6.1 JFC members declarations of interest

Committee members were requested to complete the NCL JFC declarations of interest form

7. Local DTC recommendations / minutes

7.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
RFL	Jun-19	24% sucrose oral solution	Pain management for procedures in neonates and infants	Decision: Added to NCL joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
UCLH	July-19	Burosumab	Early Access Program: X-linked hypophosphatemia in adults	Decision: Approved pending funding confirmation and use of FoC consent form Prescribing: UCLH and RNOH Tariff status: Excluded from tariff Funding: NA (FOC) Fact sheet or shared care required: No

7.2 Approved under evaluation

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Jul-19	Dexrazoxane	Prevention of anthracycline-cardiotoxicity in high dose paediatric sarcoma patients	Decision: Approved under evaluation Prescribing: UCLH only Tariff status: Excluded from tariff Funding: Not routinely commissioned – Trusts to consider internal funding until commissioned by NHSE Fact sheet or shared care required: No

8. New Medicine Reviews

Alprostadil cream (Vitaros®) for erectile dysfunction under the Selected List Scheme (SLS) (Applicant: Professor D Ralph and Mr A Muneer, UCLH)

The Committee considered an application to use alprostadil cream (300 microgram) under the Selected List Scheme (SLS) in patients with erectile dysfunction after failure of first-line phosphodiesterase-5 inhibitors (PDE5-i). The NCL Joint Formulary currently includes alprostadil in two different formulations; administered via intracavernosal injection (Caverject®) or insertion of an intraurethral stick (MUSE®).

An analysis of two Phase-III, randomised, double-blind, placebo controlled trials was undertaken, which compared alprostadil cream to placebo. The study included three co-primary outcomes using the International Index of Erectile Function (IIEF) and a Sexual Encounter Profile (SEP). Statistical significance was reached in favour of alprostadil 300 microgram cream versus placebo in the three co-primary outcomes. However, only the third co-primary outcome (mean change between baseline response of the third question in the SEP diary between baseline and final visit) indicated a clinically relevant improvement based on the minimally clinically important differences outlined in the NICE Evidence Summary (absolute difference increase of 8.9% [$p<0.001$]). There was no clinically important difference observed for other co-primary outcomes (change in score in the erectile function domain of the IIEF from the baseline to the final visit response and the mean change between baseline response of the second question in the SEP diary between baseline and final visit).

The EPAR did not identify any active comparator studies for alprostadil cream and it was not possible to perform an indirect comparison against intraurethral alprostadil due to differences in primary endpoints. An indirect comparison against PDE5-i showed alprostadil cream to be less effective than sildenafil and tadalafil.

Mr Muneer informed the Committee that alprostadil cream was minimally invasive, easier to administer and offers a second-line treatment option for patients who cannot use intracavernosal injection or intraurethral stick due to dexterity issues. It was hypothesised that alprostadil cream may salvage the need for penile implant surgery in some individuals which is costly and risks long-term adverse outcomes; however there was no evidence to substantiate this claim. Mr Muneer noted that PDE5-i should be first-line therapy in primary care and took the view that alprostadil cream could be offered by some GPs who are able to demonstrate the application effectively.

There were concerns that alprostadil cream would represent a significant cost-pressure as patients were more likely to accept treatment with a cream, as compared with intracavernosal or intraurethral application, however it was noted that the currently available formulations of alprostadil have been subject to long-standing shortage of supply.

In camera, the Committee agreed that alprostadil cream was easier to administer and less invasive that other second-line options and that other alprostadil formulations should remain on the NCL Joint Formulary as superiority of these formulations could not be excluded. In summary, the Committee approved alprostadil cream as a second-line therapy to treat erectile dysfunction under SLS following failure or intolerance to PDE5-i.

Post meeting note: The NCL Primary Care erectile dysfunction pathway recommends 1st line PDE5-i (sildenafil 50/100mg PRN, then trial tadalafil 10/20mg PRN) and then "refer to urology if no response after 8 weeks of medication ONLY IF PATIENT WISHES to consider MUSE, vacuum device or caverject injections in nurse led clinic". The pathway therefore requires an update following the approval of alprostadil cream. Alprostadil cream should remain restricted to secondary care initiation unless a decision is made to include as a primary care option.

Decision: Approved
Prescribing: Initiated in secondary care, continue in primary care (unless the NCL Primary Care pathway is updated to include alprostadil cream)
Tariff status: In tariff
Funding: Hospital/CCG
Fact sheet or shared care required: No
Additional information: Alprostadil cream to be prescribed under the Selected List Scheme

Action: NCL CCGs to request a review of the NCL 'Erectile Dysfunction Primary Care Protocol' (version 10.7).

9. Letrozole – Request to change from second-line to first-line agent for ovulation induction

The committee considered a request to use letrozole for ovulation induction in women with group II anovulation *in absentia*.

In January 2018 NCL JFC approved an application to use of letrozole second-line, following failure of clomifene, for ovulation induction women with group II anovulation. Subsequently an international guideline has recommended the use of letrozole first-line in women with PCOS; PCOS represents the major proportion of women with WHO group II anovulation.

In terms of efficacy, a Cochrane review conducted by Franik et al, updated in 2018, showed that letrozole is more effective than clomifene in terms of live births (OR 1.68 [95% CI: 1.42 to 1.99]).

In terms of congenital malformations, one new retrospective study was published since January 2018, the Cochrane 2018 review did not included this outcome. A summary of retrospective studies and RCTs comparing letrozole to clomifene did not identify a consistent trend in favour of either drug. The Committee concluded that low quality evidence showed no difference between clomifene and letrozole. Reassurance was taken from the UK Teratology Service who concluded significant exposure of the embryo appeared unlikely unless letrozole is inadvertently given for ovulation induction to a woman who is already pregnant.

Letrozole is off-label for this indication, is contraindicated in premenopausal women and the manufacturer has issued a warning letter against its use for ovulation induction. In contrast, clomifene is licensed and holds years of experience as a first-line agent for ovulation induction.

In summary, the Committee acknowledged that first-line use of letrozole is recommended by an international consensus guideline however remained concerned by:

- the warning issued by the Novartis in 2005 against the use of letrozole for ovulation induction which had not been redacted
- the low quality data relating to congenital malformation and therefore uncertainty remained as to whether or not letrozole posed an increase in congential malformations relative to clomifene
- letrozole is off-label and would be positioned ahead of a licensed medicine within its licensed indication

The Committee requested the applicant attend in person to address the following queries before a final decision could be made:

- Does the guideline represent a consensus with views of the UK clinical community?
- Has there been a request to withdraw the warning letter issued by Novartis in 2005?
- Did the previous international consensus guideline recommend the use of letrozole first-line?
- Will the manufacturers of letrozole be applying for a license extension?
- Is there a lost clinical opportunity of using a less effective first-line treatment prior to using letrozole?
- What is the current practice in Queen Charlotte's hospital?

Post-meeting note: The International guideline collaborated with RCOG and the British Fertility Group. RCOG have not issued guidance for the pharmacological management if PCOS/ women with WHO group II anovulation

Decision: Deferred

10. Pre-NICE application: Jorveza® (budesonide orodispersible tablets) to treat eosinophilic oesophagitis

JFC Support have received a pre-NICE application for budesonide orodispersible first-line for eosinophilic oesophagitis. In February 2018 the Committee approved off-label fluticasone inhaler (first-line) & budesonide nasals (second-line) for this indication.

In September 2018 budesonide orodispersible tablet was licensed for short-term use of eosinophilic oesophagitis (maximum 12 weeks). The Committee heard that eosinophilic oesophagitis is a chronic condition and did not anticipate patients to discontinue treatment after 12 weeks therefore most

patients would be using budesonide orodispersible tablet off-label. A long-term maintenance study has results in abstract form which may be used to extend the product license.

The Committee agreed it was inappropriate to review budesonide orodispersible tablet in advance of NICE (i) in order to prevent duplication of efforts with a national Committee, (ii) the low unmet need as patients already had access to effective treatments, and (iii) the high cost of budesonide orodispersible tablet making a positive NICE TA highly uncertain.

11. Guideline update - Ocular Lubricants

The Committee reviewed an update to the NCL Ocular Lubricants pathway; co-authored by MEH and Islington CCG which had undergone multiple rounds of consultation. The guideline newly included Thealoz Duo® approved by JFC in July 2019 and NHSE advice on self-care.

It was queried whether brand names should be included on the guideline however most stakeholders requested that the guideline was generic and DM+D compliant. MEH have produced an adaptation of the NCL guideline to include the most cost-effective product choices which can be provided on request.

It was not considered practical to provide definitions for 'mild', 'moderate' or 'severe' dry eye however in practical terms, if dry eye does not resolve following life-style measures and management with mild or moderate product recommendations, referral to secondary care should be considered.

The guideline was approved.

12. Factsheet update – Sacubitril valsartan

The fact sheet was approved.

13. Draft response for appeal: Catephen (camelia sinensis) to treat perianal and genital warts

In May 2019, the Committee did not approve an application to use Catephen (camelia sinensis) 10% ointment to treat perianal and genital warts. The decision was based on Catephen being similarly effective but more expensive than alternatives. There was also insufficient unmet clinical need for a new pharmacological mechanism of action as podophyllotoxin cream/solution and imiquimod cream were available.

JFC Support received an appeal against the decision however none of the grounds for appeal met the threshold for reconsideration in accordance with the JFC terms of reference. A letter was drafted to explain why each of the grounds for appeal was unsuccessful. The Committee approved the letter to be sent to the applicant.

14. Appeal against the removal of dulaglutide from the NCL Joint Formulary

The Committee received a joint appeal from 24 diabetes specialists against the removal of dulaglutide from the NCL Joint Formulary. The appeal recommended that:

- Semaglutide was the preferred GLP-1 receptor agonist
- Dulaglutide is restricted for patients:
    - who are needle-phobic and cannot use the semaglutide pen device.
    - with impaired manual dexterity (e.g. due to severe arthritis) and cannot use the semaglutide pen device.
    - with learning difficulty or mental health issues and require GLP-1 receptor agonist administration by a third-party as the dulaglutide device minimises the risk of needle-stick injury
- Liraglutide 1.2 mg (Victoza®) is restricted for patients with concurrent gastrointestinal conditions e.g. inflammatory bowel disease

The Committee heard from Dr Lamba that dulaglutide had practical advantages over semaglutide which needed to be balanced against inferior impact on HbA1c and weight loss; specifically the prefilled autoinjector (as compared to an insulin-type pen) and lack of a need to dose escalate. It was acknowledged that an increased number of similar products on formulary increased the risk of prescribing and administration error – a GLP-1RA fact sheet had been developed in an effort to reduce this risk. Patients requiring insulin who are needle-phobic/impaired manual dexterity/require third-party administration do not have autoinjector options therefore it was queried why this was required for

patients requiring GLP-1 receptor agonists; Dr Lamba suggested that care is often suboptimal for these patients and may include community services which was wasteful.

In camera, the Committee remained uncertain that the increased risk of having three similar GLP-1 receptor agonists was justified and had not seen any evidence to suggest that autoinjectors offered such a substantial advantage that it warranted prescribing a less effective treatment. Additionally many patients eventually require insulin, so while this may delay use of an insulin-type pen, the Committee noted that there is the necessary facility in place to train patients. The Committee however acknowledged the compromise and uniformity of opinion amongst diabetes specialists in creating clear prescribing criteria and agreed to accept their recommendations.

15. Fact sheet update - GLP-1 RA

The fact sheet was approved subject to the order of GLP-1 receptor agonists in the document being updated from "liraglutide, dulaglutide, semaglutide" to "semaglutide, dulaglutide, liraglutide".

16. Guideline update - Antihyperglycaemic agents for type 2 diabetes

The guideline was approved.

17. JFC chair

Dr MacAllister stepped down as Chair of the NCL JFC after completing two successful three year terms. The Committee were informed that following an open application process Dr Sofat was appointed into the role.

Dr Urquhart thanked Dr MacAllister on behalf of the Committee for his substantive efforts and pivotal role in establishing the Committee and for his years of dedication and leadership as JFC Chair.

The Committee thanked Dr MacAllister for all his work and congratulated Dr Sofat on her new appointment.

18. Next meeting

Monday 16th September 2019

19. Any other business

Nil