North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 20 January 2020
G12 Council Room, South Wing, UCL, Gower Street, WC1E 6BT

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Dr M Kelsey	WH, DTC Chair	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr S Semple	MEH, Chief Pharmacist	
	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 P Taylor	Haringey CCG, Head of Medicines Management	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Ms L Reeves	C&I, Chief Pharmacist	
	Dr A Sell	RNOH, DTC Chair	
	Mr S Richardson	WH, Chief Pharmacist	
In attendance:	Dr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Barron	NCL MEP, Project Lead	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr S O'Callaghan	UCLH, Formulary Pharmacist	
	Ms A Olukosi	Haringey CCG, Prescribing Advisor	
	Ms L Stockford	NHNN, Pharmacist	
	Ms S Tan	NEL CSU, Commissioning Pharmacist	
	Ms S Pheerunggee	Tower Hamlets CCG, Prescribing Advisor	
	Dr S Hall	Tower Hamlets CCG, Medicines Optimisation Lead GP	
	Mr S Nganizi	NHSE, Policy & Strategy Management Trainee	
Apologies:	Mr C Daff	Barnet CCG, Head of Medicines Management	
	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	
	Mr T Dean	Patient Partner	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Ms G Smith	RFL, DTC Chair	
	Ms K Davies	NEL CSU, Deputy Director Medicines Management	

2. Meeting observers

Dr Sofat welcomed Ms Olukosi (Haringey CCG, Prescribing Advisor), Ms Tan (NEL, Commissioning Pharmacist), Ms Pheerunggee (Tower Hamlets CCG, Prescribing Advisor), Dr Hall (Tower Hamlets CCG, Medicines Optimisation Lead GP) and Mr Nganizi (NHSE, Policy & Strategy Management Trainee) as observers of the meeting and explained the role of the Joint Formulary Committee in NCL.

3. Minutes of the last meeting

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

4. Matters arising

4.1 Outstanding actions: Ospemifene for moderate to severe symptomatic vulvar and vaginal atrophy (VVA) in post-menopausal women who are not candidates for vaginal oestrogen

An application to use ospemifene for VVA was deferred in November 2019 to allow the applicant to further define the cohorts considered ineligible for vaginal oestrogen. Four cohorts were subsequently submitted:

1. Women unwilling to use hormones i.e. family history of breast cancer, history of breast cancer, safety fears about hormones, history of endometriosis (either resolved or patient undergone a hysterectomy), history of endometrial cancer with subsequent hysterectomy and history of ovarian cancer with subsequent bilateral oophorectomy.
2. Women with inadequate response to vaginal oestrogen
3. Women who are unwilling to use a vaginal preparation i.e. dislike messiness associated with the formulation or due to cultural beliefs
4. Women unable to use a local vaginal product due to physical limitations, pain or intolerance to side effects from vaginal oestrogen.

The Committee considered each cohort. For the first and third cohort, the Committee agreed topical oestrogen remained a viable treatment option which was safe, effective and cost-effective therefore ospemifene was not approved. For the second cohort, there was no evidence that ospemifene was superior to topical oestrogen therefore was not approved. For the fourth cohort, the Committee agreed there were no alternative treatment options and ospemifene provided an oral alternative which may provide a small absolute improvement in clinical symptoms of vaginal dryness and dyspareunia. The Committee agreed this was the only cohort in which ospemifene was likely to be cost-effective and it was noted that the Scottish Medicines Consortium also identified this cohort as part of their review.

The Committee considered the risk of prescribing creep associated with adding a new medicine to the NCL Joint Formulary for such a restricted cohort within the product's overall license. This risk was considered to outweigh the benefit therefore the Committee agreed ospemifene should not be added to the NCL Joint Formulary but that Trust DTCs could allow individual patient access through established 'one offs' or 'Chairs' action' processes. Any approvals should be limited to 'women unable to use a local vaginal product due to physical limitations, pain or intolerance to side effects from vaginal oestrogen'.

Decision: Not added to the NCL Joint Formulary however Trusts should consider approving individual patient applications via their 'one offs' or 'Chairs' action' process only for 'women unable to use a local vaginal product due to physical limitations, pain or intolerance from side effects of vaginal oestrogen'.
Additional information: Trusts to feedback a summary of individual patient approvals in 12 months to determine if a cohort becomes more apparent.

4.2 Guideline: Chronic Spontaneous Urtiaria [update]

At the November 2019 JFC meeting, the Committee considered removing montelukast from the adult Chronic Spontaneous Urticaria (CsU) treatment pathway. Prior to making a recommendation, the Committee asked JFC Support to determine whether there was consensus amongst NCL clinicians for the proposal, and whether montelukast is used in the paediatrics management of CsU. A specialist at GOSH confirmed neither montelukast nor omalizumab are used for paediatric CsU. JFC Support are awaiting a reply from the adult CsU clinical lead at RFL; Ms Samuel offered to follow up.

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.

7. Local DTC recommendations / minutes

7.1 Rivaroxaban and aspirin for peripheral arterial disease and coronary artery disease

In February 2019, JFC considered an application submitted by vascular teams to use rivaroxaban 2.5mg BD + aspirin 75mg OD to prevent cardiovascular outcomes in patients with peripheral arterial disease (PAD). The Committee deferred their approval until there was evidence of cardiology and vascular multidisciplinary working. In October 2019, NICE approved the treatment combination for coronary artery disease (CAD) or PAD and RFL had subsequently approved the TA.

The Committee reviewed the patient pathway presented at RFL DTC. The number of patients eligible for rivaroxaban in NCL by NICE was expected to be 1,093, so to manage implementation of the NICE TA in a safe and effective manner, the pathway prioritised treatment for those who would benefit most: (i) CAD with PAD, (ii) CAD with heart failure and (iii) CAD with poor renal function.

It was requested that rivaroxaban 2.5mg + aspirin 75mg was considered for inclusion in the NCL Antiplatelet guideline to provide context for the combination and details of follow-up. JFC Support agreed to follow up with Formulary Pharmacists and NCL HoMM to ensure implementation of the TA is equitable with appropriate information provided to Primary care for continuation.

Action: JFC Support to discuss with Formulary Pharmacists and NCL HoMM to consider the implementation of the NICE Technology appraisal

7.2 Approved

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Dec-19	Sativex® (THC and CBD oromuscosal spray)	Add-on therapy for the management of moderate to severe spasticity due to Multiple Sclerosis	Decision: UCLH only; for 'complete responders' in line with NICE guidance NG144 and not approved for partial responders Prescribing: Secondary care Tariff status: In tariff Funding: CCG Fact sheet or shared care required: UCLH UMC to laisse with NCL Shared Care Group for consideration of establishing shared care guidelines
RFL	Nov-19	Atezolizumab in combination with nab-Paclitaxel	Pre-NICE FOC scheme (following closure of EAMS): Locally advanced or metastatic triple negative breast cancer	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care Tariff status: N/A Funding: FoC Fact sheet or shared care required: No

7.3 Approved under evaluation

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Dec-19	Empagliflozin	Symptomatic neutropenia secondary to glycogen storage disease type 1b (GSD1b) or glucose 6 phosphatase catalytic subunit 3 (G6PC3) deficiencies	Decision: UCLH only; approved under evaluation Prescribing: Secondary care (initiation by consultant in adult metabolic disease and consultant haematologist) Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

8. New Medicine Reviews

8.1 Proposal to remove dosulepin from the NCL Joint Formulary for depression and migraine prophylaxis (Islington CCG)

The Committee considered an application to remove dosulepin from the NCL Joint Formulary for depressive illness and migraine prophylaxis. NICE recommends against the initiation of dosulepin in depressive illness and NHSE recommends against use of dosulepin in Primary care.

In terms of its use in depression, NICE advise that all antidepressants are generally equally effective and that despite dosulepin being better tolerated than alternative treatments, its use is not recommended due to the increased cardiac risk and toxicity in overdose. Two large studies found antidepressants (predominantly tricyclic anti-depressants [TCAs]) led to an increased risk of MI (OR=5.8). A UK study identified an association between dosulepin and ischaemic heart disease (OR = 1.67 [95% CI 1.17 to 2.36]), with an increasing odds ratio with increasing dosulepin dose. Another study of deaths due to drug poisoning between 1993 to 2002 revealed dosulepin to attribute to 48.5 deaths per million prescriptions; comparatively, SSRIs accounted to one death per million prescriptions due to suicide. CIFT and BEH confirmed dosulepin is not recommended for any indication at their Trusts.

For migraine, the Committee heard that British Association for the Study of Headache (BASH) and Scottish Intercollegiate Guidelines Network (SIGN) recommend TCAs as a possible treatment for migraine prophylaxis and both specify amitriptyline, not dosulepin, as the treatment choice. A systematic review and meta-analysis by Jackson et al (n=3,176) investigated the use of TCAs in headache. 1,471 articles were identified and 37 met inclusion criteria. Although effectiveness of TCAs was demonstrated versus placebo, dosulepin was not used in any included study (with the majority of studies investigating amitriptyline). A further literature search by JFC Support found no studies demonstrating the efficacy and safety of dosulepin in migraine prophylaxis.

The Committee heard the MHRA recommend supplies of dosulepin are limited to minimise cardiovascular and epileptogenic risk in overdose. NICE warn of the high anticholinergic burden with dosulepin and higher propensity of cardiovascular adverse effects. Toxbase provides information on case studies where ingestion of large doses has led to status epilepticus, cardiac arrest and death and that ingestion of a single capsule may be sufficient to achieve toxicity in a young child.

One neurologist at RFL requested dosulepin was retained on formulary for migraine prophylaxis in those who had failed amitriptyline and where other preventative therapies were ineffective or not tolerated, particularly for patients who have a comorbidity of depression. There was a lack of evidence supporting this positioning and the Committee projected that any perceived benefit would be a placebo response – something which was not justified for a high-risk medicine. Dosulepin did not appear on the NCL primary care or draft secondary care treatment pathways. NHNN were supportive of removing dosulepin for migraine prophylaxis.

NHNN requested that dosulepin was retained on formulary for complex headache and the Committee were aware it was also used for chronic neuropathic pain. The Committee agreed that the risk of using dosulepin far outweighed any potential benefit from treatment in any indication and recommended the removal of dosulepin from the NCL Joint Formulary.

The Committee discussed the challenges in deprescribing patients from dosulepin in Primary care, with over 9,000 prescriptions issued over 12 months across the region. CCGs are supporting GPs in withdrawing dosulepin from existing patients in line with NHSE guidance. Islington CCG shared their experience in attempting to withdraw dosulepin treatment is challenging and not beneficial for all patients. Camden & Islington Mental Health Trust supported of removing dosulepin from the Joint Formulary for new initiations, but recommended that existing patients were reviewed to establish an agreed plan to safely withdraw and discontinue dosulepin.

Decision: Removal from the NCL joint formulary; no new initiations for any indication.

9. Azathioprine and mycophenolate for myasthenia gravis

The Committee considered an application to use azathioprine (AZA) and mycophenolate mofetil (MMF) in the treatment of myasthenia gravis (MG). Both medications are already used at RFL and NHNN, though they are not on the NCL Joint Formulary and are hence not included in the NCL DMARDs fact sheet for Primary care continuation. Clinicians are requesting addition of both agents to the Joint Formulary and that responsibility for prescribing and monitoring is transferred to Primary care.

Wang et al (n=808) conducted a network meta-analysis (NMA) for immunosuppressant therapies and monoclonal antibodies used in the treatment of MG; studies included within the NMA were all small (less than 50 patients for AZA and less than 160 for MMF); all studies were of moderate to low quality and risk of bias was generally difficult to assess due to the lack of detailed reporting in studies. The primary outcome was change in quantitative MG score (QMGS) and secondary outcomes were glucocorticoid reduction and adverse event count. AZA was ranked second-last for QMGS, first for glucocorticoid dose reduction and was considered well tolerated. MMF was ranked last for QMGS, showed no reduction in glucocorticoid dose and was worse tolerated than AZA. The NMA concludes AZA and MMF were not as efficacious as other agents such as eculizumab, though significance with AZA was induced only as a long-term intervention.

Older studies included in the NMA did not use the QMGS score to define improvement in disease severity and hence could not contribute to the analysis of the primary outcome.

In terms of safety, there are four MHRA safety alerts for MMF: pure red cell aplasia, hypogammaglobulinaemia, risk of bronchiectasis and teratogenicity in both men and women. The intensity of monitoring for AZA and MMF in MG was said to be the same as for other indications already approved for use in NCL. AZA is licensed for immunosuppression regimens as an adjunct to immunosuppressive agents whereas MMF is licensed for acute transplant rejection (off-label use).

Ms Stockford informed the Committee that a number of patients have been initiated on AZA and MMF and there are many cases of Primary care managing the requests for blood results with NHNN retaining prescribing responsibility.

The Committee concluded that the evidence for efficacy and safety was favourable for AZA but not for MMF. It was noted that the Association of British Neurologists (ABN) recommend AZA when patients relapse upon prednisolone withdrawal or have intolerable adverse effects and MMF is a suggested alternative where AZA has failed or is intolerable. It was unclear where MG specialists in NCL were proposing MMF in relation to high-cost evidence-based interventions such as rituximab and IVIg. The Committee subsequently agreed to defer decision making for both drugs until a treatment pathway was provided, inclusive of all therapies used to treat MG.

Decision: Deferred

Action: Specialists at NHNN and RFL to create a treatment pathway to demonstrate the place in therapy of all available immunosuppressant and monoclonal antibodies used to treat MG.

10. Risk assessment tool for established medicines

JFC Support adapted a UCLH UMC risk assessment tool to be used as part of the NCL formulary harmonisation work, particularly where DTC minutes from the Trust using the medicine under review are unavailable. The tool provides a RAG rating for efficacy, safety, governance and cost.

The Committee agreed the tool should be used for NCL formulary harmonisation work however requested the inclusion of a section addressing the intensity of monitoring required and for the budget impact to include healthcare resource utilisation.

The risk assessment tool was approved, subject to the requested amends being made.

Action: JFC Support to amend the NCL risk assessment tool

11. Semglee® (biosimilar insulin glargine)

The Committee considered a proposal to add Semglee®, a new biosimilar insulin glargine, to the NCL Joint Formulary as a cost-savings measure. The proposal was standalone, not consultant initiated and not part of a wider plan to optimise insulins across NCL.

The adoption of biosimilar insulin is slow across NCL and in England more generally which contrasts to biosimilar adoption for drugs used exclusively in secondary care (e.g. anti-TNF, rituximab, filgrastim). This slow adoption is thought to be due in part to the large number of clinicians responsible for delivering diabetes care (Type 1 & Type 2), the high number of patients on treatment (>4000 in NCL use glargine), the slow turnover of patients (glargine is a lifelong treatment) and concerns over destabilising treatment.

Semglee is only available as a pre-filled pen. The pen was reviewed by patients and clinicians in Barnet who found it to be highly similar but slightly preferable to Lantus® (originator glargine) pre-filled pens.

The cost-benefit for actively switching large numbers of patients is unfavourable as the biosimilar discount is small; assuming 25% of glargine is switched to Semglee® (best-value glargine) the estimated cost-avoidance is £60,000 per annum. LPP and the London Diabetes Clinical Network (LDCN) issued advice that the "relatively modest savings from switching patients may not justify the time it could take to implement it".

The Committee agreed Semglee® was a suitable treatment option for patients with T1 and T2 diabetes (when used in line with NICE guidance) however declined to add it to the NCL Joint Formulary as:

- The proposal in its current form was unlikely to yield significant savings
- Abasaglar could not be entirely removed from the NCL Joint Formulary as Semglee was not available in a cartridge
- Risk associated with adding another biosimilar glargine to the NCL Joint Formulary did not outweigh the benefits.

This decision could be revisited if Semglee formed part of a commissioned Lantus to biosimilar glargine switching programme (switching to Semglee is likely easier than switching to Abasaglar owing to the device similarity), the price of Semglee falls or Semglee becomes available as a cartridge.

Decision: Not approved

12. Position statement: oral liothyronine for primary hypothyroidism [update]

The updated Fact Sheet was presented to the Committee for approval, which newly made liothyronine available in line with RMOC recommendations. An NCL audit, which included 37% of all patients using liothyronine in primary care, found that 18% were using T3 monotherapy (a higher proportion than expected under current guidance), approximately half had supressed TSH levels (a sign of overtreatment) and the majority were using a higher than recommended ratio of T3:T4 (their dose of T3 is too high). The Committee were concerned about these findings and referred the topic to NCL HoMM for further consideration. The Committee approved the position statement subject to minor amends by the working group.

Post-meeting note: *NCL HoMM agreed the requirement for Blueteq could be removed as would make NCL an outlier and there were adequate measures already in place to ensure any new starters were initiated in line with NCL/RMOC guidance.*

13. Position statement: cannabis-based medicinal products [update]

JFC Support updated the NCL position statement (formerly known as the "cannabis and cannabis-related products: position statement") in response to NICE guideline for cannabis-based medicinal products, NICE TA for Epidyolex® and the modified information for the use of Sativex®. The consultation period is still ongoing and the Committee were asked to submit any comments. If no major amendments are received, approval would be sought via Chair's action.

14. Guideline: Statin prescribing and lipid modification guideline for the prevention of cardiovascular disease [update]

The updated guideline was presented to the Committee for approval. The Committee approved the guideline.

15. Annual report 2018/19

The Committee approved the annual report 2018/2019.

16. Medical devices

Evaluating medical devices is not included in the JFC Terms of Reference (ToR). Historically JFC have reviewed applications for devices that have a pharmacological mechanism of action (e.g. gentamicin beads for osteomyelitis), are administered systemically (e.g. contrast agents) or where significant pressures on pharmacy budgets are anticipated (e.g. ocular lubricants, flash glucose monitoring).

The Committee discussed whether a more formalise approached to reviewing devises was required. It was acknowledged that Trusts have dedicated committees for reviewing medical devices and agreed it was considered inappropriate to duplicate this work. Medical device committees however may have

limited experience in critically appraising literature therefore it was agreed JFC should offer to review devices with pharmacological type activity, systemic administration or particularly high-cost.

The Committee agreed that there should be no change to their ToR however any request to review medical device should first be accepted by the Committee for review, in advance of a review being undertaken (in a similar process to that used for pre-NICE schemes without FOC supply).

The Committee considered the specific case of GammaCore and agreed it should not be reviewed at JFC.

17. Next meeting

Monday 17th February 2020

18. Any other business

Nil