North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES
Minutes from the meeting held on 23rd June 2022

Present:	Prof A Hingorani	NCL JFC Chair	(Chair)
	Dr B Subel	NCL JFC Vice Chair	(Vice Chair)
	Dr K Tasopoulos	NMUH, DTC Chair	
	Dr P Jasani	RFL, Divisional Clinical Director	
	Dr A Scourfield	UCLH, DTC Chair	
	Dr M Kelsey	WH, DTC Chair	
	Ms K Delargy	BEH, Chief Pharmacist	
	Mr A Shah	RNOH, Chief Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Mr J Harchowal	UCLH, Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Ms M Singh	NCL CCG, Head of Medicines Management (Barnet)	
	Mr P Gouldstone	NCL CCG, Head of Medicines Management (Enfield)	
	Mr A Dutt	NCL CCG, Head of Medicines Management (Islington)	
	Dr L Waters	CNWL, Consultant Physician in HIV	
	Dr D Roberts	Islington Borough, Clinical Director	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Dr R Urquhart	UCLH, Divisional Clinical Director	
In attendance:	Ms S Sanghvi	North London Partners, JFC Principal Pharmacist	
	Mr G Grewal	North London Partners, JFC Support Pharmacist	
	Mr R Rajan	North London Partners, JFC Support Pharmacist	
	Ms S Amin	IPMO Programme Team, Lead Pharmacist	
	Ms M Kassam	MEH, Senior Pharmacist	
	Ms A Sehmi	NMUH, Formulary Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Ms H Thoong	GOSH, Formulary Pharmacist	
	Ms M Thacker	RFL, Clinical Lead Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr H Shahbakhti	RFL, Formulary Pharmacist	
	Mr S O'Callaghan	UCLH, Formulary Pharmacist	
	Mr J Flor	WH, Lead Pharmacist	
	Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	
	Ms A Fakoya	NHS London Shared Service, Contract & Commissioning Support Pharmacist	
	Mr I Quarm	NCL CCG, Prescribing Advisor	
	Dr G Lieberman	WH, Consultant Gynaecologist	
	Dr E Rachamim	RFL, Community Paediatrician	
	Ms S Shah	NHS London Shared Service, Contract & Commissioning Support Pharmacist	
	Dr F Rugg-Gunn	UCLH, Consultant Neurologist	
Apologies:	Dr A Worth	GOSH, DTC Chair	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Sell	RNOH, DTC Chair	
	Mr S Semple	NCL ICS, Interim Chief Pharmacist; GOSH, Interim Chief Pharmacist	
	Dr D Burrage	WH, Consultant Clinical Pharmacologist	

Ms R Clark	NCL CCG, Head of Medicines Management (Camden)
Ms E Mortty	NCL CCG, Deputy Head of Medicines Management (Haringey)
Ms L Reeves	C&I, Chief Pharmacist
Ms N Phul	MEH, Chief Pharmacist
Ms S Stern	NMUH, Chief Pharmacist

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. Ms Sanghvi asked members and regular observers to send through any outstanding forms.

4. Minutes of the last meeting

The minutes and abbreviated minutes were accepted as an accurate reflection of the May 2022 meeting.

5. Matters arising

Nil.

6. Review of action tracker

Action tracker included for information.

7. JFC Outstanding Items & Work Plan

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

8. Local DTC recommendations / minutes

DTC site	Month	Drug	Indication	JFC outcome
C&I	Feb 2022	Cariprazine	Schizophrenia	**Decision:** Not approved
UCLH	May 2022	FOC scheme: Zanubrutinib†	2nd line therapy for treatment of Waldenstrom's macroglobulinaemia (if NICE TA and commissioning for ibrutinib is removed)	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** N/A – Free of charge **Funding:** N/A – Free of charge **Fact sheet or shared care required:** No
UCLH	May 2022	Rituximab	Relapsing remitting multiple sclerosis	**Decision:** UCLH only* **Prescribing:** Secondary care **Tariff status:** Excluded from tariff **Funding:** Trust **Fact sheet or shared care required:** No
UCLH	May 2022	Nystatin vaginal tablets, nystatin + flucytosine vaginal cream, boric acid vaginal capsules	Approved on advice of ID or microbiology for the management of azole resistant non-albican vulvovaginal candidiasis • 1st line - Nystatin vaginal tablets • 2nd line - Nystatin + flucytosine vaginal cream, or boric acid vaginal capsules	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Fact sheet or shared care required:** No
RFL	April 2022	Ethanol 20%	Ophthalmology surgical procedures (on formulary historically; change in formulation)	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Fact sheet or shared care required:** No

† 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. * Subject to funding consideration.

9. New Medicine Reviews

Nil to review.

10. Appeal: Melatonin modified-release tablets (Slenyto) for autism spectrum disorders and Smith-Magenis syndrome

The Committee considered an appeal for Slenyto® (melatonin modified-release (MR) tablets), a synthetic version of the naturally occurring hormone to regulate the sleep cycle given at a dose range of 2-10mg, for the licensed indications of autism spectrum disorders (ASD) or Smith-Magenis syndrome (SMS).

NCL JFC had previously reviewed melatonin for "children or adolescents with neurological or developmental disorders" in March 2017; at the time, the Committee acknowledged the benefits of melatonin, though to carefully manage the budget impact advised that the cost-effective product (Circadin MR tablets) was used where possible and crushed where needed to aid compliance instead of using more expensive liquid formulations. At the time, breaking the MR formulation was not considered an issue as the focus was on sleep onset rather than Total Sleep Time (TST). In May 2021, the JFC reviewed Slenyto, a more expensive licensed product with the potential to displace prescribing in patients with neurological or developmental disorders (an estimated 700 patients). Slenyto was considered not to have proven an improvement in efficacy, safety, or cost-effectiveness versus Circadin, but did incur substantial budget impact (an estimated minimum of £219,000), and therefore was not approved.

The appeal was made on several grounds:

- The appellants proposed that the previous review considered a much wider cohort, though the proposed use of Slenyto would be for the licensed indications (ASD/SMS) only; it would be placed second line where Circadin was unsuccessful (e.g., ineffective, intolerable or unpalatable when crushed)
- It was therefore estimated that Slenyto would be of use in 85 patients at any one time. The new estimated budget impact was lower (£32,000 to £173,000). The appellants considered the true budget impact to be at the lower end of this range, as doses beyond 6mg are rarely used.
- The previous JFC decision was influenced by the risk of prescribing outside of the licensed indications of Slenyto. However, the appellants would adhere to the indications strictly, and proposed that an updated melatonin factsheet would help govern the formulary amendment (which would include information on the indications for use, a trial period from the specialist before transfer to the GP, clear stopping criteria, and advice not to crush Slenyto).
- The previous JFC decision was based on lack of evidence of efficacy, safety or cost-effectiveness versus available melatonin formulations. However, this did not take into account the convenience of having a substantially smaller MR tablet, which allows it to be taken whole by very young children, which was considered by clinicians to improve TST compared to immediate release formulations.
- The previous committee decision considered one clinician's clinical experience with their use of Circadin crushed. However, the appellants argue that in their clinical experience, crushing Circadin fundamentally changed the pharmaceutical properties which was not conducive to an improvement in TST in their cohort of patients. The appellants provided evidence from Chua et al, which demonstrated the difference in the dissolution profile between Circadin intact versus Circadin crushed (though noted this did not measure patient response).
- The appellants informed the Committee that Slenyto was on formulary in both SEL and CNWL under similar criteria to those proposed; this was a factor that has led to an increase in prescribing in NCL (18% of the total prescribing of Slenyto in London is already taking place in NCL). Therefore, there is an issue in equity of access to Slenyto.
- As the appellants do not have access to Slenyto, referrals are made to tertiary services after available melatonin therapies. Slenyto is usually recommended by tertiary services, which cannot be initiated by the appellants as it is non-formulary. Consequently some families, who are able to afford to do so, are obtaining private prescriptions for Slenyto. Access to Slenyto is proposed to reduce inappropriate referrals to tertiary services, and reduce inequity of access to Slenyto.
- The appellant informed the Committee that in some patients who cannot access an effective melatonin formulation (i.e., Circadin is inappropriate and Slenyto is inaccessible), tertiary services may recommend

clonidine. Compared to melatonin, clonidine requires additional monitoring due to the risk of additional adverse effects (e.g., blood pressure, ECG); therefore access to Slenyto may reduce use of a less safe medication.

- Finally, the appellants argued that issues of compliance were of particular concern to their patient cohort; although not evidence based, pragmatic reasoning would consider that a smaller tablet which can be masked in food would allow the tablet to be given whole (maintaining the modified release preparation) in young autistic patients.

The Committee heard from Dr Rachamim that whilst the appealing clinicians would be happy to use Circadin first as a trial, there is a noticeable trend of young autistic patients being unable to tolerate crushed Circadin or melatonin liquid. The inequity of access impacts not only the patient, but the whole family. Although doses of melatonin doses can extend up to 10mg, if patients do not experience benefit at up to 6mg, melatonin is usually stopped and the patient is referred back to the specialist. Treatment holidays are offered, and if required, treatment is restarted at the lowest effective dose. It was recognised that patients who start Slenyto may tolerate Circadin as they become older. The clinical team offered their support to update the NCL factsheet to reflect their advice and the formulary position.

In camera, the Committee discussed the grounds for appeal and were persuaded in particular by the inequity of access to Slenyto® experienced by some NCL service users, and knowledge that a less-safe alternative to melatonin (clonidine) may be used instead. The Committee also discussed the potential concerns with adding Slenyto to the formulary, including the risk of prescribing creep in off-label indications and the effective transfer of prescribing to primary care. However, the Committee agreed that these concerns could be mitigated against via use of digital tools in NCL (e.g., messages on prescribing systems) and an update of the NCL melatonin factsheet (by adding information on the restricted use in ASD/SMS patients under CYP/CAMHS services, pragmatic advice of treatment holidays, trial of Circadin in patients if they can tolerate when older, and appropriate details to facilitate transfer to primary care).

In summary, the Committee agreed to add Slenyto to the NCL Joint Formulary for patients with ASD/SMS under the CYP service.

Decision: Approved
Prescribing: Secondary care initiation; Primary care continuation
Tariff status: In tariff
Funding: Trust and CCG
Fact sheet or shared care required: Yes – NCL melatonin factsheet to be updated

11. Ankylosing/Axial spondylitis high-cost drug pathway

The Committee reviewed the NCL Pathway for ankylosing spondylitis and non-radiographic axial spondylitis, which was developed by a working group including clinicians from across NCL and outlines eligibility for biologics where patients have had inadequate response to ≥NSAIDs. The pathway includes NICE TA recommended drugs and a recommendation to commission 3 lines of therapy: two lines of TNF alpha inhibitors and one line of therapy with an IL-17A inhibitor.

The Committee noted that the pathway includes temporary secukinumab dose escalation to 300mg monthly (outside of NICE TA as licensed thereafter) for patients who fail on 150mg. This recommendation is outside of the scope of the NICE TA as it was added to the license and evidence available post NICE publication. Evidence from an extension study by Pavelka et al (2020) suggests improvement in BASDAI 50 response (secondary endpoint) with 300mg dose compared to 150mg, including in a subgroup of TNF inhibitor non-responders (40% vs 24% respectively). No serious adverse events were noted with the higher dose, which is established practice in other indications. Dose escalation is estimated to have a cost impact of £50K but the Committee noted that there are limited other options for these patients and treatment response criteria are defined clearly within the pathway.

The Committee clinically approved the pathway, noting that financial approval was required from the NCL CCG contracting team before implementation.

12. JFC Rapid Reviews Proposal

The Committee heard that JFC Support team increasingly receiving a high number of requests to ratify previous DTC formulary decisions for use across the sector. Many are historic uses with limited documentation to support ratification, and currently undergo a rapid review evaluation.

The Committee agreed with the suggested approach to address a backlog of rapid reviews post pandemic and support a pragmatic approach to reviews going forward. An additional sub-group meeting will be held in August to form decisions on rapid reviews currently on the workplan. The subgroup will review and test new rapid review documentation for ratification of existing DTC decisions and bring a final template back to JFC for ratification and future use.

13. Sustainability & Formulary Evaluations

Ms Sanghvi provided an update on discussions regarding opportunities to include sustainability within NCL JFC processes and evaluations of medicines. Information regarding carbon footprints and sustainability of medicines are complex and difficult to obtain, with no standards to evaluate and compare what good practice should be. It was noted that the onus should be further up the chain, with national organisations and pharma, to support with these considerations. The Committee heard that NICE, MHRA and the NHSE Medicines Sustainability Committee are working to develop assessments and tools to support APCs with sustainability assessments for medicines. The Dorset APC team are incorporating sustainability questions within their application forms, targeted at pharma, with the aim of raising awareness and benchmarking gaps in the information available.

The Committee agreed to await national recommendations regarding incorporating sustainability considerations into APC processes due to the complexity and lack of standardised information. This update can be shared with local DTCs who may be having similar discussions regarding their processes. Local work and ideas in relation to the NCL Green Plan and medicines can be fed in to NCL MOC, which oversees sustainability initiatives related to medicines and reports in to the Greener NCL Board.

14. Appeal: Brivaracetam for epilepsy

The Committee considered an appeal for brivaracetam tablets, a highly selective binder of synaptic vesicle protein 2A (SV2A) similar to levetiracetam, given at a dose range of 50 mg/day to 200 mg/day, for focal epilepsy resistant to other antiepileptic drugs (AEDs).

NCL JFC previously reviewed brivaracetam for “as an adjunct for partial onset seizures” in 2016. Despite the lack of comparative data between brivaracetam and levetiracetam, the Committee approved brivaracetam under evaluation for patients who had previously responded to levetiracetam but had to stop due to off-target effects (due to a perceived reduced risk of adverse effects with brivaracetam). In April 2022, the Committee was presented with the results of the evaluation and noted that despite results of a slightly improved adverse effect profile, the data did not support the routine use of brivaracetam in patients who suffer off-target effects with levetiracetam.

The appeal was made on the grounds that:

- NICE published a guidance titled *‘Epilepsies in children, young people and adults’ [NG217]* which recommend brivaracetam as add-on therapy option in the treatment of generalised (off-label), focal, and myoclonic (off-label) epilepsies. The current non-formulary status would prevent its use in these indications.
- A high proportion of patients (94%) in the audit had discontinued levetiracetam due to adverse effects. By comparison, 39% discontinued brivaracetam in patients who did not tolerate levetiracetam.

The Committee heard from Dr Rugg-Gunn that although the audit demonstrated similar side-effect profile to levetiracetam the magnitude of these were less. The audit supported that adverse events were less prevalent with brivaracetam compared to the same patients who took levetiracetam (low mood 59% vs 20.5%; aggressive behaviour 43.1% vs 8.5%; general side effects 24.5% vs 18%). Dr Rugg-Gunn explained that the audit findings are commensurate with clinical experience and published clinical trials, though the Committee noted that clinical trials had inherent weaknesses in study designs.

Dr Rugg-Gunn stated that approval to use brivaracetam in NCL in line with the NICE guidance was unlikely to correspond with a rise in prescribing as brivaracetam when under JFC evaluation was initiated as an add-on option at a similar treatment pathway in pharmaco-resistant focal epilepsy. Therefore, majority of patients will have previously tried levetiracetam before brivaracetam. Dr Rugg-Gunn explained that epileptologists will

exercise clinical judgement to initiate brivaracetam prior to levetiracetam in a small cohort of patients who are at high risk of behavioural adverse effects.

In camera, the Committee discussed the grounds of the appeal. As NICE made recommendations to initiate brivaracetam in off-label indications (generalised epilepsy and myoclonic epilepsy), the Committee was reassured by clinicians' prudent prescribing and demonstration of good governance during the JFC evaluation period. The Committee was reassured that brivaracetam would be initiated as second-line add on option for generalised (off-label), focal, and myoclonic (off-label) epilepsies, in line with NICE guidance, for use in patients who could not tolerate levetiracetam, or exceptionally, in patients eligible for levetiracetam but deemed by the specialist epilepsy team to be at high risk of behavioural side effects.

Decision: Approved as a 2nd line add on option for generalised epilepsy, myoclonic epilepsy and focal epilepsy, in line with NICE guidance, for use in patients who could not tolerate levetiracetam or, exceptionally, in patients eligible for levetiracetam but deemed by the specialist epilepsy team to be at high risk of behavioural side effects.
Prescribing: Secondary care initiation, primary care continuation
Tariff status: In tariff
Funding: Trust and CCG
Fact sheet or shared care required: To be discussed at NCL Shared Care Group
Additional information: Specialists to seek acceptance of primary care continuation prior to initiation.

15. Utrogestan for HRT and review of transdermal oestrogen + progesterone patches

In May 2018, the Committee reviewed an application to switch from formulary approved oral combination HRT products (containing oestrogen plus a synthetic progestin) to utrogestan capsules (micronised progesterone) plus a separate oral oestrogen product due to proposed improved tolerability. The Committee did not approve the application due to insufficient data to support tolerability benefits and significant cost pressure.

In September 2019 and interim decision was made to approve utrogestan capsules (micronised progesterone) in combination with transdermal oestrogen HRT products due to a national shortage of combination (oestrogen plus progestogen) transdermal HRT products.

The Committee reviewed this interim approval as national supply issues had now stabilised, only affecting a minority of products. The Committee were presented a proposal from women's health specialists within the region to continue utrogestan in women who had been initiated on this combination HRT regimen during the national shortage. The Committee were also asked whether to revert utrogestan back to 'not approved' on the joint formulary or consider a new proposal to remove restrictions on utrogestan due to several changes in availability and cost of HRT products since originally reviewed in 2018.

For existing patients receiving utrogestan based combination HRT, the Committee were supportive of the proposal to continue this regimen provided there were no reported issues of adherence or tolerability.

For the proposal to remove restrictions on utrogestan capsules and add as an approved treatment on the joint formulary, the Committee were presented with updated comparative cost estimates for traditional- and utrogestan-based combination HRT for oral and transdermal products, and continuous and sequential regimens. Introduction of sequential or continuous oral utrogestan-based combination HRT as a treatment option represented a small incremental annual cost either as a 2nd line option (estimated 10%) or as an equivalent 1st line option to other approved products. However, introduction of sequential or continuous transdermal utrogestan-based combination HRT represented a moderate annual cost saving.

The Committee noted that since the interim approval, there had been considerable prescribing of utrogestan within NCL, some Trusts in NCL were already using utrogestan as a first line option, and that other London regions did not restrict access. Patients who experience tolerability issues with traditional HRT combination products, who are unable to access utrogestan with NCL were reported by specialists to either stop HRT or seek private access. It was highlighted that there were many HRT products on the NCL joint formulary but limited guidance to support primary care clinicians on product selection and when to consider moving from oral to transdermal preparations.

The Committee concluded that utrogestan, a licensed HRT product (in combination with oral or transdermal oestrogen), was likely now cost neutral or cost saving, and supported its inclusion on the joint formulary as an option for hormone replacement therapy. However, the Committee recommended that an NCL HRT

pathway is developed by primary and secondary care stakeholders to support primary care clinicians offering HRT, including when utrogestan based HRT regimens could be considered.

Decision: Approved (in combination with oral or transdermal oestrogen) as an option for patients requiring HRT. Place in therapy deferred pending development of NCL HRT pathway.
Prescribing: Primary or secondary care (place of initiation to be defined in NCL pathway)
Tariff status: In tariff
Funding: Trust and CCG
Fact sheet or shared care required: No – NCL pathway to be developed

16. DOACs for non-valvular atrial fibrillation (Edoxaban update)

Generic Apixaban: The Committee heard that there has been a challenge to the apixaban patent by two generic manufacturers which was upheld by the High Court in June 2022. It was noted that at the time of the JFC review in May 2022, this information was not available to the Committee. Following discussion of communications received from NHSE (dated 23rd June), the Committee agreed to proceed with the Edoxaban work as agreed in May 2022. It was noted that supplies of generic apixaban are very limited and unlikely to increase significantly until the outcome of the appeal is known, which is currently expected to be mid-2023. As a result, the price of generic apixaban has not reduced and is still on par with branded apixaban. Edoxaban therefore remains the most cost-effective DOAC by a considerable margin due to the national DOAC framework, with NHSE commissioning recommendations for NVAF remaining unchanged.

Edoxaban Phase 1: The Committee were updated on Phase 1 which was approved in May 2022. Edoxaban should be considered as the first line option across NCL, where a DOAC is to be initiated for prevention of stroke & systemic embolism in patients with NVAF, where clinically appropriate. The interim position statement was ratified by the Committee and will be made available via the NCL MON website. It was highlighted that support is required from secondary care colleagues to assist in the full implementation of Phase 1 as soon as possible.

Edoxaban Phase 2: The Committee were updated on the progress of Phase 2, which was applicable to the switching of low-risk patients in primary care already established on a DOAC or warfarin for NVAF. This was agreed in principle by the Committee in May 2022, subject to review of the criteria for excluding high-risk patients from a switch, and oversight of an implementation plan for safe switching in primary care. The exclusion criteria will be circulated for consultation ahead of final review by the Committee and will incorporate criteria set nationally.

17. Valproate risk minimisation guideline

This item was deferred to a future JFC meeting.

18. Next meeting

Thursday 21st July 2022

19. Any other business

N/A