North Central London Integrated Care System

NHS
North Central London
Medicines Optimisation Network

Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 17th August 2023

		Present	Apologies
Members			
Prof A Hingorani	NCL JFC Chair	✓	
Dr B Subel	NCL JFC Vice Chair	✓	
Ms W Spicer	RFL, Chief Pharmacist		✓
Dr P Jasani	RFL, DTC Chair		✓
Dr K Boleti	RFL, DTC Chair		✓
Dr A Scourfield	UCLH, DTC Chair	✓	
Mr J Harchowal	UCLH, Chief Pharmacist	✓	
Ms L Coughlan	NCL ICB, ICS 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	✓	
Ms J Ballinger	GOSH, Chief Pharmacist		✓
Mr V Raman	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)		✓
Ms N Patel	NCL ICB, Prescribing Adviser (Barnet)	✓	
Dr D Roberts	NCL ICB, Clinical Director (Islington)		✓
Attendees			
Ms S Sanghvi	IPMO Programme Team, JFC Principal Pharmacist	✓	
Ms S Amin	IPMO Programme Team, Lead Pharmacist	✓	
Mr G Grewal	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms S Maru	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms P Varu	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Mr H Shahbakhti	RFL, Formulary Pharmacist	✓	
Ms H Bouattia	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		✓
Ms K Mistry	RNOH, Formulary Pharmacist	✓	
Ms S Ahmed	WH, Formulary Pharmacist	✓	
Ms R Pointon	WH, Rotational Pharmacist	✓	
Mr J Flor	WH, Finance, Business and Performance Pharmacist	✓	
Ms M Thacker	RFL, Clinical Lead Pharmacist		✓
Mr G Purohit	RNOH, Formulary Pharmacist		✓
Ms J Bloom	MEH, Associate Chief Pharmacist	✓	
Ms M Patel	NCL ICB, Prescribing Advisor (Observer)	✓	
Ms S Gillis	WH, Consultant Anaesthetist	✓	
Mr B O'Farrell	RFL, ICU Specialist Pharmacist	✓	

2. Meeting attendees

Prof Hingorani welcomed members, observers, and applicants to the meeting (see above).

3. Members' declaration of interests

The Declarations of Interests register for Committee members was included for information. No further interests were declared at the meeting.

4. Minutes of the last meeting

Minutes and abbreviated minutes were accepted as an accurate reflection of the July 2023 meeting.

5. Matters arising

Nil

5.1 Criteria for use of Budenofalk® (budesonide) in autoimmune hepatitis

In April 2023, the JFC approved the use of budesonide (Budenofalk®) for the induction and maintenance of remission in patients with autoimmune hepatitis (AIH), subject to the development and receipt of specific criteria for initiation and discontinuation. Data collection on adherence to agreed criteria at 12 months was also recommended. The Committee reviewed the criteria developed by RFL hepatology teams and JFC support, noting that the data collection recommendation has been changed to 24 months to enable suitable assessment of therapeutic response. The Committee approved the criteria, pending a minor amendment to the stopping criteria wording. The amended criteria are included for information below.

Criteria for prescribing budesonide (Budenofalk®) in patients with AIH:

Starting/switching criteria:

- First-line in patients at high risk of developing adverse effects from corticosteroids, or second-line following actual adverse effects from corticosteroids, including:
    - Psychosis
    - Poorly controlled diabetes
    - Osteoporosis
    - Intolerance to prednisolone
        - Preventative measures to control osteoporosis should be implemented at the same time as moving to budesonide, including routine prescription of calcium and vitamin D and selective use of bisphosphonate therapy

Dose:

- 3mg TDS during induction
- 3mg BD once stable
- Some patients may benefit from 3mg OD – off-label use

Stopping criteria:

- Intolerance to budesonide
- Adverse effects to budesonide
- Therapeutic response not achieved (following a minimum of 6 months of treatment)

- After two years, if treatment is successful and further treatment is not required (defined by persistent biochemical response)
- Discontinuation of budesonide (GPs must seek specialist guidance):
    - High-dose treatment (3mg BD) will not be stopped abruptly. It will be tapered off over at least 2 weeks (If the GP is prescribing, they are not expected to make decisions regarding discontinuation. The specialist team is responsible for initiating and managing discontinuation).
    - Low-dose treatment (3mg OD) can be stopped without being tapered (If the GP is prescribing, must be discussed with the specialist team first).

Timeframe before transfer of care:

- Most patients will use budesonide for up to two years; a small proportion of patients will require lifelong treatment with corticosteroids.
- A minimum of 3 months prescribing by the specialist (or longer if unstable or patient has not shown a response to treatment)
- Once the GP prescribes corticosteroids, patients will be followed-up by the specialist every six months

Data for collection:

- JFC suggested 1 year assessment, but assessment after 2 years more appropriate based on stopping criteria
    - Budesonide starting (i.e., first-line) or switching from prednisolone (i.e., second line)
    - Rationale for starting/switching
    - When budesonide was transferred to the GP
    - Duration on treatment (i.e before discontinuation)
    - Reason for stopping
        - Treatment course completed successfully
        - Stopped due to inadequate response
        - Stopped due to intolerance and/or adverse effects

5.2 AKIS® (diclofenac bolus IV injection) – outstanding action

The Committee discussed the use of AKIS®, a parenteral form of diclofenac administered via bolus intravenous injection, as an alternative to Voltarol® administered via intravenous infusion. JFC previously considered the use of AKIS® in February and March 2019 and considered the off-label use of Voltarol® in Hartmann's solution to be the appropriate comparator for a budget impact assessment (as this established practice was the standard of care employed in several NCL Trusts). The Committee understood that the manufacturers of AKIS® have recently established an LPP contract price, reducing the drug acquisition cost by almost 40%. However, despite this price reduction, AKIS remained around double the cost of Voltarol® administered in Hartmann's solution.

Other benefits of using AKIS were discussed, such as (i) the reduced risk in administering via a licensed route and in administering a bolus injection versus an intravenous infusion; (ii) reduction in the overall fluid volume delivered to patients; and (iii) theoretical improvements in day surgery flow from optimising analgesia and reducing nursing time. Limitations of using AKIS® include the risk of 'creep' into other hospital services, which could lead to an exponential increase in the use of injectable diclofenac.

The Committee heard that there is significant prescribing of AKIS® in another large London Trust, but data suggests the Trust is acquiring AKIS® at a price comparable to Voltarol® (i.e., lower than the LPP contract price). The Committee were unable to recommend the use of AKIS at the current LPP contract price and would not be seeking to undermine the pan-London process for standardised contract prices, but would consider the proposal again if the LPP price was renegotiated to be in parity with Voltarol® in Hartmann's solution.

Decision: Not approved

6. Review of action tracker

Action tracker included for information. Closed actions have been updated on the tracker.

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
RFL	December 2023	Darolutamide (Bayer plc) with Docetaxel (FOC Scheme)	FOC scheme: Hormone Sensitive Prostate Cancer	**Decision**: Added to the NCL Joint Formulary **Prescribing**: Secondary care only **Tariff status**: N/A **Funding**: FOC scheme **Fact sheet or shared care required**: N/A
RFL	January 2023	Botulinum Toxin (Dysport) BT	Shoulder instability	**Decision**: Added to the NCL Joint Formulary **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A **Additional information:** Approved subject to; protocol/guidance development, funding consideration, audit data collection and use of cost-effective brand.
RFL	January 2023	Methotrexate	Posterior non-infectious uvetitis	**Decision**: Added to the NCL Joint Formulary **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: Deferred to the NCL Shared Care Group for the development of Shared Care/Fact sheet.
RFL	January 2023	Azathioprine		
RFL	January 2023	Mycophenolate		
UCLH	November 2009	Pentosan polysulfate sodium capsules	Haemorrhagic cystitis	**Decision**: Added to the NCL Joint Formulary **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A
RFL	March 2023	Indocyanine green (Diagnostic green GmbH)	Assessment of vascular perfusion prior to colorectal anastomosis	**Decision**: Approved – RFL only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A
RFL	April 2023	Durvalumab (FOC Scheme)	In combination with standard chemotherapy as first-line treatment for patients with unresectable/advanced biliary tract cancer	**Decision**: Added to the NCL Joint Formulary **Prescribing**: Secondary care only **Tariff status**: N/A **Funding**: FOC scheme **Fact sheet or shared care required**: N/A
RFL	April 2023	Thalidomide	Tuberculosis late paradoxical reaction	**Decision**: Approved - RFL only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A

RFL	April 2023	Etanercept	DADA2 vasculitis	**Decision**: Approved – RFL only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A

8.1 Mitotane with EDP (Etoposide, Doxorubicin, Cisplatin) chemotherapy for adrenocortical carcinoma

RFL reviewed the use of mitotane as adjuvant treatment for adrenocortical carcinoma in 2013 and this decision was ratified at JFC in 2018. The evidence base for the use of mitotane in combination with EDP chemotherapy was presented to the Committee for ratification and to clarify that the combination use of mitotane with EDP is approved for use within NCL.

Medication: Mitotane with EDP chemotherapy
Decision: Added to the NCL Joint Formulary
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: N/A

9. Review of JFC processes

9.1 Drug evaluation format

A proposal to implement a 3-month pilot on a change in the JFC drug evaluation template to PowerPoint slides was presented to the Committee. A full slide set will be circulated within the agenda and to applicants, however only the key slides will be presented at the meeting. The JFC minutes will still provide a written summary of the evidence and discussion. The Committee accepted the proposal, JFC support will seek feedback after 3 months and then share a final template for other NCL formulary teams to consider adopting.

9.2 Annual report 22/23 – JFC SWOT analysis and priorities

A brief overview of the priorities for 2023/24 were presented to the Committee. The Committee were requested to review and comment on the draft SWOT analysis and priorities for JFC for the 2022/23 annual report by Thursday 24th August. The final annual report will be shared with JFC following sign-off.

10. NHSE FOC Medicines Scheme Recommendations

The NHS England 'Free of charge (FOC) medicines schemes – national policy recommendation for local systems' was published in August 2023. Key differences between the current NCL guidance (last updated December 2021) were highlighted to the Committee. It was agreed to convene a small working group to review the NCL FOC policy and process considering the NHSE recommendations. Expressions of interest to join the working group were invited from JFC stakeholders.

11. New medicine reviews

11.1 Remifentanil as a sedative in ICU

The Committee considered an application for remifentanil intravenous (IV) infusion, an opioid, for off-label use in the maintenance of sedation in mechanically ventilated adult patients in intensive care units (ICU). There is inconsistency in the use of remifentanil within NCL Trusts in an ICU setting. NMUH currently use remifentanil in ICU with a local protocol. UCLH had it on formulary in 2008 but this was removed from formulary in 2010. There is interest in using remifentanil in multiple trusts within NCL. The Committee reviewed the evidence for efficacy and safety.

Tan et. al was a meta-analysis (11 RCTs; n=1067) comparing the efficacy and safety of remifentanil (dose range 6-90 micrograms/kg/hour) with other opioids or sedative agents in mechanically ventilated patients in ICU. This meta-analysis informed the negative Use of Medicines Committee (UMC) decision in 2010. Patients received remifentanil alone or remifentanil in combination with another sedative agent compared to opioids (i.e., sufentanil, morphine, fentanyl) and sedative agents (i.e., midazolam, propofol). The primary endpoint, duration of mechanical ventilation, was not met and there was no difference when remifentanil was compared to an opioid or sedative agent (weighted mean difference [WMD]: 0 days; 95% CI -018 to 0.17; P=0.96). Time to extubation after sedation cessation was initially significantly shorter with remifentanil (WMD: -2.04 hours; 95% CI -0.39 to -3.39; P=0.02). However, after

adjustment for publication bias the difference was not statistically significant (WMD: -1.57 hours; 95% CI -3.55 to 0.41; P=not reported). Key limitations of the study were the inclusion of poor quality RCTs which were heterogenous and had small sample sizes.

Zhu et. al was a systematic review and meta-analysis (23 RCTs; n=1905) assessing the safety and efficacy of remifentanil (dose range 6-60 micrograms/kg/hour) in mechanically ventilated adult patients compared to other opioids. The majority of the RCTs included patients in ICU, however, five studies were based on remifentanil use in the recovery/operating room. Patients received remifentanil alone or in combination with a sedative agent compared to either opioids (i.e., sufentanil, morphine, fentanyl) or an opioid/sedative combination (i.e., propofol, midazolam, lorazepam). The primary endpoint, duration of mechanical ventilation (18 studies; n=1655), was statistically significantly shorter with remifentanil (reduction in mean difference: -1.46 hours; 95% CI -2.44 to -0.49; P=0.003). Time to extubation after cessation of sedation (11 studies; n=716) was also statistically significantly shorter (reduction in mean difference: -1.02 hours; 95% CI -1.59 to 0.46; P=0.0004) in favour of remifentanil. In subgroup analyses where remifentanil was compared with fentanyl (8 studies; n=624), the duration of mechanical ventilation, was significantly shorter with remifentanil (reduction in mean difference: -3.85 hours; 95% CI -7.39 to -0.39; P=0.03). Key limitations of the study were that publication bias could not be excluded, the RCTs had heterogeneous population/comparators with small sample sizes and the majority of the RCTs were of suboptimal quality.

Yang et. al was a systematic review and meta-analysis (15 RCTs; n=1233) comparing the efficacy and safety of remifentanil (dose range 6-60 micrograms/kg/hour) when compared with other opioids in adult mechanically ventilated patients. Patients received remifentanil alone compared to opioids (i.e, sufentanil, morphine, fentanyl). The primary endpoint, duration of mechanical ventilation (14 studies; n=1055), was statistically significantly shorter with remifentanil (standard mean difference [SMD]: -0.23 hours; 95% CI -0.41 to -0.06; P=0.01). Reduction in weaning time (5 studies; n=487) was statistically significantly shorter with remifentanil (SMD: -0.21 hour; 95% CI -0.40 to -0.03; P=0.02). Key limitations were similar to other studies with heterogenous comparators/population and the RCTs had small sample sizes.

In terms of safety, there is no significant difference in the side effect profile between remifentanil and other opioids. The literature suggests remifentanil may be associated with opioid-induced hyperalgesia; however, this is mostly reported in post-operative patients. Anecdotally, clinicians state they have not observed this effect.

Potential risks include differences in the administration of fentanyl and remifentanil (i.e, remifentanil should never be administered by bolus injection due to risks of serious side effects such as apnoea, hypotension, bradycardia, and death, whereas fentanyl is given by bolus injection, followed by an infusion). Due to the rapid offset action of remifentanil, residual opioid activity diminishes after 5-10 minutes and therefore background analgesia must be considered prior to discontinuation. Staff training and clearly defined risk mitigation steps will be essential for use and implementation in an ICU setting.

In terms of budget impact, remifentanil is expected to cost an additional £35,500 per annum (based on UCLH and WH patient numbers). Noting, NMUH already use remifentanil in ICU and RFL numbers were not available at the time. Assumptions of this costing model include an average adult weight of 65kg, remifentanil dose of 12 micrograms/kg/hour, average 2 days use. This was calculated based on drug acquisition costs and there are claims these costs may be offset by other efficiencies in healthcare resource utilisation in ICU. However, there are no economic data or analyses to support this.

The Committee heard from Dr Gillis that although the duration of mechanical ventilation and time to extubation/weaning time from the studies may not appear to be significant, the process of getting a patient to extubation can be very time-consuming and requires careful planning with close monitoring. The presence of sedative drugs in the system is a frequent concern for clinicians when preparing for extubation. The intended use of remifentanil in ICU is for analgo-sedation i.e using an analgesic for its sedative effects which results in a propofol-sparing effect. Similar monitoring which would be undertaken when using remifentanil anaesthesia would apply in an ICU setting. Dr Gillis highlighted that although remifentanil use for sedation would be new in ICU, other drugs used in ICU (e.g. adrenaline, noradrenaline) require frequent infusion pump changes and should not be given by a bolus injection either. Therefore, these administration concepts would be familiar to nursing staff.

Potential patient cohorts that may benefit from remifentanil use in an ICU setting could include:

- Patients receiving remifentanil during surgery and requiring post-operative care in ICU where the predicted duration of ventilation is less than 72 hours.
- Patients requiring neurological assessment e.g following neurosurgery, post-cardiac arrest, and overdose.

The importance of excluding residual opioid effects in the system would be beneficial for these patient cohorts when assessing reasons why a patient may not be waking up after sedation cessation. Dr Gillis highlighted potential risk mitigation steps for the safe use of remifentanil in ICU, including establishing very strict patient criteria, ensuring good leadership around decision-making for use, and consultant discussion before prescribing. The use of infusion pump libraries was suggested to preven inadvertent bolus dose administration.

In camera, the Committee acknowledged the variation in the results of the meta-analyses and that the evidence was limited by the contribution of a few small studies with significant treatment effect driving a small overall difference in treatment effect. The Committee noted feedback from clinicians regarding a significant clinical difference in practice, potentially due to differences between the study cohort and the proposed application cohort. It was agreed that there may be value in using remifentanil in a well-defined group of patients, however, these criteria require further clarification. A consensus across all NCL ICUs on use would be required, with consideration of risks and mitigation steps. It was highlighted that the limit of 72 hours of use is important to consider as part of this process. The Committee agreed to defer the decision pending receipt of clear pathways and criteria for establishing patients on remifentanil in ICU, as well as risk mitigation steps.

In summary, although the treatment effect based on the evidence is small, it was accepted that there may be some benefit in the use of remifentanil in ICU for a strictly defined patient cohort. Further work is required to confirm an NCL ICU clinician consensus for use. Therefore, the decision is deferred pending receipt of clear pathways, criteria for establishing patients on remifentanil in ICU and risk mitigation steps.

Medication: Remifentanil
Decision: Deferred - pending receipt of clear pathways, criteria for establishing patients on remifentanil in ICU and risk mitigation steps.
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: n/a

12. Guidelines, Pathways and Position statements

12.1 Review of NCL Ocular Lubricants guidelines vs pan-London dry eye guidelines

The Committee considered a gap analysis comparing the NCL Prescribing Guideline for Ocular Lubricants (August 2019) and the Pan-London Dry Eye Guideline (July 2022). The pan-London guideline was developed by an LPP Ophthalmology short-life working group with input from various clinicians including Moorfields (MEH) representatives. All differences between the guidelines were addressed during the production of the Pan-London guide and MEH confirmed the adoption of the Pan-London Dry Eye Guideline. The Committee agreed to retire the NCL guidelines and adopt the Pan-London Dry Eye Guideline.

12.2 Review of NCL Overactive Bladder Pathway in Primary Care

The Committee was informed that the NCL guideline for the Pharmacological Management of Overactive Bladder Syndrome in Primary Care, developed in October 2016, is overdue an update. Since the development of the NCL guideline, two primary care pathways relating to overactive bladder have been developed (for Lower Urinary Tract Symptoms in males (last updated in July 2022) and females (last updated in March 2023)) using NICE guidelines (CG97 and NG123 respectively).

The Committee reviewed and approved a proposal to retire the NCL guideline for the Pharmacological Management of Overactive Bladder Syndrome in Primary Care due to the availability of 2 primary care pathways. The Committee agreed that the NICE and JFC 'do not offer' recommendations should be included in NetFormulary monographs. The Committee recommended liaising with the ICB primary care pathway team to reassess the place in therapy of medicines suitable for overactive bladder management based on cost and to update the primary care pathways to include information about stopping criteria and treatment review periods (from section 5 of the NCL guideline). The Committee also agreed that it was important to consider how primary care pathway links can be accessed via NetFormulary.

13. Primary Care Pathways

The risk assessments for the medicines included in the; i) Adult headache, ii) Acute dizziness in adults, iii) Adult heavy menstrual bleeding and iv) Polycystic ovary syndrome (PCOS) pathways were presented to the Committee

for consideration and approval as part of the JFC support for the pathways transformation work. The risk assessment undertaken involved a review of the place in the pathway and the evidence base for each medicine including safety, efficacy, costs, prescribing and formulary position. The medicines in the pathways were discussed with the JFC clinical pathways sub-group prior to the meeting with some recommendations.

In summary, the medicines-related elements in the i) Adult headache, ii) Acute dizziness in adults, iii) Adult heavy menstrual bleeding and iv) Polycystic ovary syndrome (PCOS) pathways were approved pending some minor amendments (noted below where relevant). Other elements of the pathway (e.g., clinical and operational aspects) will be approved by other ICB groups as per the ICB primary care pathways' governance process.

13.1 Adult headache

Clarification on the clinical importance of brand prescribing carbamazepine for headaches has been requested from clinical specialists. Feedback and comments will be brought back to the JFC clinical pathways sub-group.

13.2 Acute dizziness in adults

The Clinical Knowledge Summaries (CKS) guidance for the management of dizziness in adult recommends a maximum treatment duration of 3 days due to lack of evidence on long-term use of medications. Clarification on the restriction duration in practice has been requested from clinical specialists. Feedback and comments will be brought back to the JFC clinical pathways sub-group.

13.3 Adult heavy menstrual bleeding

No pending actions

13.4 Polycystic ovary syndrome (PCOS)

The inclusion of secondary care medication suitable for continuation of prescribing in primary care (e.g metformin, eflornithine) were recommended by the JFC clinical pathways sub-group. This will be updated in the pathway and brought back to the group.

14. Next meeting

Thursday 21st September 2023

15. Any other business

The Committee thanked Gurpal Grewal for his invaluable contributions and work as part of JFC support team over the last 5 years and wished him well in his future endeavours.