Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 18th April 2024

		Present	Apologies
Members			
Prof A Hingorani	NCL JFC Chair	✓	
Dr B Subel (Chair)	NCL JFC Vice Chair	✓	
Ms L Coughlan	NCL ICB, Deputy Chief Clinical Officer & ICS Chief Pharmacist	✓	
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	✓	
Dr R Urquhart	UCLH, Divisional Clinical Director		✓
Dr K Tasopoulos	NMUH, DTC Chair	✓	
Ms A Stein	NMUH, Interim 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, Assistant Director of Medicines Optimisation	✓	
Ms M Kaur-Singh	NCL ICB, Head of Medicines Planning & Operations	✓	
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	✓	
Ms S Maru	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms K Leung	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms M Butt	IPMO Programme Team, Director	✓	
Ms T Shah	RFL, Deputy Chief Pharmacist	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Mr A Barron	UCLH, Principal Pharmacist		✓
Mr S O'Callaghan	UCLH, Formulary Pharmacist	✓	
Ms C OBeirne	UCLH, Formulary Pharmacist	✓	
Ms H Thoong	GOSH, Formulary Pharmacist		✓
Mr D Sergian	MEH, Formulary Pharmacist	✓	
Ms A Bathia	RNOH, Formulary Pharmacist	✓	
Ms S Ahmed	WH, Formulary Pharmacist		✓
Ms N Patel	NMUH, Formulary Pharmacist	✓	
Ms M Thacker	GOSH, Deputy Chief Pharmacist	✓	

Ms H Weaver	NHSE, Specialised Commissioning Pharmacist (Observer)	✓	
Ms EY Cheung	NCL ICB, Head of Medicines Quality & Improvement		✓
Mr J Flor	WH, Lead Pharmacist	✓	
Mr A Fazal	RFL, Principal Pharmacist	✓	
Mr D Ryan	UCLH, Clinical Pharmacology Registrar	✓	
Prof C Bunker	UCLH, Dermatology Consultant	✓	
Dr K Dear	UCLH, Dermatology Registrar	✓	
Dr E Uppal	UCLH, Dermatology Registrar	✓	
Dr C Kortsalioudaki	UCLH, Neonatal Consultant	✓	
Ms A Husain	UCLH, Lead Women's Health and Neonates Pharmacist	✓	
Ms P Stepney	UCLH, Neonatal Dietician	✓	
Ms J Pang	IPMO Programme Team	✓	
Mr K Simpson	IPMO Programme Team	✓	
Ms S Jalil	NCL ICB, Prescribing Advisor (Observer)	✓	

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. Prof Hingorani declared that he received a competitive 2-year industry-academia collaborative grant from Pfizer (manufacturers of etanercept) related to heart failure gene discovery, which was now finished. Mr Harchowal declared that he has worked with Pfizer on innovation projects linked to patient pathways in cancer, but not directly related to any drugs.

4. Minutes of the last meeting

Minutes and abbreviated minutes of the March 2024 meeting were ratified.

5. Review of action tracker

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

5.1. [Update] ProPrems for necrotising enterocolitis in preterm neonates (Applicants: Dr Korstalioudaki, Ms Stepney and Ms Husain; UCLH)

In January 2023, the Committee approved ProPrems® for the prevention of necrotising enterocolitis (NEC) in pre-term neonates at UCLH, a level 3 neonatal unit, under evaluation for one year. Implementation of ProPrems was delayed due to challenges with staff capacity, obtaining divisional approvals and consideration of an FDA alert in September 2023. The FDA alert highlighted risk of invasive, potentially fatal disease caused by the bacteria or fungi contained in unlicensed probiotics and noted a death of a pre-term infant linked to probiotic treatment. The Committee noted that the particular strain that caused this death (Bifidobacterium longum) is not present in ProPrems and that the use of probiotics is supported by national and European guidelines (e.g. ESPGHAN, GIRFT, WHO and MatNeoSIP).

Dr Korstalioudaki informed the Committee that the neonatal team have engaged with numerous stakeholders and experts in the UK and Europe, including via the N3 Neonatal Nutrition Network, national NEC meeting and ESPGHAN and reached consensus that it was appropriate to proceed with implementation of ProPrems®. The Committee heard mitigations adopted by UCLH to minimise risk of contamination and to ensure parents and carers were fully informed during decision-making. These mitigations included:

i. Selection of ProPrems® as a high-quality product that meets European Good Manufacturing Practice (GMP) standards and is recommended by ESPGHAN.
ii. Development of patient information leaflet to support shared decision making
iii. UCLH guideline on prescribing, administration, stopping criteria, cautions and risks
iv. Standard operating procedure for preparation and administration to minimise risk of contamination, which received approval from NICU microbiology consultants and Infection Control.
v. Training for doctors and nurses with requirements for individual sign-off.
vi. UCLH neonatal governance sign-off to proceed with the use of ProPrems®.
vii. Practice to be audited and reported to local governance and JFC

Implementation is planned to begin from 22nd April 2024.

The Committee further discussed the Cochrane review (Sharif et al, July 2023) for probiotics for prevention of NEC in neonates, which has been updated since the previous JFC evidence review. The review shows a lower risk of NEC (RR 0.54; 95% CI 0.46 to 0.65) and lower risk of all-cause mortality (RR 0.77; 95% CI 0.66 to 0.90) and late onset invasive infection (RR0.89; 95% CI 0.82 to 0.97) for probiotics compared to control, with no significant difference in neurodevelopmental impairment. This provided further reassurance regarding efficacy and safety.

In summary, the Committee agreed that the UCLH Neonatal Unit has taken appropriate measures following the FDA alert. The Committee recommended the neonatal governance group consider the inclusion of the FDA alert in the patient information leaflet to ensure full transparency with parents and carers, but for this to be balanced with (1) the totality of evidence on the use of probiotics in NEC, which indicates favourable efficacy and safety, and (2) mitigations the neonatal unit have implemented. The Committee also welcomed the reporting of interim results at 6 months before full results of the evaluation (to be undertaken by the UCLH level 3 neonatal unit) are anticipated in May 2025.

Drug: ProPrems®
Indication: For the prevention of necrotising enterocolitis in pre-term neonates
Decision: Approved under evaluation for one year
Prescribing status: Restricted to UCLH level 3 neonatal unit
Funding source: Trust
Fact sheet or shared care required: N/A
Additional information: The Committee welcomed the reporting of interim results at 6 months before full results of the evaluation are anticipated in May 2025.

6. JFC Outstanding items and workplan

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

7. Local DTC recommendations/minutes

DTC site	Month	Drug	Indication	JFC outcome
RFL	February 2024	Methylphenidate as per licensed dose	Narcolepsy in paediatrics (6 to 18 years old) as second line treatment when Modafinil has not shown improvement or led to adverse reactions	**Decision**: Conditionally approved subject to development of local guideline **Prescribing**: Secondary care initiation, primary care continuation (suitable for secondary care continuation if SEL shared care not accepted) **Funding source**: In tariff **Fact sheet or shared care required**: N/A **Additional information:** Medication to be initiated/advised by the Evelina London children's sleep service. Initial 3 months to be supplied by Evelina, with prescribing transferred to secondary care if shared care not accepted by primary care.
RFL	February 2024	Evorel patch (6.25mcg to 25mcg twice weekly for 6 months and then review as per BSPED guideline recommendation. Treatment duration: 2-3 years)	First line treatment for pubertal induction in young children with delayed puberty	**Decision**: Conditionally approved subject to development of local guideline **Prescribing**: Secondary care only **Funding source**: In tariff **Fact sheet or shared care required**: N/A **Additional information:** Medication to be initiated/recommended by GOSH, with secondary care continuation

The Committee noted that some DTCs review radiopharmaceuticals, however governance routes for these differ across NCL Trusts. The Committee agreed that radiopharmaceuticals do not fall within the remit of JFC review or ratification.

8. Matters arising

8.1. Bijuve® supply update (Applicant: Dr Talaulikar; UCLH)

In October 2022, the Committee reviewed the use of Bijuve® (lose-dose continuous combined oestrogen/ body-identical progesterone HRT) for the management of menopausal symptoms to:

(i) To replace low-dose oral combination HRT which contain an oestrogen and progestin (e.g., Kliovance® 1mg/500mcg) with a claim of a superior safety profile; and

(ii) To replace low-dose oestrogen (oral or transdermal) plus oral body-identical progesterone (Utrogestan®), with claims of superior convenience (from use of a combined product over two separate products) and improved concordance (due to difficulty in escalating progesterone doses to accompany increases in transdermal oestrogen)

The Committee did not approve the addition of Bijuve® to the NCL formulary due to the lack of robust evidence of superior efficacy or safety in comparison to the available HRT products, such as Utrogestan® (oral body-identical progesterone).

In September 2023, JFC approved the use of Bijuve® for an interim period of 6-months while Utrogestan® supplies were unavailable with a view to review the supply chain and formulary position in 6 months. Utrogestan® is now currently in stock and available to procure.

The Committee considered a request, in absentia, for the addition of Bijuve® to the NCL formulary as a replacement to Utrogestan® in the event of future Utrogestan® shortages due to the volatile HRT supply chain. The Committee approved the request to extend the approval beyond the interim period for Bijuve® to be used only if Utrogestan® is not available.

Drug: Bijuve® 1mg/ 100mg capsules, one capsule daily continuous treatment
Indication: For the management of menopausal symptoms
Decision: Approved only in the event of Utrogestan® shortages or where stock is not available.
Prescribing status: Suitable for initiation in primary and secondary care
Funding source: In tariff
Additional information: N/A
Fact sheet or shared care required: N/A

9. Medicine reviews

9.1. Etanercept for SJS/TENs (Applicants: Prof. Bunker, Dr Dear; UCLH)

The Committee considered an application for etanercept (a TNF-alpha inhibitor) 50mg subcutaneously twice weekly in addition to IV steroids in a first-line setting, for off-label use, in suspected Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TENs) in adult patients with over 30% body surface area (BSA) affected or at risk as assessed by a dermatologist.

Wang et al (2018; n=96) was an active-comparator controlled, unblinded study to compare the efficacy and safety of etanercept and IV prednisolone in patients > 4 years old with probable/definitive SJS/TENs (of which 38% of patients had a BSA >10%). Patients were randomised 1:1 to etanercept 25-50mg subcutaneously twice weekly or prednisolone 1-1.5mg/kg/day intravenously administered until skin lesions healed. The primary endpoint, time to complete skin re-epithelialization, was not significantly shorter with etanercept compared to IV prednisolone (13.8 days vs.16.5 days; p> 0.05). Mortality was not significantly lower with etanercept than IV prednisolone (8.3% vs. 16.3%; OR: 0.47, [95%CI: 0.13 to 1.72]). Key limitations of the study were the open-label design, underpowered sub-group analysis in patients with severe illness (BSA > 10%), and intervention not reflective of proposed use (etanercept with IV steroids would be a more relevant intervention).

Ao et al (2022; n=25) was an active-comparator controlled, unblinded, non-randomised study to compare the efficacy and safety of etanercept with IV methylprednisolone to IV methylprednisolone monotherapy in adult patients with suspected SJS/TENs (of which 28% of patients had a BSA > 30%). Patients were allocated to receive either etanercept subcutaneously twice weekly until steroid tapering in addition to IV steroids or IV methylprednisolone (equivalent to 1-1.5mg/kg/day). The primary endpoint, median time to complete skin re-epithelialization, was significantly shorter in the etanercept and IV steroids arm compared to IV steroids (12 days vs 16 days; p=0.0105). The study reported a significant reduction in duration of hospital stay with the addition of etanercept (figures not reported, p=0.0243). Key limitations of the study were that it was non-randomised and unblinded.

Two non-randomised observational case series (Paradisi et al 2014; n=10 and Paradisi et al 2021; n=17) reported one-off dosing of etanercept 50mg subcutaneously within 6 hours of hospitalisation. Median time to skin healing was 8 days and 8.5 days respectively.

In terms of safety, Wang et al reported no difference in mortality in the etanercept arm compared to the steroids arm (OR: 0.47[95% CI: 0.13-1.72]). Etanercept has a lower risk of serious adverse effects compared to IV steroids (10% vs. 21%). Etanercept has a known safety profile from use in the rheumatology cohort.

In terms of budget impact, etanercept is expected to cost an additional £4000 per annum for approximately 5 patients per annum, as compared to IV steroids monotherapy.

The Committee heard from Prof Bunker that due to the rarity, severity and heterogeneity of the disease, it is difficult to obtain high quality trial data. The inclusion of etanercept in societal guidelines is anticipated to take a few years till publication. There is no formal multi-disciplinary team (MDT) currently in place to manage these patients, but an informal North London TENs MDT is available. Prof Bunker emphasised the severity of the condition and urgency in reaching a treatment decision, noting that the number of cases is rising in NCL due to the growth in haematology and oncology services.

In camera, the Committee noted that etanercept is widely used for other indications, relatively safe and inexpensive but that the efficacy remained uncertain from the limited evidence base. The Committee acknowledged that the limited evidence base (uncontrolled case series, one non-randomised, unblinded study and anecdotal experience) may be reflective of the rarity and severity of the condition. In terms of the clinical outcomes, the Committee noted a modest benefit in terms of time to skin re-epithelialisation and mortality rate (with wide confidence intervals). However, the Committee noted that the evidence base for steroids (the current standard of care treatment) is equally poor and steroids may cause more adverse effects, despite being licensed for this indication. The use of etanercept in conjunction with steroids may mitigate harm from steroids.

The Committee raised a concern regarding potential variation in practice and suggested that consensus guidelines and a more formal cross-Trust MDT process would ensure a consistent approach. In addition, the Committee noted that management of SJS/TENs is an NHSE commissioned service and to support equity of access to care, it would be appropriate to submit an NHSE Specialised Commissioning policy proposal for national consideration.

In summary, the Committee agreed to conditionally add etanercept to the NCL Joint Formulary in addition to IV steroids in a first-line setting in suspected Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TENs) in adult patients with over 30% BSA affected or at risk, as assessed by a dermatologist. The conditions of approval are:

i) Development of consensus guidelines across the specialist dermatological services including inclusion, exclusion and stopping criteria,

ii) Establishment of a formal MDT process across NCL, or joining an existing MDT (e.g. HLH MDT),

iii) Submission of an NHSE Preliminary Policy Proposal, and,

iv) Presentation of an audit in 12 months that demonstrates that an appropriate governance and operational process (e.g. MDT) is in place and being followed routinely.

Drug: Etanercept injections 50mg SC twice weekly for 4 doses (up to 10 doses may be required if patients relapse); off-label
Indication: In addition to IV steroids in a first-line setting in suspected Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TENs) in adult patients with over 30% BSA affected or at risk, as assessed by a dermatologist.
Decision: Conditionally approved subject to i) Development of consensus guidelines across the specialist dermatological services including inclusion, exclusion and stopping criteria, ii) Establishment of a formal MDT process across NCL, or joining an existing MDT (e.g. HLH MDT), iii) Submission of an NHSE Preliminary Policy Proposal, and, iv) Presentation of an audit in 12 months that demonstrates that an appropriate governance and operational process (e.g. MDT) is in place and being followed routinely.
Prescribing status: Restricted to secondary care only
Funding source: Internally funded High Cost Drug
Fact sheet or shared care required: N/A

10. Position Statements and Guidelines

10.1. NCL Fluoroquinolones Position Statement

The NCL Safe Prescribing of Fluoroquinolones Position Statement has been updated by the NCL Antimicrobial Pharmacist Group (APG) in line with new MHRA drug safety alert recommendations (Sept 2023 and Jan 2024) and circulated for NCL consultation. All comments received have been addressed. The Committee approved the updated position statement.

10.2. NCL Glaucoma Guideline

Deferred.

10.3. NCL DOACs NVAF Position Statement

In 2022, the NHSE national DOAC procurement framework placed edoxaban as the best-value DOAC. The NCL Position Statement was updated to recommend edoxaban as the preferred DOAC for non-valvular atrial fibrillation (NVAF), and an active-switch program of existing DOAC patients to edoxaban was implemented in accordance with NHSE recommendations. In January 2024, NHSE updated their commissioning recommendations, noting the availability of generic apixaban. The update placed generic apixaban as the best value 'twice-a-day' DOAC and edoxaban as the best-value 'once-a-day' DOAC for AF.

Following this update, the following changes have been made to the NCL position statement for choice of DOAC in NVAF:

i. Generic apixaban has been placed as the first-line DOAC where clinically appropriate.

ii. Rivaroxaban has been placed as an alternative as a 'once-daily' preparation as the pricing difference between apixaban and rivaroxaban is minimal and the patent expiry for rivaroxaban is expected to be sooner than for edoxaban.

iii. An active-switch program to apixaban is not mandated for existing patients so existing patients can be continued on existing treatment. Clinicians will be supported if they wish to review and switch patients to apixaban.

The Committee approved the updated position statement.

11. NHSE Updates

11.1. NHSE Specialised Commissioning NICE Appraisals Update

The Committee noted an NHSE Circular (SSC2614) providing an update on Specialised Commissioning from February 2024. This was included for information only.

11.2. Desflurane decommissioning

The Committee noted NHSE guidance on desflurane decommissioning and clinical use published in March 2024. Significant work across NCL to reduce desflurane use has led to very low existing use across the system. Following NCL consultation, no issues were identified on adopting the NHSE guidance and decommissioning desflurane. Therefore, the Committee were supportive of:

i) Designating a non-formulary status for desflurane across NCL except for the specific limited circumstances outlined by NACCS (intracranial surgery where the duration of anaesthesia is anticipated to be long (e.g. > 10 hours) and the intention is to wake the patient at end of surgery), and,

ii) Any further clinical exceptions identified locally should be fed back to NACCS to inform the national position.

Decision: Non-formulary

12. Tocilizumab biosimilar: Tyenne®

The Committee considered the use of the tocilizumab biosimilar (Tyenne®) for its licensed indications by NCL Trusts. The products available, licensed indications, efficacy and pharmacokinetic data are similar across the biosimilar (Tyenne®) and the originator (RoActemra®).

In terms of safety, the APTURA I study reported a similar frequency of side effects between Tyenne® and RoActemra® (9.3% vs 9.9%). However, more frequent injection site reactions were reported with Tyenne® than RoActemra® after 24 weeks (11.3% vs 4.6%), with the difference decreasing after 63 weeks (12.3% vs 8%). Given the well-characterised similarity between Tyenne® and RoActemra® from a quality and pharmacokinetics perspective, the EMA concluded that the observed difference in injection site reactions between the trial arms might be a random finding that does not indicate a true difference. Minor differences in excipients between Tyenne® and Roactemra® were noted. In the EMA assessment report, the manufacturers of Tyenne® reported that none of the excipients used are expected to induce clinically relevant ISR or would have any other safety impact.

The Committee noted that operational concerns have been highlighted regarding homecare supply and the choice and capacity of the homecare providers specified by the biosimilar manufacturers. Potential solutions (e.g. unbundling drug and homecare costs) are under discussion between the Trusts and High Cost Drugs team.

In summary, the Committee approved the use of the tocilizumab biosimilar (Tyenne®) for its licensed indications by NCL Trusts. The Committee recommended that Trusts monitor rates of injection site reactions resulting in switch back to originator. Trusts were recommended to try to maximise savings by implementing the biosimilar, acknowledging the logistical issues related to homecare that are currently under discussion.

Drug: Tocilizumab biosimilar (Tyenne®)
Indication: In line with NICE TA/NCL JFC approved indications

Decision: Approved
Prescribing status: Restricted to secondary care only
Funding source: ICB-commissioned High Cost Drug
Fact sheet or shared care required: N/A
Additional information: Trusts to monitor rates of injection site reactions resulting in switch back to originator. Trusts are recommended to try to maximise savings by implementing the biosimilar, acknowledging the logistical issues related to homecare that are currently under discussion.

13. Next meeting

Thursday 16th May 2024

14. Any other business

Nil