

Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 18th May 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; NCL ICS, Interim 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)	✓	
Dr D Roberts	NCL ICB, Clinical Director (Islington)	✓	
Attendees			
Ms S Amin	IPMO Programme Team, JFC Principal Pharmacist	✓	
Mr G Grewal	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms S Maru	JFC Support Pharmacist	✓	
Ms P Varu	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 Gabriela	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 Blochberger	NHSE, Specialised Commissioning Pharmacist		✓

Ms A Fakoya	NCL ICB, Contracts & Commissioning Pharmacist		✓
Dr A Hosin	UCLH, Clinical Pharmacology Registrar	✓	
Ms EY Cheung	NCL ICB, Deputy Head of Medicines Management (Camden)		✓
Ms K Mistry	RNOH, Formulary Pharmacist	✓	
Ms S Ahmed	WH, Formulary Pharmacist	✓	
Ms L Garubova	WH, Formulary 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 C Weaver	Senior Prescribing Advisor, NCL ICB (Camden)	✓	
Ms G Gungor	NCL ICB, Assistant Director of Transformation		✓
Ms P Panesar	Lead Antimicrobial Pharmacist, UCLH	✓	
Dr D Lowe	Consultant Infectious Diseases, RFL	✓	
Dr N Sotiris	Consultant Anaesthetist, WH	✓	
Ms M Lanzman	Lead Antimicrobial Pharmacist, RFL	✓	
Dr M Brown	Consultant Infectious Diseases, UCLH	✓	
Dr E Sanchez	Consultant Virologist, UCLH	✓	
Ms O Odejide	Senior Prescribing Advisor, NCL ICB (Camden)	✓	
Ms M Corpus	Clinical Nurse Endoscopist/VCE Senior Lead Nurse (Observer)	✓	
Ms R Saujani	NMP Student (Observer)	✓	
Mr Z Zarar	NMP Student (Observer)	✓	
Mr D Kahan	PCN Pharmacist, Barnet Federation (Observer)	✓	

1. Meeting apologies

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

2. Meeting observers

Prof Hingorani welcomed observers to the meeting (see above).

3. Members' declaration of interests

The Declarations of Interests register for Committee members was included for information.

4. Minutes of the last meeting

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

5. Matters arising

5.1 End of the lenalidomide FOC scheme

Lenalidomide was ratified at JFC under a FOC scheme for relapsed lymphoma in November 2022. It was brought to the attention of the committee that the FOC scheme has ended, and the company (Bristol Myers Squibb) are no longer accepting new FOC Scheme applications for lenalidomide.

5.2 Amendment to the March 2016 JFC meeting minutes for testosterone gel

The Committee were informed that minutes from the March 2016 JFC meeting state that testosterone gel for poor libido post menopause or due to premature ovarian insufficiency stated that it was red listed. The red list status was reviewed by the NCL Shared Care Group, and it was agreed that the treatment should be available in primary care, supported by an NCL factsheet. An addendum has been added to the March 2016 minutes to reflect this change. The Committee agreed with the addendum.

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 Amin.

8. Local DTC recommendations / minutes

DTC site	Month	Drug	Indication	JFC outcome
UCLH	March 2023	Artiss®	Subcutaneous tissue sealant in major head and neck procedures	Decision: Approved – UCLH only Prescribing: Secondary care only Tariff status: In tariff Funding: Trust Fact sheet or shared care required: N/A
UCLH	March 2023	Intravesical bupivacaine	Bladder spasm pain post Robotic-Assisted Laparoscopic Prostatectomy (RALP)	Decision: Approved – UCLH only Prescribing: Secondary care only Tariff status: In tariff Funding: Trust Fact sheet or shared care required: n/a
UCLH	March 2023	Sodium cromoglicate (oral capsules)	Management of gastrointestinal symptoms in systemic mastocytosis	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
UCLH	March 2023	Chlorhexidine Gluconate gel 1%	-After head and neck cancer treatment on the recommendation of a Head and Neck Consultant or Restorative/Special Care Dental Consultant. -For patients receiving palliative care as part of ongoing symptom control. -Management of Sjogren's syndrome as per advice from a Dental specialist.	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care initiation, primary care continuation Tariff status: In tariff Funding: Trust Fact sheet or shared care required: N/A
UCLH	March 2023	Hydrogen Peroxide mouthwash 6%		
UCLH	March 2023	Sodium Fluoride mouthwash		
RFL	April 2023	FOC Scheme: Durvalumab †	With gemcitabine and cisplatin for locally advanced, unresectable or metastatic biliary tract carcinoma	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: N/A - Free of charge Funding: FOC scheme Fact sheet or shared care required: N/A
DHSC	October 2020	Restandol®	Product discontinued	Removed from formulary

8.1 FOC Scheme: Durvalumab for mBTC

Durvalumab was ratified for use via a FOC Scheme with gemcitabine and cisplatin for locally advanced, unresectable, or metastatic biliary tract carcinoma. The letter of agreement was updated to meet the NCL FOC wording criteria. The FOC application form was amended to allow RFL to provide anonymised patient data back to the manufacturer (Astra Zeneca). Other NCL Trusts interested in use can follow the same process.

8.2 NeoKay oral drops for patients with vegetarian and vegan diets where Konakion MM is unsuitable

The Committee were informed that Konakion MM is unsuitable for vegetarians as one of the excipients is derived from cattle. NeoKay oral drops were an alternative preparation of phytomenadione for use in neonates which were vegetarian- and vegan-friendly with little difference in cost. The Committee were satisfied that an option should be available on the NCL Joint Formulary for patients with vegetarian & vegan diets and agreed to add NeoKay oral drops to formulary as a second-line option.

Medication: NeoKay oral drops

Decision: Added to the NCL Joint Formulary

Prescribing: Secondary care

Tariff status: In tariff

Funding: Trust

Fact sheet or shared care required: N/A

8.3 Discontinuation of Restandol

The Committee was informed that Restandol 40mg capsules was discontinued from the UK market in October 2020 and will therefore be removed from the NCL Joint Formulary. There are no other suppliers of oral testosterone formulations. Testosterone transdermal and long-acting injection formulations remain available.

9. New medicine reviews

9.1 Rapid reviews : Midazolam, Clonidine and Ketamine

The use of midazolam, clonidine, and ketamine for sedation as premedication in paediatric patients prior to general anaesthesia is historical practice at GOSH. Some of the pre-medications are on the Whittington Hospital (WH) formulary, whereas others are not. WH formulary team have undertaken rapid reviews, and these were presented to the Committee to harmonise practice across NCL. In general, most patients requiring sedation as premedication for general anaesthesia have learning disabilities and/or spectrum disorders and therefore the choice of pre-medication will depend on the patient specific situation.

The Committee heard from Dr Sotiris that no new significant cost implications are expected, as clonidine and ketamine IV preparations are already stocked in theatres and will be used via the oral route. Although anaesthetists have their own preferences, reassurance was provided that the approval of these medicines in combination with a local guideline written by experts and clinicals leads in the department would be adopted by the wider team. Risk mitigation associated with the use of parenteral formulations orally has been considered and can be highlighted in the guidance. It was accepted that the guideline can be updated to include a hierarchy of treatment choice and the inclusion of additional notes can be incorporated to help rationalise and guide choice for clinicians using the guidance.

In camera, it was highlighted that although the range of medications requested is wide, this is required due to the complexities with this patient group and the range of patients presenting at WH. It was agreed that the pathway could be simplified, and the inclusion of preferences seem sensible and appropriate. The guideline should clearly specify that use is intended in anaesthesia only, and use is not intended by other specialists such as A&E, trauma, dental etc. Although this has been presented to the Committee by WH formulary team, use may apply to other NCL Trusts but, before adoption elsewhere, guidance should be in place/adapted according to local requirements and use. It was highlighted that brand-specific bioequivalence should be clarified in the guidance (e.g., for midazolam formulations).

In summary, the Committee supported the approval of the midazolam, ketamine, and clonidine for sedation as premedication in paediatric patients prior to general anaesthesia. Further work on the guideline is required to rationalise the inclusion of each agent and a treatment hierarchy with clarification that the guideline is intended for use in anaesthesia only.

Decision: Approved pending update of local guideline

Prescribing: Secondary Care only

Tariff status: In tariff

Funding: Trust

Fact sheet or shared care required: N/A

Additional information: Local guidance is required for use.

9.2 Therapies for COVID-19

9.2.1 Paxlovid, sotrovimab and remdesivir for severely immunocompromised hospitalised adult patients, irrespective of oxygen requirement or days since symptom onset

The Committee considered the use of three COVID therapies to reduce viral load in immunocompromised patients whether due a disease that compromises immune function or a disease that requires treatment with immune modulating therapies. NCL cares for many such patients through its specialist services. It is recognised that such patients may have prolonged illness with COVID because of difficulty in clearing the virus This Committee review therefore encompassed the anti-viral agents Paxlovid® and remdesivir, and the monoclonal antibody sotrovimab.

The pivotal clinical trials that led to licensing of these agents were primarily in immunocompetent patients, and some were in patients with no oxygen requirement presenting early in their illness. For this reason, Paxlovid® and sotrovimab are licensed specifically in patients who do not require supplemental oxygen and are within 5 days of symptom onset. Remdesivir is licensed specifically for use in patients requiring supplemental oxygen at any timepoint or who do not require oxygen within 7 days of symptom onset. Therefore, as part of

the evaluation, other types of evidence (e.g., from case series or non-randomised observation studies) were sought for off-label use of these agents in immunocompromised patients.

The Committee were informed that NICE had recently provided a negative recommendation for remdesivir in mild or severe COVID-19, although this was currently under appeal from the manufacturer on several grounds, such as patients on low-flow oxygen not being considered as a separate subgroup. Therefore, the JFC review focused on:

- Paxlovid and sotrovimab use in immunocompromised patients >5 days since symptom onset, or who have an oxygen requirement.
- Remdesivir use in immunocompromised patients who require no oxygen, or who require supplemental oxygen or mechanical ventilation, at any time from symptom onset.

All treatments were intended for use as per their respective licensed dosing regimen. The Committee understood that immunocompetent patients can mount an immune response to SARS-CoV-2, creating antibodies and eliminating the virus. However, immunocompromised patients are unable to eliminate the virus and the patient can remain symptomatic and infectious for extended periods of time. There was no RCT data for the proposed COVID therapies in these settings, particularly in seronegative patients. The Committee were informed that RCT data available for seronegative patients (who were immunocompetent but had no prior exposure to SARS-CoV-2) was from the RECOVERY trial using the monoclonal antibody Ronapreve®. This found that Ronapreve® significantly reduced 28-day mortality compared with standard of care alone in seronegative patients (24% vs 30%; RR = 0.79 [95% CI 0.69 to 0.91]), but no difference was found in the total population (i.e., including both seropositive and seronegative patients combined). Ronapreve was not approved by NICE due to uncertainty on its efficacy against current predominant variants of SARS-CoV-2.

As there was no RCT data, a literature review was conducted to find all relevant publications where the three proposed therapies were used in off-label indications. Data to support the use of Paxlovid when used after 5 days of symptom onset was from one positive case report in a seronegative patient with repeated hospital admissions and in one registry study in 144 hospitalised patients, 12 of which were immunocompromised patients prescribed Paxlovid >5 days since symptom onset; viral elimination was described as being longer in immunocompromised patients, although the time to viral elimination was not described. There was no data to support the use of Paxlovid in patients requiring oxygen. Other data to support the use of Paxlovid was described, which included the pivotal RCT in which 47% of patients who did not require oxygen within 5 days of symptom onset was seronegative; the reduction in viral load was consistent regardless of baseline serology status, and in an exploratory analysis the primary outcome of hospitalisation or death was significant in favour of Paxlovid versus placebo in both seropositive and seronegative populations respectively. Further data was available in a case-series which found Paxlovid to be effective in avoiding hospitalisation in immunocompromised patients with rheumatic disease, and a propensity-matched cohort study which found Paxlovid was more effective in unvaccinated patients compared with vaccinated patients and in patients who were vaccinated and severely immunocompromised compared with immunocompetent vaccinated patients (RR = 0.66 [95% CI 0.50 to 0.89]).

Data to support the use of sotrovimab when used after 5 days of symptom onset was seen in two separate case reports, both of which demonstrated sotrovimab administered to immunocompromised patients led to resolution of symptoms and confirmed elimination of virus 4-5 weeks post discharge (one patient also had an oxygen requirement). A prospective cohort study in which sotrovimab was administered to 17 immunocompromised patients when they were admitted to hospital after a median of 10 days following symptom onset demonstrated efficacy with 16 patients successfully discharged (a proportion of these patients also required oxygen, though the exact number is unknown). A retrospective cohort study where sotrovimab was administered to 32 immunocompromised patients with bilateral pneumonia and/or need for oxygen a median of 9 days from symptom onset demonstrated progression of respiratory support or death in 7 patients. Other data to support sotrovimab use in immunocompromised patients include two case reports of successful sotrovimab administration to immunocompromised patients in the outpatient setting, a cohort study (n=7,706) which showed the risk of hospitalisation or death at 28 days in an immunocompromised subgroup was lower with all monoclonal antibodies, a retrospective observational study which found 81.1% of immunocompromised patients without oxygen did not progress to severe COVID-19, and a retrospective study in which a large proportion of hospitalised immunocompromised patients were given sotrovimab, of which 30.2% remained hospitalised and 5.3% died within 90 days.

Data to support remdesivir in patients with no or low-flow supplemental oxygen came from Amstutz et al (n=10,480), who performed a systematic review and meta-analysis for the use of remdesivir in hospitalised

adult patients with COVID-19 compared with no remdesivir. The meta-analysis included studies considered in the NICE appraisal and additional data. Symptom onset was a median of 9 days (IQR 6-12 days). In the primary outcome, all-cause mortality at day 28, was significantly lower with remdesivir compared to no remdesivir (12.5% vs 14.1%; adjusted OR = 0.88 [95% CI 0.78 to 1.00; p=0.045]). A subgroup analyses demonstrated that all-cause mortality at day 28 in patients who received no or low-flow oxygen was significantly lower with remdesivir compared to no remdesivir (adjusted OR = 0.80 [95% CI 0.70 to 0.93]), although this effect was not consistent in patients with high-flow, non-invasive ventilation or ECMO adjusted (OR = 1.10 [95% CI 0.88 to 1.38]). It was recognised that “no remdesivir” could include standard of care or placebo (therefore the comparator was not consistent), the data was not specific to an immunocompromised population, and it did not include data for delta or omicron variants.

Data to support remdesivir in patients without oxygen but >7 days from symptom onset was supported in part by Amstutz et al, but also with a further case report in a single immunocompromised patient who successfully eliminated the SARS-CoV-2 virus using remdesivir on two separate admissions without oxygen. Data to support remdesivir use in patients with mechanical ventilation was supported by a case series in 4 patients who received remdesivir whilst in ICU, in which two patients survived. Further evidence was provided through a literature review of case reports (in which 7 cases utilised remdesivir alone, of which 6 survived), a propensity matched cohort study (mortality rate at day 28 was 18% with remdesivir vs 22% with no remdesivir [p<0.0001]), and many other case reports alluding to successful viral elimination with remdesivir (although 3 case reports had reported unsuccessful viral elimination with remdesivir).

In terms of safety, all treatments were known to clinicians with substantial experience in their use. Paxlovid was known to interact with many CYP3A inducers and inhibitors. Sotrovimab carries a risk of resistance, and several case reports discussed the risk of escape variants, particularly in immunocompromised patients with persistent viral shedding.

From April 1st 2023, COVID therapies became the commissioning responsibility of the ICB. It was estimated that there would be a total of 48 eligible patients for each drug per annum in UCLH and RFL combined; this would be 5.5% of the total number of therapies offered via the CMDU in the previous year. The Committee were informed that whilst treatments were currently available free of charge for a limited time in licensed indications, there may costs associated with off-label use. The estimated budget impact for 48 patients was £89,000 for sotrovimab and £102,800 to £188,500 for remdesivir respectively (a budget impact for Paxlovid could not be calculated as the Drug Tariff price was not available).

The Committee heard from Dr Brown and Dr Sanchez that there is a large amount of evidence and experience in the use of these agents throughout the pandemic, although the distinction for use in the immunocompromised cohort is using these agents outside of their normal window of time from symptom onset or outside their usual oxygenation status due to the individuals ability to clear the virus on their own and often remain symptomatic and seronegative for extended periods of time. There is a need for all three agents based on the issues of eligibility to each treatment, although Paxlovid would be considered first, and patients who are ineligible due to interactions may be eligible for sotrovimab.

The Committee acknowledged the evidence was largely of low quality, although were reassured by the overwhelming volume of evidence and clinical rationale for immunocompromised patients requiring additional support for viral elimination. The Committee considered it would be pragmatic to proceed with the addition of all three agents to the NCL Joint Formulary, but would need further understanding of eligibility criteria, stopping criteria, confirmed numbers of patients eligible for each treatment and risk mitigation measures in a treatment protocol, with a requirement for MDT consideration prior to use and a single point of data collection. The Committee agreed that treatments should be reviewed once NICE publish their technology appraisal guidance following appeal later in the year.

In summary, the Committee approved the use of Paxlovid, sotrovimab and remdesivir in *severely immunocompromised hospitalised adult patients*, irrespective of oxygen requirement or days since symptom, onset pending receipt of a protocol that should include eligibility criteria, stopping criteria, confirmed patient numbers eligible for each treatment, risk mitigation measures and requires the use of an MDT prior to initiation and data collection.

9.2.2 Remdesivir for hospitalised adult patients categorised as high-risk with COVID pneumonitis and require supplemental oxygen

The Committee considered the use of remdesivir for hospitalised patients categorised as being high-risk for progression with COVID pneumonitis and requiring supplemental oxygen. Much of the evidence to support this

application had been discussed in 9.1.1. The Committee agreed that this application could be incorporated into the same protocol (including MDT decision making and data collection) as described in 9.1.1, and should also be reviewed once NICE publish their technology appraisal guidance following appeal later in the year.

9.2.3 COVID therapies delivered via the COVID Medicines Delivery Unit (CMDU)

NCL JFC have been asked to provide medicines governance for the use of COVID-19 therapies delivered via the COVID Medicines Delivery Unit (CMDU), which includes Paxlovid® and sotrovimab. The Committee understood that the initial model being developed will allow GPs within the CMDU to prescribe Paxlovid® for patients eligible under NICE TA criteria (which will initially be dispensed from specific community pharmacies), and those who cannot tolerate Paxlovid® can be offered sotrovimab (which will be administered at UCLH). This is an evolving model, and operational leads are looking into the prospect of creating a standardised Patient Specific Direction (PSD) to avoid duplication of prescribing across care settings, and potentially community administration of sotrovimab in certain clinical situations. The Committee agreed with the use of Paxlovid and sotrovimab within the context and criteria of NICE TA878, which does not restrict the setting which therapies are prescribed and administered in.

JFC Chairs and Support team have been responding to individual requests for JFC governance support and deciding whether each fit the remit of the Committee, with recent requests pertaining to prescribing of Paxlovid off-label in patients 12-18 years following paediatric MDT recommendation (with concerns of accountability and responsibility), and administration of sotrovimab in the community setting (with concerns of risk and safety with the potential for anaphylaxis). JFC Chairs and Support team have requested the development of a pathway, within which the Committee could review and ratify elements related to medicines and formulary (although operational and implementation aspects would need to be reviewed via other Primary care operational groups).

Medicine: Paxlovid® and sotrovimab for use as per NICE TA878

Decision: Approved

Prescribing: Primary care (via CMDU) and Secondary Care

Tariff status: In tariff

Funding: ICB

Fact sheet or shared care required: N/A

10. Primary Care Pathways

10.1 Actinic Keratosis pathway: risk assessments for 5-FU cream, diclofenac 3% gel and liquid nitrogen

As below

10.2 Acne Vulgaris pathway: risk assessments for Epiduo, Treclin®, Duac®, Azelaic acid, Benzoyl peroxide, Adapalene, Doxycycline, Lymecycline, Erythromycin, Co-cyprindiol, combined oral contraceptives and Isotretinoin

The risk assessments for the medicines included in the Actinic Keratosis and Acne Vulgaris Primary Care Pathway were presented to the Committee for consideration and approval as part of the JFC support for the pathways transformation work agreed previously. The medicines in the pathway are currently in use within NCL and align with the NCL prescribing recommendations. The risk assessment undertaken involved a review of the place in the pathway and the evidence base for each medicine including safety, efficacy, costs and prescribing and formulary position. The medicines in the pathways were discussed with the JFC clinical pathways sub-group prior to the meeting with no issues identified. Specific recommendations related to the pathway will be fed back to clinical pathways group. It was noted that liquid nitrogen for cryotherapy in the Actinic Keratosis pathway is only available in some practices in primary care and patients can be referred to the practice if unavailable at their local practice. Overall, the Committee were supportive of the medicines included in the pathways.

In summary, the medicines in the Actinic Keratosis and Acne Vulgaris Pathway were approved pending ratification at the next meeting (as the Committee was not quorate when this item concluded). The process for reviewing Primary Care pathways may require further iterations and remains under review.

11. Next meeting

Thursday 15th June 2023

12. Any other business

Nil