Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 16th March 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)	✓	
Mr T Dean	Patient partner		✓
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	✓	
Dr J Levy	NCL ICB, Integrated Medicines Committee (IMOC) Chair Clinical Director, Kentish Town South PCN (Camden Borough)	✓	
Ms C Weaver	Senior Prescribing Advisor, NCL ICB (Camden borough)	✓	
Ms G Gungor	NCL ICB, Assistant Director of Transformation	✓	
Ms K Roy	UCLH, Respiratory Consultant	✓	
Ms M Formica	WH, Lead Respiratory Pharmacist	✓	

2. Meeting observers and members

Prof Hingorani welcomed members, applicants and observers 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 relevant to the agenda were declared by members.

4. Minutes of the last meeting

Minutes and abbreviated minutes were accepted as an accurate reflection of the February 2023 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 Amin.

8. Local DTC recommendations / minutes

8.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
MEH	October 2022	Ciprofloxacin eye ointment 3mg/g	Infection prophylaxis in osteo-odonto-keratoprosthesis (OOKP)	**Decision**: Approved – MEH only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A
MEH	January 2022	Amphoteric solution (Diphoterine)	Severe chemical eye burns in A&E	**Decision**: Approved – MEH only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: n/a **Additional information:** pending pathway development and training/dissemination to A&E staff

UCLH	February 2023	Empaglifozin	Management of neutropenia in Glycogen storage disease 1b (GSD1b) and glucose 6 phosphatase catalytic subunit 3 (G6PC3) deficiency	**Decision**: UCLH only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A
UCLH	February 2023	Eurartesim®	First episode of P. falciparum malaria with slow response to artesunate or Riamet®, and second episode of P. falciparum malaria without intervening travel to a malaria-endemic country (presumed recrudescence)	**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	February 2023	Gardasil-9®	Recurrent respiratory papillomatosis	**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	February 2023	FOC Scheme: Glofitamab	Relapsed or refractory high grade B cell lymphoma or transformed follicular lymphoma	**Decision**: Added to the NCL Joint Formulary **Prescribing**: Secondary care only **Tariff status**: N/A - FOC scheme **Funding**: N/A - FOC scheme **Fact sheet or shared care required**: N/A
UCLH	February 2023	Levofloxacin	Management of community or hospital acquired pneumonia when first line and second line options are unsuitable	**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:** on the advice of microbiology/ID only

UCLH	February 2023	Tisseel® (tissue sealant)	For mesh fixation in hernia repair, as an alternative or adjunct to sutures or staples. For supportive treatment where standard surgical techniques are insufficient: - for improvement of hemostasis - as a tissue glue to promote adhesion/sealing, or as suture support: *o in gastrointestinal anastomoses* *o in neurosurgery where contact with cerebro-spinal fluid or dura mater may occur*	**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. New Medicine Reviews

9.1 Review of GOLD guidance for inhaled therapies in COPD: use of triple therapy (ICS/LABA/LAMA) in place of LABA/ICS as initial therapy in patients with eosinophils ≥300 cells/µL

The Committee considered a request from NCL respiratory clinicians to follow a recommendation from the Global initiative for chronic Obstructive Lung Disease (GOLD) to 'consider' the use of triple therapy (ICS/LABA/LAMA) inhaler devices as initial therapy in patients with ≥2 moderate or ≥1 severe exacerbation (i.e. requiring hospitalisation) in the previous 12 months if they have blood eosinophils ≥300 cells/µL, a small proportion of which may be treatment naïve. This is in contrast with NICE guidance, which recommends '*consider*' LABA/ICS as initial maintenance therapy in COPD patients with asthmatic features or features suggesting steroid responsiveness (the definition of which includes '*raised eosinophils'*); triple therapy is '*offered*' after LABA/ICS if symptoms affect daily quality of life, or the patient suffers further exacerbations. The Committee was requested to consider whether the NCL COPD guideline could adopt the GOLD recommendation of initiation of triple therapy in COPD patients with eosinophils ≥300 cells/µ regardless of a prior trial of LABA/ICS.

GOLD guidance recommendations were based on pivotal studies previously considered by JFC for the formulary reviews of triple-therapy devices. This includes the FULFIL and KRONOS studies, which demonstrated significant improvements in pre-dose trough FEV_1 for triple therapy compared with LABA/ICS devices, amongst other outcomes. GOLD states that the results from these studies demonstrate triple therapies are significantly better than LABA/ICS. However, the recommendation is limited as the included populations in these studies were previously treated COPD patients only (i.e., there is no data on triple therapy vs LABA/ICS as the initial treatment option in treatment naïve patients).

The Committee considered meta-analyses conducted by NICE during the development of their 2019 guideline comparing LABA/ICS with triple therapy. In terms of prior medication received; triple therapy significantly reduced the risk of moderate to severe exacerbations in those who received any prior COPD medication (RR = 1.34 [95% CI 1.05 to 1.37]) and in those who previously used LABA/ICS (RR = 1.17 [95% CI 1.02 to 1.35]). In terms of previous exacerbations, triple therapy significantly reduced the risk of moderate to severe exacerbations in patients who had no previous exacerbations in the past 12 months (RR = 1.35 [95% CI 1.10 to 1.66]) and was associated with a non-significant risk reduction in patients who did have an exacerbation in the past 12 months (RR = 1.13 [95% CI 0.97 to 1.32]). There was no data for treatment naïve COPD patients.

In the NICE economic analysis, LAMA/LABA was found to be the most cost-effective inhaled maintenance therapy for COPD, although there was no clinical or economic evidence for patients with COPD and features of asthma. The NICE guideline committee considered it logical that any regimen recommended for COPD patients with features of asthma to include an ICS and adding an ICS into LAMA/LABA therapy was a logical next step. However, they took a conservative approach as there was uncertainty in the cost-effectiveness and lack of evidence in using triple therapy in patients with COPD and features of asthma; therefore, LABA/ICS was recommended first, and triple therapy was only considered in patients who remain uncontrolled on therapy.

NICE also reviewed eosinophil thresholds; triple therapy significantly reduced the risk of moderate to severe exacerbations compared with LABA/ICS in patients with "higher" eosinophil counts (RR = 1.16 [95% CI 1.06 to 1.26]) and in those with "lower" eosinophil counts (RR = 1.40 [95% CI 1.26 to 1.56]), though definitions varied between studies. NICE determined that it was unclear whether eosinophils should be used to initiate triple therapy or what the threshold should be, and decided it was important not to rely on eosinophil counts to make decisions on predicting response to therapy or set a threshold. The results from the meta-analysis by NICE suggested a role for LAMA in patients with COPD, regardless of their eosinophil blood count. The GOLD definition of eosinophil threshold was based on a review by Stockley et al (2019), which itself was based on post-hoc analyses of LABA/ICS vs LABA alone studies and did not appear to be conclusive in terms of a single defining threshold of eosinophils from which patients demonstrated steroid responsiveness.

In terms of safety, there is experience in the use of triple therapies for COPD. Triple therapies will possibly increase the risk of LAMA-related adverse events (e.g., headache, glaucoma, tachycardia etc).

A budget impact was estimated based on the NICE impact resource template. NICE predicted 2.11% of COPD patients with asthmatic features or features suggesting steroid responsiveness will use LABA/ICS; the use of triple therapies replacing ICS/LABA was expected to cost up to £18,390 per annum. A very small proportion of patients may be treatment naïve, though the exact number was difficult to predict.

The Committee heard from Dr Roy that NCL respiratory specialists support the use of dual bronchodilation in all COPD patients to aid with breathlessness (which is the predominant feature in COPD); clinicians will step-up to triple therapy (i.e., add in an ICS) after further investigations which includes (but are not limited to) eosinophil counts, or when the patient experiences further exacerbations on treatment. Patients with COPD may experience indirect benefits from having better COPD control at an earlier timepoint, such as reduction in co-morbidities. Dr Roy indicated that COPD is likely to be underdiagnosed in the general population, and there is belief that many patients may have been mis-labelled as having asthma rather than COPD, therefore the true population of patients who may benefit from triple therapy could be in the region of 33%. There is a view that evidence from the previously treated population can be extrapolated to the treatment naïve population.

In camera, the Committee noted the paucity of data to support initiation of triple therapy for maintenance treatment. In addition, the robust evidence and cost effectiveness reviews undertaken by NICE were acknowledged (compared with GOLD guidance which is a narrative summary without a rigorous evidence review equivalent to that undertaken by NICE). The Committee was therefore cautious about making a recommendation that contradicts NICE completely. However, the Committee also acknowledged NICE had less certainty of their recommendation to *consider* LABA/ICS as initial treatment than they were to *offer* triple therapy following exacerbations. The Committee also appreciated that triple therapy may be a logical treatment option in certain patients, and there was some evidence to demonstrate triple therapy was superior to LABA/ICS in previously treated patients. The Committee were not convinced of the proposed eosinophil threshold defined by GOLD as, again, there was paucity in data. Additionally, primary care clinicians who would also be using this pathway would not always have eosinophil counts available to them upon which to make prescribing decisions.

In summary, the Committee encouraged the development of a pathway using the NICE definition of asthmatic features or signs suggesting steroid responsiveness; using the NICE criteria for initiation of LABA/ICS; but allowing clinician discretion to opt for triple therapy in place of LABA/ICS from the outset, without an initial trial with LABA/ICS in patients who are considered likely to benefit from two bronchodilators in addition to ICS because of symptom severity, comorbidity or exacerbation risk. JFC Support will continue to work with authors in preparing a final guideline to bring back to a future meeting.

10. Request for NCL JFC to review primary care pathways

The Committee reviewed a request to undertake the role of approving the medicine and prescribing elements of NCL ICB primary care pathways. Prior to the formation of NCL ICB in July 2022, the CCG Medicines Management Committee (MMC) was the responsible committee for these approvals; post ICB formation this responsibility lies with the NCL ICB Integrated Medicines Optimisation Committee (IMOC), with the MMC

disbanded in July 2022. IMOC is intended to be a high-level strategic committee overseeing medicines governance in NCL and therefore it has been requested if the role of approving the medicines and prescribing elements of the pathways can be undertaken by the JFC as part of an overall governance process, with final ratification via IMOC.

It was highlighted that there are currently 18 pathways pending sign-off for which NCL JFC support has been requested. The Committee acknowledged that until the process is undertaken, there remain uncertainties regarding the requirement of a sub-group, additional resource impacts on both the Committee and JFC support team, and the level of input needed from relevant clinicians to support this function.

In summary, the Committee agreed that this function can be taken on by NCL JFC on a short-term basis (period to be defined) to support in the sign-off of the pending pathways. The short-term period of this agreed function will fulfil the need of scrutinising the process for signing off the pathways, understand better the optimal way of doing this work and what the resource impact is likely to be. At the end of this agreed short-term function (timeline to be defined) the Committee will be in a better position to assess whether the function is feasible to maintain in the long-term and what an ideal process should be.

11. Principles for commissioning high-cost drug pathways for ICB commissioned drugs

The guiding principles for commissioning of high-cost drug pathways for ICB commissioned indications was presented to the Committee for approval. The principles will support consistent, timely and equitable suite of high-cost drug pathways to be agreed, updated, and commissioned. The Committee were in support of adopting the guiding principles and JFC will form its basis for review and final approval of high-cost drug pathways for ICB commissioned indications on these principles. It was agreed the guiding principles will be taken to IMOC for final approval.

12. NICE response to NCL JFC letter regarding new evidence for DOACs

The Committee discussed a response to a letter sent on behalf of the NCL JFC to NICE and NHSE regarding current NICE guidelines for diagnosis and management of atrial fibrillation (AF). The letter highlighted that the initial recommendation for NICE guideline NG196 'Atrial fibrillation: management - Draft for consultation', September 2020, (section 1.6.3 and 1.6.4) to offer '*anticoagulation with apixaban or dabigatran to people with atrial fibrillation*' based on the findings of a network meta-analysis. This network meta-analysis concluded: '*apixaban 5mg twice daily was ranked as being the most cost-effective intervention for several outcomes evaluated including stroke or systemic embolism, myocardial infarction, and all-cause mortality. It was also ranked as the safest with the lowest incidence of major and gastrointestinal bleeding'*.

However, after stakeholder consultation, the NICE guideline committee amended this recommendation to '*apixaban, dabigatran, edoxaban and rivaroxaban are all recommended as options for the treatment of atrial fibrillation...*'. The reason for this change in position was given as follows (p 56 of evidence review supplement G1): '*Initially the committee were satisfied that the coherence of the model was adequate; that is, there were no differences in populations between direct treatment comparisons that could lead to invalid treatment estimates. However, after discussions, and after listening to the review of stakeholders, it was felt that the coherence of the model could not be assumed*'. Following this, a national DOAC procurement exercise identified edoxaban as having the lowest acquisition cost, and NHSE published commissioning recommendations placing edoxaban as the first line DOAC for non-valvular AF where clinically appropriate. In addition, an Investment and Impact Fund indicator giving preference to edoxaban was released.

In December 2022, a letter was submitted to NICE and NHSE on behalf of the Committee. NICE and NHSE were informed that new evidence from analysis of electronic health records was available that supports the findings of the original network meta-analyses about the potential position that apixaban offers an optimal balance between efficacy and safety. NICE and NHSE were asked to reconsider whether they still felt that all DOACs had equivalent safety and efficacy based on the findings of the original network meta-analysis and the electronic health record dataset analysis.

NICE have since responded stating that the new evidence does not sufficiently change their position that all DOACs have equivalent safety and efficacy and does not force reconsideration of the evidence that underpins the network meta-analysis which contributed to the NICE AF guideline. The position of NHSE that the DOAC with the lowest acquisition cost should be preferred therefore stands, however it was noted that NHSE have not yet responded to the letter sent from JFC.

The Committee agreed that comments from NHSE should be sought before a final decision is made. In parallel, the Committee agreed that opinions from authors of both publications, the original network meta-analysis and the electronic health records dataset analysis, should be sought on the critique of the methodology raised by NICE and then respond to NICE on their critique. It was highlighted that the NCL JFC DOAC prescribing position

for the management of non-valvular AF remains unchanged, i.e. edoxaban is the preferred DOAC, where clinically appropriate.

13. Semaglutide red list review

The publication of the NICE TA [TA875] for the use of semaglutide (Wegovy®) in weight management has resulted in a high volume of requests for NHS prescribing in primary care. To support the high volumes of requests in primary care, a 'Red List review' was undertaken and brought to the NCL JFC for urgent consideration.

Wegovy® is a pre-filled pen injection formulation that is administered weekly and suitable for self-administration. Initially, a 16-week dose-escalation period is recommended to reduce the likelihood of gastrointestinal side effects. No major safety concerns were identified as part of the 'Red List review'. The NICE TA recommends that eligible patients are managed within a specialist weight management service providing multidisciplinary management of overweight patients or obesity (including but not limited to tier 3 and 4 services). During the NICE committee discussion, it was acknowledged that access to specialist weight management services is not equitable across England and Wales and the service provision is under review.

The Committee agreed to add Wegovy® to the NCL Red List, noting that the Red List status could be revisited in the future as NCL weight management services are reviewed. Therefore, Wegovy® should only be prescribed in secondary care within specialist weight management services. GPs should not be asked to continue prescribing in primary care from NHS or private specialists.

14. Next meeting

Thursday 20th April 2023

15. Any other business

Nil