North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 19th August 2021

Present:	Dr M Kelsey	WH, DTC Chair	(Chair)
	Dr K Tasopoulos	NMUH, DTC Chair	
	Ms G Smith	RFL, DTC Chair	
	Mr A Dutt	NCL CCG, Head of Medicines Management (Islington)	
	Dr A Sell	RNOH, DTC Chair	
	Mr S Semple	MEH, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Dr R Urquhart	UCLH, Divisional Clinical Director	
	Ms R Clark	NCL CCG, Head of Medicines Management (Camden)	
In attendance:	Mr A Barron	UCLH, Principal Pharmacist	
	Mr G Grewal	North London Partners, JFC Support Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Ms S Amin	UCLH, Formulary Pharmacist	
	Ms S Maru	UCLH, Formulary Pharmacist	
	Ms S Y Tan	NEL CSU, Contracting and Commissioning Pharmacist	
	Ms A Fakoya	NEL CSU, Commissioner Support Pharmacist	
	Ms A Sehmi	NMUH, Formulary Pharmacist	
	Ms H Thoong	GOSH, Formulary Pharmacist	
	Mr D Sergian	MEH, Formulary Pharmacist	
	Dr A Hosin	UCLH, Clinical Pharmacology Registrar	
	Ms S Lever	NCL CCG, Deputy Head of Medicines Management (Barnet)	
	Mr G Kitson	WH, Deputy Chief Pharmacist	
	Ms C Gates	UCLH, Specialist Pharmacist	
	Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	
	Ms P Panesar	UCLH, Lead Microbiology Pharmacist	
	Ms M Lanzman	RFL, Lead Microbiology Pharmacist	
	Dr I Balakrishnan	RFL, Consultant Microbiologist	
	Dr M Forster	UCLH, Consultant Medical Oncologist	
	Dr M Linch	UCLH, Consultant Medical Oncologist	
Apologies:	Prof R Sofat	NCL JFC Chair	
	Ms W Spicer	RFL, Chief Pharmacist	
	Mr T Dean	Patient Partner	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Ms L Reeves	C&I, Chief Pharmacist	
	Mr A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Dr A Scourfield	UCLH, Interim DTC Vice Chair	
	Ms M Singh	NCL CCG, Head of Medicines Management (Barnet)	
	Mr P Gouldstone	NCL CCG, Head of Medicines Management (Enfield)	
	Ms S Stern	NMUH, Chief Pharmacist	
	Dr D Burrage	WH, Consultant in Emergency Medicine	

2. Meeting observers

Ms Weaver (NHSE, Specialised Commissioning Pharmacist) was welcomed as an observer of the meeting.

3. Minutes of the last meeting

The minutes and abbreviated minutes of 15 July 2021 meeting were accepted as accurate reflections of the meeting.

4. Matters arising

4.1 Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban

In July 2021, the Committee provisionally recommended that andexanet alfa (NICE TA697) should be restricted to Consultant Haematologist recommendation only, acknowledging that it would be used second-line to prothrombin complex concentrate (PCC). JFC Support consulted on this provisional recommendation and the majority of Consultant Gastroenterologists who responded agreed. The Committee therefore agreed to add andexanet alfa for the reversal of anticoagulation from apixaban or rivaroxaban in adults with life-threatening or uncontrolled gastrointestinal bleeds, restricted to the recommendation of a Consultant Haematologist only.

Each Trust should make a local decision for local stock and supply arrangements.

Decision: Approved; Consultant Haematology recommendation only
Prescribing: Secondary care
Tariff status: Excluded from tariff
Funding: CCG
Primary and secondary care Fact sheet or shared care required: No

4.2 Neutralising monoclonal antibodies for the treatment of COVID-19

The Committee was updated on the recent developments of neutralising monoclonal antibodies for the treatment of COVID-19. The first licensed neutralising monoclonal antibody is expected imminently for use in hospitalised patients supported by a NHSE/I Commissioning Policy. Once available, the drug will follow a JFC formulary review process with a Chair's action decision for implementation across all Acute Trusts. The commissioning policy for use in community (non-hospitalised) patients will follow thereafter, and will likely coincide with the availability of further neutralising monoclonal antibodies as they become licensed.

5. JFC Outstanding Items & Work Plan

These items were included for information only. Any questions should be directed to Mr Grewal.

6. Members declarations of conflicts of interest

Nil

7. Local DTC recommendations / minutes

7.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
NMUH	June 2021	Intranasal Dexmedetomidine	Sedation for paediatric imaging as monotherapy for children >15kg and as top-up sedation where chloral hydrate has failed in children <15kg	Decision: NMUH only Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
RFL	June 2021	Indocyanine green	Intraoperative diagnostic	Decision: RFL only Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

RFL/ JFC	June 2021	Cefazolin	Gram positive infections (in any patient group) where other antibiotic options are not suitable (e.g., resistance/ allergy/ interaction). MSSA bacteraemia (in any patient group) – 2nd line treatment if intolerance to flucloxacillin and no known allergy to other beta-lactams.	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

8. New Medicine Reviews

8.1 Free of Charge scheme: Lutetium-177-PSMA-617 for PSMA-positive metastatic castrate resistant prostate cancer (Applicant: Dr M Linch, UCLH)

The Committee considered a pre-NICE free-of-charge (FOC) scheme for lutetium-177-PSMA-617, a PSMA targeting ligand conjugated to a beta-emitting radioisotope, for PSMA-positive metastatic castrate resistant prostate cancer (mCRPC) in patients who have progressed or failed on LHRH-antagonists, abiraterone or enzalutamide and docetaxel; it could be administered before cabazitaxel if the patient refuses or physician considers the patient unsuitable for a second taxane therapy.

The VISION study was an international, Phase III, open-label study to compare the efficacy and safety of lutetium-177-PSMA-617 given with standard of care (SoC) versus SoC alone for patients who have mCRPC with one PSMA-positive lesion and at least one androgen receptor inhibitor and at least one taxane regimen (n=831). Patients were randomised 2:1 to receive 7.4GBq lutetium-177-PSMA-617 with SoC or SoC alone (SoC could include hormonal treatments, bisphosphonates, radiation therapy, denosumab or glucocorticoids). The study used two alternate primary outcomes. In the first alternate outcome, median imaging-based progression-free survival (analysed in a population of patients from March 2019 to the end of the study; n=581), was significantly longer with lutetium-177-PSMA-617 compared to SoC alone (8.7 months vs. 3.4 months; HR = 0.40 [99.2% CI 0.29 to 0.57]). In the second alternate outcome, median overall survival (analysed in the ITT population; n=831) was significantly longer with lutetium-177-PSMA-617 compared with SoC alone (HR = 0.62 [95% CI 0.52 to 0.74]). Key limitations of the study were the open-label design, progression-free survival measured in a subgroup, and that the study was pharma-supported.

In terms of safety, lutetium-177-PSMA-617 had a higher risk of grade 3 adverse events compared to SoC alone. The most frequent adverse events in the lutetium-177-PSMA-617 arm were fatigue, dry mouth and diarrhoea. There were also five grade 5 adverse events in the lutetium-177-PSMA-617 arm (due to pancytopaenia, bone marrow failure, subdural haematoma and intracranial haemorrhage) and none in the SoC alone arm. Additional risks of note were the unlicensed radioactive status of the treatment, the requirement for appropriate storage and handling, and requirement for additional counselling and appropriate pre-treatment.

In terms of budget impact, lutetium-177-PSMA-617 is free of charge, with each patient requiring an individual contract with the company.

The Committee heard from Dr Linch that he has given lutetium-177-PSMA-617 in the private sector and within clinical trials to good effect, and was well tolerated compared with other treatments. In terms of additional healthcare resource utilisation, the use of lutetium-177-PSMA-617 would require the capacity to administer the therapy and PSMA PET scans every 12 weeks. The current positioning of lutetium-177-PSMA-617 is as per the VISION study (including any relative contraindications), and is not being positioned earlier in the treatment pathway (although this is the subject of further clinical trials that are underway).

In camera, the Committee discussed the efficacy and safety outcomes of the study; the Committee were satisfied with the study demonstrating an improvement in median overall survival, though were concerned by the grade 5 adverse events experienced and potential for toxicity. As the applicants have indicated the therapy would be used as per the VISION study, it was felt appropriate to restrict the use of lutetium-177-PSMA-617 to patients with an ECOG status of 0 to 2. Non-drug resource impact was considered acceptable, given the improvement in overall survival. Equity of access for patients with mCRPC in other NCL Acute Trusts was discussed, and the Committee was satisfied that the uro-oncology network in NCL was strong

and patients eligible for treatment at other Acute Trusts would be appropriately referred for consideration of treatment at RFL or UCLH.

In summary, the Committee agreed to add free-of-charge lutetium-177-PSMA-617 to the NCL Joint Formulary, for PSMA-positive metastatic castrate resistant prostate cancer (mCRPC) in patients with an ECOG status of 0 to 2, who have progressed or failed on LHRH-antagonists, abiraterone or enzalutamide and docetaxel.

Decision: Approved. NHSE/I should be notified in line with NCL Free of Charge scheme guidance.
Prescribing: Secondary care
Tariff status: N/A – Free of charge
Funding: N/A – Free of charge
Primary and secondary care Fact sheet or shared care required: No

8.2 Early Access to Medicines Scheme: Osimertinib as adjuvant treatment for non-small cell lung cancer with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations (Applicant: Dr M Forster, UCLH)

The Committee considered an Early Access to Medicines Scheme (EAMS) for osimertinib, a tyrosine kinase inhibitor, for adjuvant treatment of stage IB to IIIA non-small cell lung cancer (NSCLC) with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations following complete tumour resection.

ADAURA was a 3-year, Phase III, placebo-controlled, double-blind study to assess the safety and efficacy of osimertinib for patients with completely resected EGFR mutation-positive NSCLC (n=682). Patients were randomised to receive osimertinib 80mg once daily or placebo, both with or without adjuvant chemotherapy. The primary endpoint, the percentage of patients alive and disease-free in the stage II to IIIA NSCLC cohort (n=470), was significantly better with osimertinib compared to placebo (90% vs. 44%; HR: 0.17 [99.06% CI: 0.11 to 0.26])). The secondary endpoint, the percentage of patients alive and disease-free in the stage IB to IIIA NSCLC cohort (n=682), was significantly better with osimertinib compared to placebo (89% vs. 52%; HR: 0.20 [99.12% CI: 0.14 to 0.30])). Key limitations of the study were the early termination of the blinded phase due to the large treatment effect, which leaves the data immature and currently lacks overall survival data.

In terms of safety, osimertinib had a higher risk of adverse events (including diarrhoea, paronychia, dry skin, pruritus and cough) compared to placebo. Other risks to consider include incidence of interstitial lung disease, QT-level prolongation, reduced ejection fraction and mild to moderate hepatic impairment.

In terms of budget impact, osimertinib is available free of charge via an NHSE Early Access to Medicines Scheme, which is available to all Acute Trusts in NCL.

The Committee heard from Dr Forster that osimertinib was a meaningful development in the adjuvant setting; whilst adjuvant chemotherapy is available, many people decline treatment as benefit is marginal. Osimertinib is already available for use in advanced NSCLC, therefore there is experience in its use. The use of osimertinib would mirror that of the trial (in which use of chemotherapy prior to osimertinib was permitted, and treatment would be for a maximum of 3 years).

In camera, the Committee acknowledged the large treatment effect when compared with placebo, whilst also noting that the primary analysis was performed two years early and data on overall survival is absent. Whilst acknowledging osimertinib is being considered for a NICE TA, the Committee agreed it would be suitable to consider the NHSE EAMS in advance of a Final Appraisal Document from NICE.

In summary, the Committee agreed to add osimertinib to the NCL Joint Formulary for adjuvant treatment in patients with NSCLC with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.

Decision: Approved
Prescribing: Secondary care
Tariff status: N/A – free of charge
Funding: N/A – free of charge
Primary and secondary care Fact sheet or shared care required: No

9. Early Access to Medicines Scheme: Tepotinib monotherapy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) harbouring mesenchymal-epithelial transition (MET) exon 14 skipping alterations

The Committee reviewed an MHRA Early Access to Medicines Scheme (EAMS) for tepotinib, an oral selective MET kinase inhibitor, for the treatment of adult patients with advanced non-small-cell-lung-cancer (NSCLC) harbouring mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping alterations.

In April 2021, the Committee ratified a UCLH decision to approve tepotinib via a Free of Charge Scheme for:

- First-line treatment of advanced/metastatic NSCLC with METex14 skipping mutations for patients with brain metastases who are unsuitable for chemotherapy
- Second-line treatment of advanced/metastatic NSCLC with METex14 skipping mutations

The MHRA EAMS launched in July 2021 has an updated broader indication for the use of tepotinib as monotherapy treatment for adult advanced NSCLC patients with METex14 skipping mutation.

The UCLH and MHRA EAMS reviews were both based on the VISION study, an ongoing, open-label, single-arm Phase 2 study, with a primary completion date in December 2021, to assess the safety and efficacy of tepotinib for adults with advanced or metastatic NSCLC with METex14 skipping mutations. The MHRA review benefits from a larger (n=149) and more mature dataset than was available at the time the UCLH review (n=99). Results however were very similar. The primary outcome, objective response (defined as all complete and partial responses) was 46% (95% CI: 36.0 to 57.0) when reviewed by the UMC and 45.2% (95% CI: 37.0 to 53.6) when reviewed by the MHRA. Secondary outcomes were median progression-free survival (8.5 months when reviewed by UMC and 8.9 months when reviewed by the MHRA EAMS) and median overall survival (17.1 months when reviewed by the UMC and 17.6 months when reviewed by the MHRA EAMS).

In terms of safety, data reviewed by UCLH was from the FDA USPI which reported common grade 3- 4 toxicities as oedema, pleural effusion and pneumonia. There were 3 fatalities reported from the VISION study (n=255) due to pneumonitis secondary to interstitial lung disease, hepatic failure and dyspnoea from fluid overload. Additional reported adverse events from the ongoing VISION study as described in the EAMS include interstitial lung disease, hepatobiliary disorders and increases in creatinine, amylase and lipase.

The Committee agreed that the additional data reviewed by the MHRA EAMS from the VISION study further supported the data already reviewed by UCLH. In summary, the Committee approved the use of tepotinib in METex14 skipping NSCLC under the MHRA EAMS for the updated indication for the treatment of adult patients with advanced non-small-cell-lung-cancer (NSCLC) harbouring mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping alterations.

Decision: Approved
Prescribing: Secondary care
Tariff status: N/A – free of charge
Funding: N/A – free of charge
Primary and secondary care Fact sheet or shared care required: No

10. Formulary position of vancomycin and fidaxomicin for *C. difficile* infection (NICE Guideline 199 update

The Committee were informed that NICE NG199 was supported by NCL Microbiology Leads and CCG MMTs. The guidance recommends that metronidazole is removed as a first-line treatment for *C. difficile* and replaced with vancomycin. Fidaxomicin is also recommended for three indications:

- After failure of fist-line vancomycin for first episode
- Relapse (i.e. within 12 weeks of resolution of first episode)
- As an alternative to vancomycin for recurrent (i.e. more than 12 weeks after resolution) episodes, noting that vancomycin is preferred for less severe, or first recurrent episodes, or if there had been a long time between episodes

The budget impact associated with implementing this guidance was £155,000 across NCL (split between NCL Providers and CCG), but the budget pressure being driven by increased use of fidaxomicin. It was noted that the patent expiry date for fidaxomicin was 2026. There were no major implementation issues identified

for NCL Providers. Several implementation hurdles for primary care were identified and would be resolved off-line of this Committee.

In October 2012, the Committee recommended that fidaxomicin was restricted for 2nd or 3rd recurrence. The Committee agreed this recommendation should be replaced by the NICE recommendation; specifically that fidaxomicin should be used:

- After failure of fist-line vancomycin for first episode *C. difficile*
- Relapse (within 12 weeks of resolution of first episode)
- As an alternative to vancomycin for recurrent (more than 12 weeks after resolution) episodes, noting that vancomycin is preferred for less severe, or first recurrent episodes, or if there had been a long time between episodes

Drug: Fidaxomicin for the above three cohorts
Decision: Approved
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Trust and CCG
Primary and secondary care Fact sheet or shared care required: No

11. NCL MON Annual Report 2019-2021

The Committee approved the NCL MON annual report for 2019-2021.

12. Vagirux® for vaginal atrophy due to oestrogen deficiency in postmenopausal women

The Committee were informed of a new application for Vagirux® (estradiol hemihydrate vaginal tablets) for the treatment of vaginal atrophy due to oestogen deficiency in postmenopausal women. Vagirux® is a newly licensed product that was determined to be therapeutically equivalent to a Vagifem® (a medicine which is on the NCL Joint Formulary). Vagirux® has a lower acquisition cost; the only identifiable difference was the use of a multiuse applicator (whereas Vagifem® uses a single disposable applicator for each dose). The Committee considered whether Vagirux® should be adopted on to formulary.

The Committee recognised that using Vagirux® would reduce waste and have a positive environmental impact, whilst also acknowledging that some patients may not want to wash the reusable applicator. The Committee concluded that Vagirux® should be added to the NCL Joint Formulary and, in line with principles of the Long Term Plan, should be promoted as the preferred device. Vagifem® would remain on formulary for women who prefer a disposable applicator.

Drug: Vagirux® (estradiol hemihydrate vaginal tablets) for vaginal atrophy due to oestogen deficiency in postmenopausal women
Decision: Preferred treatment
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Trust and CCG
Primary and secondary care Fact sheet or shared care required: No

Drug: Vagifem® (estradiol hemihydrate vaginal tablets) for vaginal atrophy due to oestogen deficiency in postmenopausal women
Decision: Alternative treatment for women who prefer a disposable applicator (otherwise use Vagirux®).
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Trust and CCG
Primary and secondary care Fact sheet or shared care required: No

13. Any Other Business

13.1 Communication of JFC decisions

Following JFC stakeholder feedback, JFC Support received a request for a prompt turnaround of JFC decisions for certain medication requests in order to implement decisions in a timelier manner. The Committee agreed that an interim decision can be considered on a case-by-case basis and communicated

as a very brief summary whilst the minutes are drafted and finalised to facilitate successful and swift implementation in Trusts.

13.2 Shortage of tocilizumab

The Committee were informed of a shortage of tocilizumab, an IL-6 inhibitor, in the supply chain. Tocilizumab is licensed for rheumatoid arthritis, juvenile idiopathic arthritis, CAR-T cell induced cytokine storm and giant cell arteritis. It was recently made available for the treatment of hospitalised COVID-19 patients, which has resulted in a global shortage.

Another IL-6 inhibitor, sarilumab, is also recommended for COVID-19 and there are sufficient stocks to meet the current demand for COVID-19 patients. The supporting evidence-base however is less robust (5 trials; 489 patients) than for tocilizumab (14 trials; 3221 patients).

NICE recommend the same eligibility criteria for tocilizumab and sarilumab, however tocilizumab is preferred owing to the superior evidence-base. NHSE/I currently have different eligibility criteria for each drug and have a preference order, however this is under review and an updated Commissioning Policy is expected imminently.

The Committee agreed that at the current time, and given current supplies of tocilizumab, sarilumab should be considered for COVID-19 only if tocilizumab cannot be used or is unavailable.

14. Next meeting

Thursday 16th September 2021