North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 2nd July 2020

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Dr P Taylor	NCL JFC Vice Chair	
	Dr M Kelsey	WH, DTC Chair	
	Ms G Smith	RFL, DTC Chair	
	Mr P Gouldstone	NCL CCG, Head of Medicines Management (Enfield)	
	Mr A Dutt	NCL CCG, Head of Medicines Management (Islington)	
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Ms R Clark	NCL CCG, Head of Medicines Management (Camden)	
	Ms P Taylor	NCL CCG, Head of Medicines Management (Haringey)	
	Mr S Semple	MEH, Chief Pharmacist	
	Mr T Dean	Patient Partner	
	Ms K Delargy	BEH, Deputy Chief Pharmacist*	
	Mr S Richardson	WH, Chief Pharmacist	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist*	
	Mr A Stein	NMUH, Deputy Chief Pharmacist	
	Ms S Lever	NCL CCG, Pharmaceutical advisor (Barnet)	
In attendance:	Dr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Barron	NCL MEP, Project Lead	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Ms S Amin	UCLH, Formulary Pharmacist	
	Ms SY Tan	NEL, Contracting and Commissioning Pharmacist	
	Ms H Thoong	GOSH, Formulary Pharmacist	
	Mr D Abdulla	NMUH, Critical Care and Formulary Pharmacist	
	Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr F Master	RFL, Formulary Pharmacist	
	Ms A Fakoya	NEL, Senior Prescribing Advisor High Cost Drugs	
	Mr J Flor	WH, Formulary Pharmacist	
	Ms M Powell	NCL CCG, Prescribing Advisor (Haringey)	
	Ms P McCormick	WH, Lead Pharmacist Integrated Medicine	
	Dr J Fullerton	UCLH, Clinical Pharmacology SpR	
	Dr D Thompson	UCLH, Clinical Pharmacology SpR	
	Prof H Payne	UCLH, Consultant Clinical Oncologist	
	Prof J Bridgewater	UCLH, Professor of Medical Oncology	
Apologies:	Ms L Reeves	C&I, Chief Pharmacist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Dr A Bansal	NCL CCG, GP Clinical Lead Medicines Management (Barnet)	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Dr A Sell	RNOH, DTC Chair	
	Mr A Tufail	MEH, DTC Chair	

**Deputising for Committee member*

2. Meeting observers

Dr Sofat welcomed Ms Weaver (NHSE, Specialised Commissioning Pharmacist) and Ms P Powell (NCL CCG, Prescribing Advisor) as observers of the meeting.

3. Minutes and abbreviated of meeting on 21st May, 2nd June and 18th June

The minutes were accepted as accurate records of the meetings.

4. Matters arising

4.1 Siponimod for treating secondary progressive multiple sclerosis

Subsequent to the last meeting, NICE issued a negative Appraisal Consultation Document (ACD) for siponimod. The Committee agreed to continue to defer their decision, rather than rejecting the scheme outright, giving time for the company FOC scheme to improve the exit strategy. A 'post meeting note' was added to the minutes.

4.2 Infliximab subcutaneous

Subsequent to the last meeting, the UK Government announced that shielding is expected to be paused from 1st August 2020. Corresponding, the Committee agreed approval for the subcutaneous formulation (as an alternative to the intravenous formulation) would also pause on this date. Additionally, the CMHP recommended a license extension to include IBD for which a new JFC application would be required and considered only in the event that shielding is unpaused or a business case with Commissioner support is presented. A 'post meeting note' was added to the minutes.

5. JFC Outstanding Items & Work Plan

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

6. Members declarations of conflicts of interest

Nil

7. Local DTC recommendations / minutes

7.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
GOSH	March 2004	Triptorelin	Precocious puberty	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: Referred to SCG
RFL, UCLH, RNOH	Pre-dates DTC	Prilocaine 1%	Local anaesthesia for short-acting nerve block	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
MEH	July 2012	Moxifloxacin eye drops	Corneal ulcer associated with bacterial keratitis	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

WH, RFL, UCLH	Pre-dates DTC	Oral Voriconazole	Fungal infection	Decision: Added to the NCL Joint formulary Prescribing: Secondary care (micro approval) Tariff status: Excluded from tariff Funding: NHSE Fact sheet or shared care required: No
UCLH	March 2020	Gadoxetate (Primovist®)	Liver-specific contrast agent	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
UCLH	March 2020	Propantheline Bromide	Post-operative hypersalivation/sialorrhea in patients undergoing invasive head and neck surgery or injury	Decision: UCLH only Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
UCLH	May 2020	Futibatinib	Free of charge scheme: Second-line treatment of metastatic cholangiocarcinoma with FGFR2 gene fusions following progression with CisGem	Decision: UCLH only Prescribing: Secondary care Tariff status: n/a Funding: FoC Fact sheet or shared care required: No Additional information: Approved as an interim measure whilst relevant clinical trials are suspended due to COVID-19.
UCLH	May 2020	Niraparib	Pre-NICE Free of Charge: Maintenance therapy of advanced ovarian cancer after response to first line platinum-based chemotherapy in patients without a BRCA mutation	Decision: UCLH only Prescribing: Secondary care Tariff status: N/A Funding: FoC Fact sheet or shared care required: No
RFL	Feb 2020	Milrinone	Short term treatment of acute heart failure in patients with acute decompensated right sided heart failure or severe congestive heart failure unresponsive to/unable to tolerate conventional therapy	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
RFL	March 2020	Avelumab and Axitinib	EAMS: Metastatic renal cell carcinoma	Decision: RFL only Prescribing: Secondary care Tariff status: N/A Funding: FoC via EAMS Fact sheet or shared care required: No

RFL	March 2020	Encorafenib and cetuximab	Pre-NICE Free of charge scheme: Treatment of metastatic BRAF V600E mutated colorectal cancer	Decision: Added to the NCL Joint formulary Prescribing: Secondary care Tariff status: N/A Funding: FoC Fact sheet or shared care required: No

8. New Medicine Reviews

8.1 Pre-NICE FoC scheme: Darolutamide for non-metastatic prostate cancer (Applicant: Prof H Payne)

The Committee considered a pre-NICE free-of-charge (FoC) scheme for darolutamide, a second-generation androgen receptor inhibitor, for non-metastatic castration resistant prostate cancer (nmCRPC).

The evidence to support this application was provided via the ARAMIS trial, a phase III, double-blind, placebo-controlled study to assess the safety and efficacy of darolutamide in adults with nmCRPC, with a prostate specific antigen (PSA) doubling time of 10 months or less, PSA ≥ 2 ng/mL at screening and castrate level of serum testosterone < 1.7 nmol/L. The primary endpoint, 'metastasis free survival' (MFS) was significantly longer with darolutamide than with placebo (median MFS: 40.4 months vs. 18.4 months; HR: 0.41 [95% CI: 0.34 to 0.50]). A statistically significant improvement in 'overall survival' (OS) was also observed (HR: 0.69 [95% CI 0.53-0.88]). QoL was not adversely affected by treatment with darolutamide, as measured by the Functional Assessment of Cancer Therapy–Prostate (FACT-P) score and the European Organisation for Research and Treatment of Cancer quality of life questionnaire (EORTC-QLQPR25) urinary symptoms subscale.

With regards to safety, more patients experienced Grade ≥3 adverse events with darolutamide than placebo (24.7% vs. 19.5%). Serious adverse reactions occurring in ≥1% of patients who received darolutamide were urinary retention, pneumonia, and haematuria.

In May 2018, NCL JFC approved a similar FoC application for apalutamide, another second-generation androgen receptor inhibitor. NICE however did not recommend enzalutamide [TA580] due to lack of a statistically significant improvement in OS at time of review and the high cost of the intervention. A comparison of the reported MFS data for each of the second-generation androgen receptor inhibitors; apalutamide (SPARTAN), enzalutamide (PROSPER) and darolutamide (ARAMIS), showed similarity. Whilst early reporting of OS showed a non-significant improvement with apalutamide and enzalutamide, survival advantages for both have now been demonstrated (HR: 0.75 [95% CI: 0.59-0.96] and HR: 0.73 [95% CI: 0.61 to 0.89] respectively).

The Committee heard from Prof Payne that use of darolutamide in nmCRPC precluded the use of enzalutamide in the metastatic setting (TA377 & TA316) however other treatment options recommended via a NICE TA remain available. For the indication under consideration, there are no alternative treatment options and multiple trials have demonstrated that using second-generation androgen receptor inhibitors earlier in the treatment pathway improves overall survival. Apalutamide and enzalutamide are under review by NICE for first-line treatment of hormone sensitive metastatic prostate cancer, therefore they are unlikely to compete with darolutamide for the proposed indication.

Darolutamide appears to have a lower risk of neurological toxicity than enzalutamide and apalutamide, however a direct comparison is not available. The Committee noted that patients with high cardiovascular risk (uncontrolled hypertension, heart failure NYHA III or IV, or CV event within last 6m) were excluded from the study. Prof Payne informed the Committee that hypertension is the main adverse event reported in clinical trials and blood pressure is monitored throughout treatment. Long-term experience of the use of a second-generation androgen receptor inhibitor in the general population has been provided with enzalutamide.

In camera, the Committee agreed there were no routinely commissioned options for nmCRPC and that darolutamide was likely to confer a survival advantage when used in this setting, without any significant impairment in QoL. The FoC scheme has favourable terms in the event of a 'not recommended' decision by NICE. In terms of patient numbers, approximately 10-15 patients across NCL would be eligible if the

application is approved in advance of the NICE TA (expected November 2020). It was noted that treatment would be associated with an increase in outpatient activity, specifically for treatment initiation and monitoring, however the benefits of treatment would outweigh any such costs.

In summary, the Committee agreed to add darolutamide to the NCL Joint Formulary for adults with nmCRPC, with a prostate specific antigen (PSA) doubling time of 10 months or less, PSA ≥ 2 ng/mL and castrate level of serum testosterone < 1.7 nmol/L.

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

8.2 EAMS: Nivolumab for unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (Applicant: Prof J Bridgewater)

The Committee considered an 'early access to medicines scheme' (EAMS) for nivolumab as second-line treatment for unresectable advanced, recurrent or metastatic oesophageal cancer after prior chemotherapy. A NICE appraisal is underway with an expected publication date in January 2021.

The evidence to support this application was provided via the ATTRACTION-3 trial, a randomised, open-label, phase 3 study of nivolumab versus investigator's choice of chemotherapy (paclitaxel or docetaxel) in unresectable advanced or recurrent oesophageal squamous cell carcinoma refractory or intolerant to one previous fluoropyrimidine-based and platinum-based chemotherapy. The primary outcome, overall survival (OS), was significantly longer with nivolumab than with chemotherapy (median OS: 10.9 months vs 8.4 months; HR: 0.77 [95% CI: 0.62 to 0.96]). QoL, as assessed with EQ-5D, showed an on-treatment improvement for patients given nivolumab versus chemotherapy.

With regards to safety, fewer patients experience Grade ≥3 treatment-related adverse events (TRAE) with nivolumab than chemotherapy (10% vs. 19%). The most frequent Grade ≥3 TRAE was anaemia (2%) in the nivolumab group compared with 9% in the chemotherapy group. Five deaths were deemed treatment-related: 2 in the nivolumab group (one each of interstitial lung disease and pneumonitis) and 3 in the chemotherapy group (one each of pneumonia, spinal cord abscess, and interstitial lung disease).

The Committee heard from Prof Bridgewater that adenocarcinoma and squamous oesophageal cancer had different treatment pathways and that this application was for squamous cell carcinoma only.

In camera, the Committee agreed that patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma had a high unmet need, with a median overall survival of less than 12 months. Nivolumab was likely to confer a survival advantage when used in this setting, whilst also improving QoL compared to chemotherapy.

In summary, the Committee approved nivolumab EAMS for unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma.

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

9. Review of licensed omeprazole suspension (Rosemont Pharmaceuticals Limited)

The Committee reviewed licensed omeprazole suspension as an alternative to off-label and unlicensed PPI use. Current practice in NCL is to use lansoprazole capsules or orodispersible tablets in an off-label capacity where clinically indicated or unlicensed PPI suspensions where solid dosage forms are impractical.

The EPAR for omeprazole suspension highlights that this newly licensed product has demonstrated equivalent bioavailability, safety and efficacy to omeprazole capsules. It was noted that use of the licensed omeprazole suspension may be slightly more convenient for patients (or their parents / carers)

than unlicensed or off-label alternatives although it requires refrigeration and has a short expiry once reconstituted.

In line with SMC and AWMSG methodology, NCL JFC assessed the cost-effectiveness of licensed omeprazole suspension compared to off-label and unlicensed PPI use. This analysis identified a substantial increase in cost without any meaningful health benefit therefore the Committee agreed that licensed omeprazole suspension did not present an efficient use of NHS resources.

In summary, the Committee did not approve licensed omeprazole suspension (Rosemont Pharmaceuticals Limited) for its licensed indications. Trusts were asked to review their PPI guidance, particularly for reflux in neonates in whom the majority of PPI suspension is prescribed.

Decision: Not approved

10. Emerade (adrenaline auto-injector)

The Committee reviewed a 'Prevention of Future Deaths report' relating to a patient dying of acute anaphylaxis. The patient was prescribed Emerade®, the adrenaline autoinjector of choice in North Central London (replacing EpiPen®) approved in August 2015.

The case however provided opportunity to reflect on JFC processes and the Committee agreed:

- Where there is no direct application from a specialist the committee will engage, where necessary, with appropriate specialists and stakeholders. However, the lack of a direct application will not preclude review.
- Medicines Safety Officer (MSO) contribution to JFC discussions would be beneficial in order to identify in-use medication risk across primary and secondary care. JFC Support will write to the NCL MSO Group to request that they nominate a representative to join JFC membership.

Owing to the ongoing supply challenges with adrenaline auto-injectors, the Committee agreed to not prefer one brand over another (i.e. a flat recommendation for Emerade®, EpiPen® and Jext® based on availability).

11. Esmya (ulipristal acetate) - suspension of the licence and medicines recall

On 9 March 2020 the EMA commenced a review of Esmya (ulipristal acetate) following a new case of liver failure requiring liver transplant; the case occurred despite measures put in place following a previous review to minimise the risk of liver injury. Due to the risk of serious liver injury the Marketing Authorisation for all ulipristal acetate 5mg products (for uterine fibroids) was suspended in the UK for the duration of the review. The MHRA has issued an alert advising patients currently taking Esmya for uterine fibroids to stop taking the medicine and advising healthcare professionals that no new patients should start treatment. The MHRA has also issued a class 2 medicines recall of ulipristal acetate from pharmacies, wholesalers, and patients.

Decision: Removed from the NCL Joint Formulary

12. Adalimumab: New CMU contract to use Idacio (biosimilar adalimumab) for new patients

Idacio® (biosimiar adalimumab) was added to the NCL Joint Formulary Committee for new patients. A review is underway to establish whether a switch of patients currently on a higher cost brand of adalimumab (i.e. Hyrimoz) to Idacio® is appropriate.

13. Choice of DOAC for the treatment of VTE – Position Statement

The Committee reviewed a position statement that was approved by NCL Haematologists and reflects discussions at the JFC February 2020 meeting. The position statement was approved.

14. Next meeting

Thursday 16th July 2020

15. Any other business

Nil