North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 16th July 2020

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Dr P Taylor	NCL JFC Vice Chair	
	Dr M Kelsey	WH, DTC Chair	
	Mr P Gouldstone	NCL CCG, Head of Medicines Management (Enfield)	
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	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 S Tomlin	GOSH, Chief Pharmacist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Dr A Sell	RNOH, DTC Chair	
	Mr A Stein	NMUH, Deputy Chief Pharmacist	
	Ms I Shaban*	NCL CCG, Deputy Head of Medicines Management	
	Ms E Mortty*	NCL CCG, Deputy Head of Medicines Management	
	Ms L Reeves	C&I, Chief Pharmacist	
In attendance:	Dr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Barron	North London Partners, MEP Project Lead	
	Mr G Grewal	North London Partners, JFC Support Pharmacist	
	Ms M Kassam	North London Partners, JFC Support Pharmacist	
	Ms S Amin	UCLH, Formulary Pharmacist	
	Mr S O'Callaghan	UCLH, Formulary Pharmacist	
	Ms SY Tan	NEL CSU, 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	
	Dr D Burrage	WH, Consultant in Emergency Medicine	
	Mr I Taylor	NCL Nutrition Group, Co-Chair	
	Ms R Stennett	NCL Nutrition Group, Co-Chair	
	Dr S Yardley	CNWL, Palliative Care Consultant	
	Mr H Vakharia	RFL, Consultant Obstetrician and Gynaecologist	
	Mr H Hafeez	RFL, Specialist Pharmacist	
Apologies:	Ms G Smith	RFL, DTC Chair	
	Mr A Dutt	NCL CCG, Head of Medicines Management (Islington)	
	Ms R Clark	NCL CCG, Head of Medicines Management (Camden)	
	Ms P Taylor	NCL CCG, Head of Medicines Management (Haringey)	
	Ms S Lever	NCL CCG, Pharmaceutical advisor (Barnet)	

Dr A Bansal	NCL CCG, GP Clinical Lead Medicines Management (Barnet)
Mr A Shah	RNOH, Chief Pharmacist
Mr A Tufail	MEH, DTC Chair

**Deputising for Committee member*

2. Meeting observers

The Chair welcomed Dr Burrage (WH, Consultant in Clinical Pharmacology and Acute Medicine) and Ms Weaver (NHSE, Specialised Commissioning Pharmacist) as observers of the meeting.

3. Minutes of the last meeting

The minutes of the 02 July 2020 meeting were accepted as an accurate reflection of the meeting.

4. Matters arising

Nil

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
UCLH	June 2020	Acalabrutinib monotherapy	Pre-NICE FoC scheme: Previously untreated Chronic Lymphocytic Leukaemia without a 17p deletion and/or TP53 mutations	Decision: Added to NCL Joint Formulary Prescribing: Secondary care Tariff status: N/A Funding: FoC Fact sheet or shared care required: No
UCLH	June 2020	Subcutaneous daratumumab	FoC scheme: Relapsed and refractory multiple myeloma, as a replacement of IV daratumumab in chemotherapy regimens, only if approved and reimbursed by CDF	Decision: Added to NCL Joint Formulary Prescribing: Secondary care Tariff status: N/A Funding: FoC Fact sheet or shared care required: No

7.2 Not Approved

DTC site	Month	Drug	Indication	JFC outcome
UCLH	June 2020	Tocilizumab	Hyperinflammation following COVID-19 infection for haematology patients excluded from COVACTA trial (NCT04320615)	Decision: Not approved

8. New Medicine Reviews

8.1 Feraccru® (ferric maltol) for iron deficiency anaemia in inflammatory bowel disease (Applicant: Dr F Rahman, UCLH)

The Committee considered an application *in absentia* for ferric maltol (Feraccru®), an iron tablet, for iron deficiency anaemia associated with inflammatory bowel disease (IDA-IBD) amongst individuals have failed two prior oral iron products and have either (i) an allergy to intravenous iron or (ii) are eligible for intravenous iron but oral therapy is preferred owing to an extended clinic wait list, severe needle phobia or poor venous access.

Gasche et al. report two identical phase III, double-blind, placebo-controlled trials; AEGIS-1 and AEGIS-2 to assess the efficacy and safety of ferric maltol for IDA-IBD in adults (Hb of 9.5-12g/dL for women and 9.5g-13g/dL for men; n = 128). Patients were required to be in remission or have mild – moderate UC or

CD and have previously failed an oral ferrous product. The primary endpoint, mean change in haemoglobin concentration, was significantly higher in the ferric maltol arm (2.25g/dl; one sided 97.5% CI: 1.81) at week 12.

AEGIS H2H (abstract only) was a 12 week, Phase IIIb, open-label, active-comparator controlled study to compare the efficacy and safety of oral ferric maltol (Feraccru®) and intravenous ferric carboxymaltose (Ferinject®) for IDA-IBD in adults (Hb 8.0-11.0 g/dL for women, 8.0-12.0 g/dL for men; n=250). Patients were randomised to ferric maltol 30mg twice daily or ferric carboxymaltose dosed according to the SPC. The primary endpoint was the 'Hb responder rate', defined as the proportion of patients achieving either ≥2 g/dL increase in Hb or normalisation of Hb. The study was powered to detect non-inferiority with a non-inferiority margin of 20%. Results show that non-inferiority was demonstrated for the *Per Protocol* population however it was not demonstrated for *Intention-To-Treat* population. A major limitation of this dataset in supporting this application is the absence of its results being published in a peer reviewed journal.

With regards to safety, when compared against placebo, ferric maltol was associated with an increase in adverse events considered to be related to treatment (25.0% and 11.7% respectively); the most common AEs were abdominal pain, constipation and flatulence. When compared against ferric carboxymaltose, ferric maltol was associated with an increase in treatment-emergent adverse events (TEAE; 59% vs. 36%) and serious TEAE (15% vs. 9%).

With regards to budget impact, ferric maltol is less costly than intravenous iron and may save £22,000 per annum excluding activity (assuming ferric maltol is discontinued after 12 weeks).

The Committee acknowledged that an oral intervention to reduce the need for intravenous iron infusion was advantageous from both an operational perspective (reduction in patient visits to hospitals, supporting the reduction in long clinic wait lists) and a patient safety perspective (reducing the risk of anaphylaxis). The Committee's conclusion from the available data was that ferric maltol is superior to placebo but inferior to intravenous iron, however the degree of inferiority could not be assessed owing to the absence of full results for the AEGIS H2H study. Principally, it was unknown how many patients treated with ferric maltol would ultimately require intravenous iron and therefore the cost-effectiveness of this intervention could not be established. It was noted that both SMC and AWMSG have rejected ferric maltol.

The Committee broadly agreed with the proposed place in the treatment pathway, however raised a number of concerns which required clarification:

- What is the existing Hb threshold (male/female) for treatment with intravenous iron vs oral iron
- What would be the proposed Hb threshold for treatment with ferric maltol locally (note that AEGIS H2H recruited patients with Hb ≥8 g/dL whereas Gasche et al. recruited patients with Hb ≥9.5 g/dL)
- The application makes reference for GPs to monitor the effectiveness of ferric maltol and to discontinue treatment after 12 weeks. It was unclear whether this represents a change in responsibilities or whether GPs already undertake such monitoring for other oral iron formulations
- What would be the thresholds for determining effectiveness of therapy to warrant continuation and discontinuation:
    - Hb threshold for continuation at 4 weeks
    - Hb threshold for discontinuation at 12 weeks
    - Plan for patients who do not adequately respond to ferric maltol after 4 or 12 weeks
- What measures would be put in place to prevent the use of ferric maltol outside any agreed indication

Based on the uncertainty with both efficacy and budget impact, the Committee were unable to recommend ferric maltol. However, the Committee agreed that it was plausible in some people who are not responding to ferrous products, and were unable to receive intravenous iron, that ferric maltol may be beneficial. In absence of published RCT evidence to support this hypothesis, the Committee agreed it was not appropriate to recommend the use of ferric maltol. The Committee therefore deferred their decision pending publication of the AEGIS H2H study and recommended that the applicant submit a one-page treatment pathway for the management iron deficiency anaemia associated with inflammatory bowel disease to support the application at the time this is revisited.

Decision: Deferred until data from the AEGIS H2H clinical trial is published and a one-page treatment pathway is submitted

8.2 Carbetocin for the prevention of post-partum haemorrhage after Caesarean section (Applicant: Dr H Vakharia, RFL)

The Committee considered an application for carbetocin, a long-acting oxytocin analogue, as a first-line option for the prevention of post-partum haemorrhage (PPH) in patients undergoing Caesarean section.

Gallos et al (Cochrane Library) undertook a network meta-analysis (NMA) to compare the efficacy and safety of various uterotonic agents, placebo and 'no treatment' for the prevention of PPH in the third stage of labour following vaginal or caesarean birth. 196 randomised or cluster-randomised trials were included (n=135,559). The primary outcome of 'prevention of PPH ≥500mL' was significantly better with carbetocin compared to oxytocin (RR: 0.72, [95% CI: 0.56 to 0.93]) however 'prevention of PPH ≥1000mL' was not better (RR: 0.87 [95% CI: 0.62 to 1.21]). The outcome (reduction in need for) 'additional uterotonic agents used' was significantly better with carbetocin compared to oxytocin (RR: 0.45, [95%CI: 0.34 to 0.59]). Key limitations of the NMA were inclusion of studies from a time period which may not reflect clinical practice today and the grouping together of routes and doses of each medicine together.

An NIHR economic evaluation was also reviewed. The data underpinning the economic analysis was from an earlier and separate NMA with fewer trials than the Cochrane review (n=87,466). In the model where no data was assumed for caesarean section, patients and adverse events were accounted for, carbetocin was estimated to be the least expensive and second-most effective uterotonic agent. Carbetocin dominated oxytocin in every analysis. A key limitation of the evaluation was missing data; the authors recommend larger trials for the use of carbetocin to take place. The Cochrane review addresses these limitations by including larger trials which adds more certainty to the evidence base for the efficacy of carbetocin in Caesarean section.

With regards to safety, the Cochrane review did not demonstrate any additional adverse events for carbetocin over oxytocin. A risk assessment demonstrated lower risk from using carbetocin compared to oxytocin. With regards to budget impact, carbetocin is expected to cost NCL an additional £98,400 per annum however this does not account for cost-offsets from system savings which will result from its use but are hard to quantify.

The Committee reviewed an audit of carbetocin used at WH which showed some consistency with the NMA results such as a reduction in 'additional oxytocic use' with carbetocin, however there was no improvement observed in 'median blood loss'. The audit also showed a meaningful reduction in 'median time spent on labour ward' although there was no difference in 'the time from delivery to discharge'.

The Committee heard from Mr Vakharia who confirmed the WH audit results were reflective of his personal experiences at WH and other Trusts using carbetocin.

In camera, the Committee agreed that the results from the NMA were difficult to interpret as it did not account for differences in the dose and route of oxytocin used. A key challenge in interpretation of the available data is that whilst carbetocin appears to be more convenient to administer than oxytocin, it presents a high cost burden to the NHS compared with oxytocin. The audit data from WH indicated carbetocin was most advantageous in lower risk patients (Category 3 & 4) however the Committee agreed that separate treatment pathways for higher and lower risk caesarean sections would be impractical to implement. The Committee concluded that a pathway was required to standardise uterotonic agent use across NCL and asked specialists to consider whether the addition of carbetocin could displace carboprost (the most expensive uterotonic agent) to help with offsetting a proportion of the budget impact. The Committee therefore deferred their decision pending receipt of a treatment pathway which would be applied across all relevant centres across NCL.

Decision: Deferred pending submission of a harmonised NCL one-page pathway for the prevention and treatment of post-partum haemorrhage after Caesarean section to support the above application.

9. Rapid risk assessment: Methadone for pain in palliative care

The Committee considered a rapid risk assessment of the use of methadone for pain within the palliative care setting in patients who have inadequate analgesia with conventional strong opioids i.e. where the opioid dose is rapidly escalating with incomplete clinical benefit, or where the dose increase is limited by

clinically significant adverse or toxicity symptoms. The proposal was brought by the CNWL Palliative Care team who have developed guidance on the use of methadone for this indication in order to reduce unwarranted variation across NCL and to support non-specialists in prescribing. In line with prescribing of other medicines for palliative care in primary care, the proposal is for GPs to prescribe methadone with high levels of support from specialists, for example, a GP would not be expected to autonomously initiate, wean or titrate the dose.

The Scottish palliative care guidance, Palliative Care Adult Network Guidelines, Palliative Care Formulary and the Oxford Handbook of Palliative Care all support the use of methadone in this setting.

With regards to efficacy, Nicholson et al conducted a systematic review (6 RCTs, n=388) of adult participants with various types of cancer who required strong opioids to control their pain. A quantitative analysis was not possible owing to variation in study methodology and comparisons. A qualitative analysis suggest, based on limited data, that there were no clear differences in participant-reported pain intensity or pain relief between methadone and morphine or transdermal fentanyl. Similar proportions of participants were able to tolerate each medicine and achieve a level of pain control that was probably similar to mild pain. Adverse events were typical for opioids but inconsistently reported.

The Committee heard from Dr Yardley that methadone would be used after 3 to 4 opioids have been trialled and have not been effective or tolerated. Patient numbers are small and treatment is usually initiated in the acute hospital. Patients who are on methadone prior to entering the palliative care setting will require an individual patient care plan in combination with the substance misuse service.

In summary, the Committee agreed to add methadone for 'palliative care in patients who have inadequate analgesia with conventional strong opioids' to the NCL Joint Formulary. The Committee asked that the NCL Shared Care Group produce an interface document to facilitate prescribing in primary care with input from the Medicine Safety Group within primary care. This document should exclude children as GOSH will review paediatric practice independently.

Decision: Approved, subject to NCL SCG agreeing an interface document
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Primary and secondary care
Fact sheet or shared care required: No, but an interface document is required

10. NCL Position Statement on the prescribing of Ensure® Plus Advance

Ms Stennett and Mr Taylor presented a position statement for Ensure® Plus Advance. The NCL Nutrition Group do not recommend Ensure® Plus Advance for any indication as there is no robust clinical evidence to support the claimed additional benefits. Calories and protein provided by the supplement can be obtained by food fortification; if oral nutritional supplements are indicated, alternative cost-effective supplements are available on formulary. The Committee were supportive of the recommendation and the proactive efforts from the NCL Nutritional Group. The Committee approved the Position Statement.

11. High cost drug treatment pathway for psoriasis

NEL CSU updated the guideline which includes the treatment pathway previously approved at JFC in June 2019.

12. Next meeting

Thursday 20th August 2020

13. Any other business

Nil.