North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 9 April 2020

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Dr M Kelsey	WH, DTC Chair	
	Mr S Richardson	WH, Chief Pharmacist	
	Mr S Semple	MEH, Chief Pharmacist	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Ms W Spicer	RFL, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Dr A Sell	RNOH, DTC Chair	
In attendance:	Dr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Barron	NCL MEP, Project Lead	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Ms SY Tan	NEL CSU, Commissioning Pharmacist	
	Ms S Amin	UCLH, Formulary Pharmacist	
	Prof K Moore	RFL, Consultant Hepatologist	
	Mr R Schulman	UCLH, Critical Care Pharmacist	
	Mr B O'Farrell	RFL, Critical Care Pharmacist	
	Mr D Abdulla	NMUH, Critical Care and Formulary Pharmacist	
	Mr S O'Callaghan	UCLH, Formulary Pharmacist	
	Dr Kay Dhadwal	RFL, Intensive Care Consultant	
	Dr Amit Adlakha	RFL, Respiratory and Intensive Care Consultant	
Apologies:	Mr C Daff	Barnet CCG, Head of Medicines Management	
	Ms L Reeves	C&I, Chief Pharmacist	
	Prof D Hughes	RFL, Consultant Haematologist	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr T Dean	Patient Partner	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	

2. Meeting observers

There were no meeting observers.

3. Minutes of the last meeting

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

4. Declarations of relevant conflicts of interest

No additional declarations were noted for the new medicine applications.

5. New Medicine Reviews

5.1 Neublised prostacyclin (iloprost and epoprostenol) for respiratory failure

The Committee considered an application for nebulised iloprost or epoprostenol to treat COVID-19 associated Acute Respiratory Distress Syndrome (ARDS) in the critical care setting. This was a prioritised review following the publication of clinical experience in UK intensive care setting published by NIHR, UCL Partners and the Intensive Care Society, which states "nebulised or IV prostacyclins may be helpful as part of therapeutic trial if using wet mechanical ventilation circuits in COVID-19 patients".

In terms of the management of ARDS outside the context of COVID-19; joint guidance from the American Thoracic Society, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine, did not address adjunctive therapies such as inhaled vasodilators. In addition, separate guidelines from the Intensive Care Society and the Faculty of Intensive Care Medicine did not identify any studies in their search strategy for inhaled prostacyclins. Two systematic reviews and meta-analyses were identified. The first was a Cochrane review (n=81) which identified two single-centre RCTs. No difference in mortality (the primary outcome from the review) was identified however data for this outcome was only available from a single cross-over study in critically ill children. There was also no difference in PaO2/FiO2 ratio however a favourable trend was identified (mean difference -25.35 [95% CI -60.48 to 9.78; p=0.16]). The second systematic review and meta-analysis included randomised and non-randomised studies (n=606); this study reported trends for improved oxygenation (PaO2/FiO2 ratio, improved PaO2 and decrease in mean pulmonary arteria pressure) although significant heterogeneity amongst studies were noted. The authors found adverse event reporting was disproportionate amongst studies, such as higher rates of hypotension reported in non-randomised studies that the RCTs.

Specific to COVID-19 associated ARDS, JFC Support did not identify any relevant trials that have either been carried out or are ongoing. Joint guidance from the European Society of Intensive Care Medicine and the Society of Critical Care Medicine also report that no adequately powered RCTs have evaluated inhaled prostacyclins and therefore they could not recommend their use for severe ARDS in COVID-19 patients. They recommend against routine inhaled nitric oxide but do recommend a trial of "inhaled pulmonary vasodilator" as rescue therapy in patients refractory to other strategies. No specific guidance from NHS England was identified at the time of discussion.

In terms of safety, nebulised iloprost is a licensed therapy for pulmonary arterial hypertension, with bleeding events, bronchospasm or hypotension reported as major adverse effects. The most common adverse events are hypotension, headache and cough. Nebulised epoprostenol is off-label (licensed for intravenous use only) therefore safety data is limited; it has a high pH (10-12) though the inhalation of alkaline agents appears to be safe when given via nebuliser. Both drugs require specific equipment for safe and effective administration. Risks of using such equipment include aerosolization and clogging of filters. Nebulised epoprostenol administration requires a syringe pump which is itself a finite resource in the context of a pandemic.

In terms of procurement, NHS England Specialised Commissioning have written to Trusts requiring that medicines are not used off-label as the medicines currently within the supply chain are required for the treatment of patients on treatment for licensed indications. The estimated budget impact for an estimated 30 patients would be in the region of £100,000 per month.

The Committee commented on the lack of evidence to support the use of nebulised prostacylin in COVID-19 associated ARDS, and that a reduction in mortality has not been demonstrated outside the context of COVID-19. The Committee heard from specialists across NCL that nebulised prostacyclin was likely to be therapeutically useful for some critically ill patients and that a clinical trial was feasible. The Committee stated a preference for avoiding the off-label of prostacyclins, in line with Spec Comm letter, the likely availability of the drug given the higher usage if approved which may compromise use in licenced

indications. Specialists from RFL, who have experience of using nebulised iloprost, advised that the eligibility criteria would require refinement. The Committee therefore recommended a pilot of nebulised iloprost in 10 patients at RFL to inform the clinical trial proposal. The clinical trial proposal should be submitted to the NIHR via the Urgent Public Health application portal. Dr Dhadwal and Dr Adlakha agreed to lead on both the pilot and the clinical trial proposal.

Decision: Nebulised iloprost approved for use in 10 patients under an evaluation; Dr Dhadwal and Dr Adlakha to lead on defining initiation criteria with other intensivists in NCL before enrolling 10 patients at RFL. Further use should be in the context of a clinical trial.
Prescribing: Secondary Care
Tariff status: Tariff excluded
Funding: Not routinely commissioned
Fact sheet or shared care required: No

Post meeting note: NHS England ICU guidance published on 08 April 2020 recommends prostacyclin for pneumonitis. JFC Support to seek further information from NHS England and report back at the next meeting.

6. Position Statement: Use of investigational antiviral agents for COVID-19 in adults

JFC Support are working with UK virologists and infectious disease specialists to form the COVID-19 Therapeutics Advise & Support Group (CTAG). This group have developed a position statement which bring together recommendations from National bodies, the CMO office and evidence from clinical trials. The statement is endorsed by the British Infection Association and the UKCPA Pharmacy Infection Network and is available by the NCL MON website.

7. Discussion: Tocilizumab, sarilumab and anakinra for hyperinflammation

There is a requirement to produce a position statement, similar to the antivirals Position Statement (see Item 6), to guide on the appropriate use of immunomodulatory agents. Dr Manson (Co-chair of HLH Across Specialty Collaboration; HASC) has agreed for HASC to work collaboratively with CTAG to produce the statement. This statement is currently under development.

8. JFC Terms of Reference during the COVID-19 pandemic

The Committee approved the interim Terms of Reference was presented to the Committee.

9. Next meeting

To be determined.

10. Any other business

Nil