North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 14th December 2021

Present:	Prof R Sofat	NCL JFC Chair	(Chair)
	Dr B Subel	NCL JFC Vice Chair	
	Dr M Kelsey	WH, DTC Chair	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Mr S Semple	MEH, Chief Pharmacist	
	Mr J Harchowal	UCLH, Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Dr A Scourfield	UCLH, Interim DTC Vice Chair	
	Ms E Mortty	NCL CCG, Deputy Head of Medicines Management (Haringey)	
	Mr P Gouldstone	NCL CCG, Head of Medicines Management (Enfield)	
	Ms K Delargy	BEH, Chief Pharmacist	
	Mr A Dutt	NCL CCG, Head of Medicines Management (Islington)	
	Ms M Singh	NCL CCG, Head of Medicines Management (Barnet)	
	Ms N Phul	MEH, Chief Pharmacist	
	Ms S Stern	NMUH, Chief Pharmacist	
	Dr R Urquhart	UCLH, Divisional Clinical Director	
In attendance:	Ms E Fiori	NCL CCG, Director of Acute Commissioning	
	Dr J Hawdon	RFL, Consultant Neonatologist	
	Ms C Dollery	WH, Executive Medical Director	
	Dr F Bennett	UCLH, Clinical Pharmacology Registrar	
	Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	
	Dr M Brown	UCLH, Consultant in Infectious Diseases	
	Ms A Fakoya	NHS London Shared Service, Contract and Commissioning Support Pharmacist	
	Ms O McGarrity	GOSH, Lead Microbiology Pharmacist	
	Ms S Sanghvi	North London Partners, Principal Pharmacist	
	Mr G Grewal	North London Partners, JFC Support Pharmacist	
	Mr R Rajan	North London Partners, JFC Support Pharmacist	
	Ms N Ngoka	RFL, Commissioning Pharmacist	
	Dr S Brill	RFL, Consultant in Respiratory Medicine	
	Ms I Samuel	RFL, Group Medicines Optimisation Pharmacist	
	Ms M Thacker	RFL, Senior Pharmacist	
	Ms S Amin	North London Partners, Lead Pharmacist	
	Mr S O'Callaghan	UCLH, Medicines Safety Officer	
	Mr A Barron	UCLH, Principal Pharmacist	
	Mr G Kitson	WH, Deputy Chief Pharmacist	
Apologies:	Mr T Dean	Patient Partner	
	Ms W Spicer	RFL, Chief Pharmacist	
	Ms G Smith	RFL, DTC Chair	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Ms L Reeves	C&I, Chief Pharmacist	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	

Dr A Sell	RNOH, DTC Chair
Ms R Clark	NCL CCG, Head of Medicines Management (Camden)
Dr D Burrage	WH, Consultant in Emergency Medicine

2. Meeting observers

Prof Sofat welcomed subject matter experts to the meeting.

3. New Medicine Reviews

3.1 Ronapreve and molnupiravir for non-hospitalised patients with SARS-CoV-2 and risk for severe COVID-19

The Committee considered an application for Ronapreve (casirivimab/imdevimab - two SARS-CoV-2 neutralizing antibodies administered by subcutaneous injection) and molnupiravir (an oral anti-viral agent) for non-hospitalised patients with COVID-19 who meet the inclusion criteria and none of the exclusion criteria as outlined in the NHSE/I Interim Commissioning Policy.

Pre-hospitalised patients are eligible for consideration if:

- SARS-CoV-2 infection (PCR confirmed within the last 72 hours); AND
- Onset of symptoms of COVID-19 within 7 days; AND
- The patient is in the 'highest' risk group as per the commissioning policy; AND
- Does not meet any of the exclusion criteria:
    - Patients requiring hospitalisation for COVID-19;
    - Patients requiring supplemental oxygen;
    - Children weighing <40kg; and
    - Children aged <12 years.

Patients should initially be considered for Ronapreve (if aged 12 years and at least 40kg). If a neutralising monoclonal antibody (nMAB) is contraindicated, not recommended (due to efficacy against Omicron variant) or if administration is not possible, a 5-day course of molnupiravir may be considered in patients aged 18 or over (but not recommended in pregnant women due to risk of reproductive toxicity).

The evidence underpinning the use of Ronapreve was from Weinreich et al (2021), who conducted a randomised, double-blind, placebo-controlled study to compare the efficacy and safety of Ronapreve versus placebo in non-hospitalised patients with SARS-CoV-2 and at least one risk factor for severe COVID-19 (n=4,057). The primary endpoint, the proportion of patients with COVID-19 related hospitalisation or death by day 29, was significantly lower with Ronapreve 1.2g compared with placebo (1.0% vs. 3.2%; RRR: 70.4% [95%CI 31.6% to 87.1%]). Key limitations of the study were the exclusion of vaccinated patients, the adaptive design allowing for protocol amendments, the composite primary outcome being driven primarily by hospitalisation and the unknown efficacy against the Omicron variant.

The evidence underpinning the use of molnupiravir was from the MOVe-OUT Study [unpublished; data obtained from the FDA review]. MOVe-OUT was a randomised, double-blind, placebo-controlled study to compare the efficacy and safety of molnupiravir versus placebo in non-hospitalised adult patients with SARS-CoV-2 with symptom onset within 5 days and at least one risk factor for severe COVID-19 (n = 1,433). The primary endpoint, the proportion of patients with COVID-19 related hospitalisation for ≥24 hours for acute care or died from any cause by day 29, was significantly lower with molnupiravir compared with placebo (6.8% vs. 9.7%; RRR: 30%, ARR = 3.0% [95% CI 0.1% to 5.9%]). Key limitations of the study was that it was unpublished at the time of review, enrolment was stopped early based on interim results which were substantially different to the unpublished data (ARR 6.8%), the exclusion of vaccinated patients and the unknown efficacy against the Omicron variant.

In terms of safety, Ronapreve is associated with a risk of infusion and hypersensitivity reactions (including anaphylaxis), therefore should only be administered where management of severe hypersensitivity reactions is possible. Ronapreve may interfere with development of an immune response to COVID-19 vaccinates (and this risk is ongoing, owing to the long half-life).

The most common adverse reactions with molnupiravir were diarrhoea, nausea, dizziness and headache. The mechanism of action has the potential for mutagenicity and genotoxicity (for which the risk was deemed as low by the FDA), and potential for embryofoetal and bone & cartilage toxicity from animal studies (for which the risk remains uncertain). Therefore, molnupiravir is not recommended during pregnancy (with people of childbearing potential advised to use effective contraception). The mechanism

of action of molnupiravir (increasing mutational frequency in the viral genome) suggests a potential risk of changes to the viral spike protein, however the clinical and public health risk of this remains uncertain.

Ronapreve is a single 1.2g intravenous or subcutaneous dose which must be administered in COVID Medicines Delivery Units (CMDUs). Molnupiravir is administered as an oral 5 day course and will be offered to eligible patients via delivery to the patients' home.

The following items were discussed and agreed:

- The use of both Ronapreve and molnupiravir in the vaccinated population was cautiously accepted, acknowledging that data would continue to be collected in all patients (via ISARIC and the PANORAMIC study for molnupiravir).
- The Committee noted that Omicron was expected to shortly become the dominant variant in London. There is uncertainty in the efficacy data for both Ronapreve and molnupiravir against Omicron. The Committee were informed of another nMAB (sotrivimab), for which interim results demonstrate a significant reduction in hospitalisations and deaths (ARR 6%; RRR 85%; p=0.002) and pre-clinical studies suggest efficacy against the Omicron variant. The Committee agreed that any updates to the commissioning policy regarding sotrovimab should be reviewed via Chair's action.
- Capacity may become an issue for CMDUs to deliver nMAB treatment due to original impact analysis using pre-Omicron population figures. Clarification over the use of molnupiravir as an alternative in this scenario is being sought from NHSEI.
- The Committee discussed the teratogenic potential of molnupiravir. The commissioning policy recommends 'effective contraception' for the duration of molnupiravir and for four days after. Barrier methods are not considered an appropriate form of contraception. People of childbearing potential who are not already on effective contraception, should be advised to abstain. The Committee discussed logistical challenges of pre-treatment pregnancy testing, and agreed to seek clarity from NHSEI regarding requirement for pregnancy testing and patient information.

In summary, the Committee agreed to add Ronapreve and molnupiravir to the NCL Joint Formulary for non-hospitalised patients with SARS-CoV-2 and a risk factor for severe COVID-19, in line with the NHSE/I commissioning policy.

Decision: Approved
Prescribing: Secondary Care - COVID Medicines Delivery Units (CMDUs) only
Tariff status: NA
Funding: Free-of-charge – commissioned via NHSE/I
Primary and secondary care Fact sheet or shared care required: No

Post-Meeting Update (16th December 2021): Two CAS alerts were published on 16th December with updates to the commissioning policies for COVID-19 treatment. With evidence that the efficacy of Ronapreve may be compromised against the increasingly prevalent Omicron variant, the following amendments to NHSE guidance were made:

- Non-hospitalised high-risk patients are recommended to be considered for sotrovimab in place of Ronapreve as the first line option as per commissioning criteria.
- Patients with hospital onset COVID-19 are eligible for Ronapreve if genotyping is available and confirms a non-Omicron variant, otherwise sotrovimab may be considered in line with the commissioning criteria.
- Patients hospitalised with acute COVID-19 should only be considered for Ronapreve if patients are infected with a non-Omicron variant OR the local hospital prevalence of the Omicron variant is <50%.

These updates to the use and criteria for nMABS and antivirals for COVID-19 was approved via Chair's action in line with the NHSE commissioning policies.

4. Next meeting

20th January 2022