North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES
Minutes from the meeting held on 17th March 2022

Present:	Dr B Subel	NCL JFC Vice Chair	(Chair)
	Mr S Semple	NCL ICS, Interim Chief Pharmacist; GOSH, Interim Chief Pharmacist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Dr G Smith	RFL, DTC Chair	
	Dr M Kelsey	WH, DTC Chair	
	Mr A Sell	RNOH, DTC Chair	
	Dr D Roberts	Islington Borough, Clinical Director	
	Dr R Urquhart	UCLH, Divisional Clinical Director	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Ms K Delargy	BEH, Chief Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr J Harchowal	UCLH, Chief Pharmacist	
	Mr S Richardson	WH, Chief Pharmacist	
	Ms M Singh	NCL CCG, Head of Medicines Management (Barnet)	
	Mr P Gouldstone	NCL CCG, Head of Medicines Management (Enfield)	
	Mr A Dutt	NCL CCG, Head of Medicines Management (Islington)	
	Ms E Mortty	NCL CCG, Deputy Head of Medicines Management (Haringey)	
In attendance:	Ms S Sanghvi	North London Partners, JFC Principal Pharmacist	
	Mr G Grewal	North London Partners, JFC Support Pharmacist	
	Mr R Rajan	North London Partners, JFC Support Pharmacist	
	Ms S Amin	IPMO Programme Team, Lead Pharmacist	
	Mr A Barron	UCLH, Principal Pharmacist	
	Ms A Sehmi	NMUH, Formulary Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Ms M Thacker	RFL, Clinical Lead Pharmacist	
	Ms A Blochberger	NHSE, Specialised Commissioning Pharmacist	
	Ms S Y Tan	NHS London Shared Service, Contract and Commissioning Support Pharmacist	
	Prof J Cunningham	RFL, Consultant Nephrologist	
	Prof D Thorburn	RFL, Consultant Hepatologist	
	Dr P Pemberton	RFL, Consultant Anaesthetist	
	Dr H Wilson	UCLH, Consultant Neurologist	
	Ms N Dass	Camden, Medicines Management Pharmacist	
	Ms S Patel	Enfield, PCN Pharmacist	
	Ms M Kassam	MEH, Senior Pharmacist	
	Ms P Gudka	RFL, Renal Pharmacist	
	Mr A Grout	RFL, Clinical Nurse Specialist Pain Management	
	Ms N Kanani	RFL, Hepatology Pharmacist	
	Ms R McGaw	RFL, Hepatology Pharmacist	
	Ms S Maru	UCLH, Senior Pharmacist	
	Ms A Shields	UCLH, Neurology Pharmacist	
Apologies:	Dr A Worth	GOSH, DTC Chair	
	Prof A Tufail	MEH, DTC Chair	
	Dr A Scourfield	UCLH, DTC Chair	
	Dr D Burrage	WH, Consultant Clinical Pharmacologist	

Ms L Reeves	C&I, Chief Pharmacist
Ms N Phul	MEH, Chief Pharmacist
Ms S Stern	NMUH, Chief Pharmacist
Ms R Clark	NCL CCG, Head of Medicines Management (Camden)

2. Meeting observers

Dr Subel welcomed Dr Roberts as a new GP member to JFC.

3. Minutes of meeting on Thursday 17th February 2022

Page 4, update 8.1 to clarify that ProPrems® is a prophylactic not treatment. The minutes and abbreviated minutes were otherwise accepted as an accurate reflection from February 2022 meeting.

4. Matters arising

No other matters were raised.

5. JFC Outstanding Items & Work Plan

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

6. Members declarations of conflicts of interest

Nil.

7. Local DTC recommendations / minutes

DTC site	Month	Drug	Indication	JFC outcome
RFL	Jan 2022	FOC scheme: Nivolumab and Ipilimumab†	Neuroendocrine carcinoma	Decision: RFL only Prescribing: Secondary care Tariff status: N/A – Free of charge Funding: N/A – Free of charge Fact sheet or shared care required: No
RFL	Jan 2022	ActaSolve Smoothie	Dietary management of patients at risk of malnutrition	Decision: Added to the NCL Joint Formulary Prescribing: Primary and secondary care Tariff status: In tariff Funding: Trust and CCG Fact sheet or shared care required: No
MEH	Oct 2021	Vitamin A (oral and IM)	Vitamin A deficiency	Decision: MEH only Prescribing: Secondary care only Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No
Barnet borough	Dec 2019	Epimax Oatmeal	Emollient cream (suitable for vegans; cost-effective alternative to Aveeno)	Decision: Added to the NCL Joint Formulary Prescribing: Primary and secondary care Tariff status: In tariff Funding: Trust and CCG Fact sheet or shared care required: No

† The relevant commissioner should be notified in line with NCL Free of Charge scheme guidance. Approval is conditional on the provision of a free of charge scheme agreement and funding statement

7.1 Oral ketamine solution for pain

JFC had previously discussed the use of oral ketamine under evaluation at RFL in 2017. The results of the evaluation conducted were presented to the Committee. The intention is to use oral ketamine in four specific cohorts of patients with a need for inpatient pain management – those with neuropathic pain & persistent postsurgical pain; patients with a history of high opioid consumption prior to surgery or trauma; patients with a poor opioid response; and patients in hyperalgesia states.

The evaluation was conducted in 61 patients from June 2019 to May 2021, who were initiated on either oral ketamine 10mg QDS or 25mg QDS. The oral morphine equivalent dose (OMED), pain score and

functional activity score (FAS) were measured at baseline and at follow-up on day 1, 3 and 5 post-initiation. Amongst patients initiated on 10mg QDS, the clinicians found that patients had a 72% reduction in OMED from baseline to day 5; those receiving 25mg QDS has a 40% reduction in OMED from baseline to day 5. There were improvements in pain score from baseline (in the case of FAS, the greatest improvements were seen in those with significant limitations at baseline).

In terms of safety, known adverse effects include drowsiness, dysphoria, respiratory depression, and small increases in heart rate and blood pressure. In the evaluation, six patients discontinued on day 1 due to drowsiness and dysphoria. RFL have a clinical guideline in use to advise on monitoring.

Oral ketamine is on formulary for inpatient use only at RFL, and there are requests from other NCL sites including WH to utilise treatment. The estimated budget impact at RFL for 50 patients is £750 per annum (based on a dose of 25mg QDS, with bottles shared between patients). Treatment is usually for 5-7 days.

Dr Pemberton informed the Committee that ketamine oral solution was used to successfully bridge to other neuropathic pain treatments or a stable morphine dose. Anecdotal evidence suggests that patients do not suffer from rebound pain once ketamine is stopped. Patients are not discharged on oral ketamine, which is of particular importance given the risk of misuse. Oral ketamine also provided a convenient option for administration compared with intravenous ketamine.

The Committee recognised that low-dose oral ketamine solution is an appropriate option for pain in specific, restricted circumstances as outlined within the RFL clinical guideline. The Committee emphasised its use for inpatients only, and supported the addition to the NCL Joint Formulary, though organisations should develop a clinical guideline to support clinicians prior to adoption in routine practice. The RFL team offered to share their clinical guideline for other Trusts to adapt.

Decision: Approved
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: No
Additional information: 10mg or 25mg QDS (dose based on hepatic/renal function). For acute pain in 4 specific cohorts (neuropathic pain & persistent postsurgical pain; patients with a history of high opioid consumption prior to surgery or trauma; patients with a poor opioid response; patients in hyperalgesia states). Trusts to create local clinical guideline for the use of oral ketamine before adding to local formularies.

7.2 MHRA EAMS: Voxelotor for the treatment of haemolytic anaemia in patients with sickle cell disease

The Committee were informed that voxelotor had recently been approved for an MHRA EAMS, which is open to Acute Trusts in NCL. JFC had previously approved a FOC scheme in a limited number of patients in NCL, and the data which informed the original approval was also the basis of the MHRA EAMS. The Committee were satisfied that the previous approval could be applied to the MHRA EAMS.

Decision: Approved under EAMS
Prescribing: Secondary care only
Tariff status: N/A – Free of charge
Funding: N/A – Free of charge
Fact sheet or shared care required: No

8. New Medicine Reviews

8.1 Cladribine for highly-active relapsing-remitting multiple sclerosis in years 3 and 4 (Applicant: Dr H Wilson, UCLH)

The Committee considered a free-of-charge (FOC) scheme for cladribine, a nucleoside analogue that is cytotoxic to lymphocytes and monocytes, for the treatment of highly active or rapidly evolving severe relapsing-remitting multiple sclerosis (RRMS) in years 3 and 4 post-initiation. To date, cladribine has been available for initiation in patients with RRMS for a duration of two years only as per NICE TA616. It is now proposed that re-initiation of cladribine during years 3 or 4 post-initiation may be preferable in patients who have demonstrated a response to cladribine and tolerated 2 years of treatment, rather than switching to an alternative therapy.

The data to support the use of cladribine in years 3 and 4 comes from an extension to the pivotal CLARITY study. CLARITY was a 96-week, Phase III, placebo-controlled double-blind study to compare the efficacy and safety of cladribine and placebo for patients with RRMS with at least 1 relapse in the past 12 months and a maximum score of 5.5 on the EDSS disability scale (n=1,326). Patients were randomised to cladribine 3.5mg/kg over 2 years, cladribine 5.25mg/kg over 2 years or placebo. The primary endpoint, annualised rate of relapse at 96 weeks, was significantly lower with cladribine 3.5mg/kg compared to placebo (0.14 vs. 0.33; relative risk reduction 58% [p<0.001]). Cladribine 3.5mg/kg gained licensure following this study for up to 2 years treatment.

An extension to the CLARITY study was subsequently conducted. Patients were eligible if they had completed CLARITY and had normal lymphocyte counts and haematological results. There was a median of 40.3 weeks gap between CLARITY and enrolment into the extension study. All patients who previously received placebo were placed on cladribine 3.5mg/kg over 2 years; all patients who previously received cladribine were randomised to either cladribine 3.5mg/kg over 2 years or placebo (i.e., 5 treatment groups in total). Two key subgroups were identified; those who received cladribine for 2 years followed by placebo for 2 years, with a total cumulative dose of 3.5mg/kg over 4 years (CP3.5) and those who received cladribine for 4 years in total, with a total cumulative dose of 7mg/kg over 4 years (CC7). Compared with the CP3.5 group, there was a non-significant trend to a lower annualised relapse rate (0.10 [95% 0.06 to 0.13] vs 0.15 [95% CI 0.09 to 0.21]), with a relative reduction in risk by 35.54% [RR = 0.65 [95% CI 0.39 to 1.08]). In other outcomes, there were small improvements in the proportion of patients who remained relapse-free (81.2% vs 75.6%) and the proportion of patients free of confirmed 3-month EDSS progression (77.4% vs 72.4%) in favour of patients in the CC7 group. Limitations of the extension study include the lack of a pre-planned protocol (and hence all outcomes were exploratory), the length of gap between CLARITY and the extension study, and patients were not selected to continue into the extension based on their disease activity.

In terms of safety, compared with the CP3.5 group, cladribine use in the CC7 group was associated with a higher proportion of patients with lymphopenia (36.6% vs. 9.2%) and leukopenia (10.2% vs 1.0%). Rates of lymphopenia and leukopenia in the CC7 group were also higher than patients who received placebo for years 1+2, followed by cladribine 3.5mg/kg in years 3 and 4. The SPC for cladribine does suggest a higher rate of neoplasm or malignancy versus placebo, though results of a meta-analysis by Pakpoor et al found no difference in malignancy rate versus other treatments of multiple sclerosis versus placebo over two years of treatment (though no evidence currently exists to demonstrate similar results after 4 years of cladribine treatment). According to a study by Sormani et al, patients receiving cladribine had a full response to the COVID vaccine (though other possible multiple sclerosis treatments, such as fingolimod, ocrelizumab, ofatumumab and rituximab demonstrated a significantly impaired response to the vaccine). A recent MHRA alert has recommended that liver monitoring is undertaken before each treatment course of cladribine. Cladribine is associated with an increased risk of Herpes Zoster infection.

In terms of convenience, cladribine is a pulsed oral therapy (up to 20 treatment days over 2 years), whereas other RRMS treatments are typically given as either IV infusion, SC injection or daily oral tablets. Cladribine is one of several treatment options which do not require outpatient clinic attendance. Several alternative RRMS treatments list serious adverse effects such as progressive multifocal leukoencephalopathy, which cladribine does not; therefore, cladribine is considered to have a lower overall burden to the patient.

In terms of budget impact, cladribine is being offered free of charge by the manufacturer for this cohort of patients. There are an estimated 40 patients within NCL who may benefit from treatment. The use of cladribine would reduce outpatient clinic attendance, and reduce costs of alternative treatments given by IV infusion in clinic.

The Committee heard from Dr Wilson that cladribine is a preferred treatment option for reasons of convenience and safety. Dr Wilson highlighted that there was also limited evidence in switching to alternative treatments for years 3 and 4, however this was accepted in practice. Lymphopenia is usually transient, appearing for 2-3 months during treatment but resolving over the following 9 months (subsequent courses can be held until lymphopenia resolves). Patients have routine blood tests to check LFTs and lymphopenia, with patients who have severe lymphopenia receiving prophylactic acyclovir to reduce the risk of Herpes Zoster infection. There are several limitations with other treatment options, and

clinicians are reassured with the information to support cladribine use in patients receiving the COVID vaccine.

In camera, the Committee discussed the available evidence and were persuaded by several arguments in terms of safety and convenience of using cladribine versus other available therapies. The Committee discussed whether the FOC scheme potentially undermines use of alternative NICE approved licensed therapies, but noted previous precedents for expanding the useful life of a treatment where this offered significant advantage over switching to alternatives. The Committee were informed that discussions are taking place at NHSE regarding cladribine treatment in years 3 and 4 and beyond, which may impact the outcome of the NCL JFC decision. In order to reduce the possibility of inequity of access to treatment, the Committee agreed to defer the decision until more information was available from the NHSE discussion; if a policy is not imminent, the Committee will consider a decision for NCL patients at the April JFC meeting.

Decision: Deferred

8.2 Medicines used in the management of cholestatic pruritus (Applicant: Prof D Thorburn, RFL)

The Committee considered an application for medicines used in the management of cholestatic pruritus (including colestyramine, colesevelam, bezafibrate, naltrexone, sertraline and rifampicin) for patients with Primary Biliary Cholangitis (PBC) or Primary Sclerosing Cholangitis (PSC). JFC had previously approved rifampicin and naltrexone in 2016. Bezafibrate was reviewed in December 2020, but the decision was deferred until a treatment pathway was created. The order of therapies suggested by JFC did not align with guidance from the British Society of Gastroenterology (BSG) or the European Association for the Study of the Liver (EASL), hence further consideration of treatment hierarchy was requested. A proposed pathway was presented to the Committee, which included the addition of colesevelam and sertraline (not previously reviewed by JFC), and consideration for rifampicin to be used 3rd line ahead of naltrexone and sertraline (JFC had previously recommended rifampicin to be used last-line due to concern about the effects on the liver with rifampicin and wanted to support antimicrobial stewardship).

Colestyramine, a bile acid sequestrant, was historically on the NCL Joint Formulary and is the only licensed therapy for the relief of pruritus with primary biliary cirrhosis. Colesevelam, an alternative bile acid sequestrant, was considered for patients who have a contraindication or intolerance to colestyramine. Colesevelam was studied by Kuiper et al in a 3-week, double-blind, placebo-controlled study to compare the efficacy and safety of colesevelam and placebo for patients with cholestatic pruritus (n=38). Patients were randomised to colesevelam 1875mg daily or identical placebo for 3 weeks; 14 patients had PBC and 14 patients had PSC. The primary endpoint, ≥40% reduction in pruritus measured on a 10-point visual analogue scale (VAS), was not significantly different between groups (36% vs. 35%; [p=1.0]). Mean serum bile acid levels were comparable at baseline, though bilirubin levels at the end of treatment was significantly lower with colesevelam compared to placebo (73 micromol/L vs 212 micromol/L [p=0.01]). Key limitations of the study include the imbalance of liver aetiologies between groups, patients enrolled included those who were previously treated and those who were treatment naïve, the relatively small sample size and short duration.

Sertraline, an SSRI, was considered for use in patients as a last-line therapy. It was studied by Mayo et al in a two-part study for patients with pruritus due to liver disease. Part A was a dose-escalation study (n=21); following exclusions, patients entered into Part B – a double-blind, placebo-controlled crossover study to compare the efficacy and safety of sertraline and placebo (n=12). Patients were randomised to sertraline (at the dose previously determined to be optimal for that individual) or matching placebo for 6 weeks; following a 4-week washout period, patients were re-assigned to the other therapy for a further 6 weeks. The primary endpoint, the mean itch improvement on a 10-point VAS, was significantly better with sertraline compared to placebo (-1.86 points vs 0.38 points [p=0.009]). In secondary outcomes, the proportion of patients who met the pre-defined threshold of ≥20% improvement in pruritus score, was significantly better with sertraline compared with placebo (8 out of 12 patients vs 0 out of 12 patients [p=0.002]). Key limitations of the study include having only those who were successful on sertraline continuing into the double-blind phase (and therefore had a lower baseline itch at the start of Part B), the possibility of carryover effects from other treatments, the small sample size and short duration.

A further study investigating the role of sertraline which was available in abstract only was discussed. Ataei et al conducted a 4-week, single-blind, active-comparator study to compare the safety and efficacy of sertraline versus rifampicin for the management of cholestatic pruritus (n=36). Patients with either PBC or PSC were randomised to either sertraline 100mg daily or rifampicin 300mg daily for 4 weeks. The authors

state that pruritus was relieved in both groups, with no statistical difference in "pruritus management" [p=0.740] or total bilirubin level [p=0.106], though hepatobiliary enzyme levels were significant raised with rifampicin compared with sertraline [p<0.01]. As the study was in abstract, it could not be critiqued further.

The Committee were provided with an overview of evidence which supported previous evaluations, including evidence from the BEZURSO and FITCH studies previously reported in the JFC December 2020 minutes. Rifampicin and naltrexone were previously considered by the Committee with evidence from a Cochrane review by Siemens et al; an updated meta-analysis found the standard mean difference in pruritus scores (using different VAS scales) with rifampicin was -1.73 (3 studies [95% CI -2.45 to -1.02]) and the mean difference in pruritus scores on a 0-10 VAS scale with naltrexone was -2.26 [2 studies [95% CI -3.19 to -1.13]). Limitations of the studies reviewed include that they were relatively short with small sample sizes, and due to different methods of measuring the outcome in the rifampicin studies, it is not possible to directly compare rifampicin and naltrexone results. The Cochrane review did not include the study by Ataei et al (above) or a study by Mansour-Ghanaei et al, who conducted a 2-week single-blind crossover study in patients with cholestatic pruritus with various aetiologies (including PBC and PSC). Patients were reviewed at baseline, then given placebo for 1 week, followed by naltrexone 50mg for 1 week. Statistical improvements were seen with both placebo and naltrexone in day and night itch scores measured on a 0-10 VAS scale, though the reduction in VAS was significantly better at the end of treatment with naltrexone compared to placebo [p<0.001]. Limitations of the study include the single-blind crossover design and the mix of aetiologies.

In terms of safety, the risk of adverse events of most treatments were fairly well established due to use in other indications. However, there were concerns of note with rifampicin. Firstly, there is a risk of thrombocytopenia, haemolytic anaemia and renal failure. Secondly, there is a risk of hepatotoxicity (supported by findings from the Ataei et al study amongst others). Finally, there has historically been concern with the use of rifampicin for non-infectious indications. A consultation was conducted prior to JFC with microbiology specialists in NCL. Feedback includes that rifampicin is useful, particularly for TB, staphylococci and MRSA as it has good tissue and biofilm penetration. Therefore, clinicians were concerned of the risk of antimicrobial resistance, particularly if patients demonstrate poor compliance. Whilst the risk of resistance may be reduced if used in very small patient numbers, it would be prudent to reserve the use of rifampicin as a last-line therapy in patients for whom all other therapies were exhausted, not tolerated or contraindicated.

In terms of budget impact, treatment costs range from £18 per patient per annum, to £970 per patient per annum. It was estimated that there would be 30-40 new patients requiring treatment per year; based on the proposed pathway, approximately 10 patients may benefit from rifampicin per annum. The budget impact was difficult to estimate as it was dependent on the choice of therapy used, and patients seen by the service may reside outside of NCL. The highest potential budget impact was considered to be £9,400 per annum. Patients who do not respond to treatment would be considered for a liver transplant, which is a significantly larger resource impact to the NHS.

The Committee heard from Professor Thorburn in acknowledgement of the available data being sparse, and the apparent high response to placebo in studies. He highlighted the national and international guidance, and the impact of cholestatic pruritus on patients' quality of life, in particular due to disturbed sleep. Therapies are rarely used in combination as they are stopped if intolerable or not efficacious, however this may be considered if there is a partial response.

In camera, the Committee were supportive of a treatment pathway to support management of cholestatic pruritus which included colesevelam (for patients who were intolerant to colestyramine), and sertraline as treatment options. There was, however, concern with the proposed use of rifampicin ahead of naltrexone and sertraline, particularly given the feedback from the microbiology community and the study by Ataei et al – which although in abstract only, is one of the few active comparator studies and found no difference in efficacy between rifampicin and sertraline. The Committee concluded that all medications were suitable for addition to the NCL Joint Formulary, but required a pathway which placed rifampicin as last-line. A guideline to support ongoing prescribing in primary care was encouraged.

In summary, the Committee agreed to add colestyramine (first line), colesevelam, bezafibrate, naltrexone, sertraline and rifampicin (last line) to the NCL Joint Formulary for the management of cholestatic pruritus.

Decision: Approved
Prescribing: Secondary care initiation; primary care continuation
Tariff status: In tariff
Funding: Trust and CCG
Fact sheet or shared care required: No
Additional information: RFL hepatology to update pathway and create a guideline to support ongoing prescribing in primary care, including monitoring requirements.

8.3 Sucroferric oxyhydroxide (Velphoro) for hyperphosphataemia for patients with CKD (Applicant: Prof J Cunningham, RFL)

The Committee considered an application for sucroferric oxyhydroxide (SFOH), an iron-based phosphate binder for hyperphosphataemia in adult chronic kidney disease (CKD) stage 4 or 5 patients on dialysis, and paediatric patients with CKD stages 4 or 5 (eGFR <30ml/min/1.73m^2) or with CKD on dialysis.

The Committee first reviewed the evidence for adult patients. Floege et al was a 27-week, Phase III, active-comparator controlled, unblinded study to compare the efficacy and safety of SFOH and sevelamer carbonate (SC) for adults on dialysis. Patients with a serum phosphate at least 1.94mmol/L were included in the study (n=1,059). Patients were randomised 2:1 to 1g to 3g of SFOH or SC 4.8g to 14.4g per day. The primary efficacy endpoint was an analysis of the superiority of SFOH maintenance dose compared with SFOH low dose in maintaining the phosphate lowering effect in people on haemodialysis; low dose was proven to be ineffective in a previous phase II study. The secondary endpoint of interest, an analysis of the non-inferiority of SFOH compared with SC in lowering serum phosphate in people on dialysis found that the difference of 0.10 (0.03) mmol/L (97.5% CI –infinity to 0.16) was less than the predefined margin and therefore SFOH was non-inferior to SC. Key limitations of the study were its open-label design, different starting dose than a licensed dose (1.5g daily), last observation carried forward approach with imputed data, differing patient characteristics (8% patients on peritoneal dialysis), and lack of patient-orientated outcomes. The study met its sample size calculation at recruitment to demonstrate 80% power in secondary outcomes.

A European public assessment report (EPAR) reports that the change from baseline to week 12 in phosphate levels was statistically significantly greater with SC than with SFOH. At week 12, more patients on SC were within a target range compared to SFOH (54.7% compared with 44.8%, OR 0.69, 95% CI 0.52 to 0.91, p=0.01). However, by week 24 there was no statistically significant difference between the groups based on observed cases (54.4% with SC compared with 52.6% with SFOH, p=0.949).

The Committee further reviewed the available evidence in paediatrics. Greenbaum et al was a 24-week, Phase III, active-comparator controlled, unblinded study to assess the safety and efficacy of SFOH in paediatric patients with CKD. Children aged between 2 to 18 years old with eGFR<30ml/min (20%) or stage 5 CKD, on at least 2 months of dialysis were included in the study (n=85). The primary efficacy endpoint, change in serum phosphate levels from baseline to the end of stage 1 in the SFOH group was not statistically significant. Secondary outcomes included change in serum phosphate from baseline to the end of stage 2 in both treatment groups. In the overall population 80% were CKD patients on dialysis (67% on haemodialysis and 13% on peritoneal dialysis). A sample size calculation was conducted but not met.

NICE guideline (NG203) recommends SFOH as a treatment option in adults with CKD stages 4 or 5 who have raised serum phosphate after calcium acetate or sevelamer carbonate, in patients who do not require a calcium-based phosphate binder. NICE reviewed the evidence in paediatrics by Greenbaum et al and did not recommend SFOH in children with CKD to manage hyperphosphataemia.

In terms of safety, SFOH had a higher risk of gastrointestinal disorders such as diarrhoea, vomiting, gastritis and discoloured faeces compared to SC in adult patients. Side-effect profile was similar in paediatric patients.

In terms of budget impact, 50 adults at RFL and 50 children at GOSH are anticipated to receive treatment with SFOH, which will incur an additional cost of £217,783 per annum.

The Committee heard from Prof Cunningham that SFOH is better tolerated and reduces pill burden for CKD patients who are already subject to polypharmacy. Improved compliance by reducing polypharmacy is clinically meaningful as a main cause of hyperphosphataemia in CKD patients is non-adherence to phosphate binders. Prof Cunningham stated that lanthanum chewable tablets cause significantly more

gastrointestinal side-effects compared to SFOH, thus its use a last line therapy in NICE guidelines is appropriate for patients who have failed calcium and non-calcium containing phosphate binders.

Prof Cunningham proposed that patients would be initiated in secondary care with ongoing monitoring and dose adjustments taking place in dialysis units. He proposed that ongoing prescriptions could be supported in primary care, with any dose changes communicated to primary care via clinic letters.

In camera, the Committee was in consensus that the evidence supported clinical use of SFOH in line with NICE guidance, i.e. for adults with CKD stage 4 or 5 on dialysis after calcium acetate and sevelamer carbonate (in whom a calcium-based phosphate binder is not required). The Committee noted that the NICE guidance found the evidence in paediatrics extremely limited, and therefore did not include SFOH as a treatment option in the NICE guideline (NG203) for management of hyperphosphataemia in children or young people with CKD. The Committee agreed that the NICE position should also be adopted for paediatrics in NCL.

The Committee heard that Velphoro® is a high-cost drug commissioned by NHSE that will be included in the block contract for 2022-23. The Committee requested the contract and commissioning team to confirm whether the anticipated patient numbers were appropriately accounted for within block calculations. The Committee noted that block funding arrangements may create a financial barrier to transfer of prescribing to primary care, but agreed that this was the preferred option to facilitate patient care closer to home.

In summary, the Committee agreed to add Velphoro® to the NCL Joint Formulary for adult CKD patients on dialysis in line with NICE guideline (NG203) pending clarification that appropriate funding is in place via the block contract. Clarification was also sought on whether financial mechanisms would be a barrier to transfer of prescribing to primary care. With the aid of a shared care protocol or fact sheet, Velphoro® was considered clinically suitable for transfer to primary care prescribing.

Decision: Approved
Prescribing: Secondary care initiation, primary care continuation (pending clarification of funding mechanism for primary care prescribing and development of a shared care protocol or fact sheet)
Tariff status: TBC
Funding: NHSE commissioned via block contract (to be confirmed by NCL Contract & Commissioning Team)
Fact sheet or shared care required: Yes

9. Review of budget impact from use of sustainable inhalers

In January 2022, the Committee considered a request to amend the inhaler choices on the NCL Joint Formulary in favour of those which are more environmentally sustainable. The Committee requested further review of potential mechanisms to offset the significant budget impact.

JFC Support presented an update to the Committee. The budget impact estimated previously was based on data from PrescQIPP which included an assumption that patients on salbutamol inhalers each receive two inhalers per annum. The average number of salbutamol inhalers per patient in NCL is 4.4 per annum; therefore, the estimated budget impact if all inhalers in NCL were switched to the new inhaler choices would be closer to £1m (if no changes to current prices, product selection and prescribing rates). The majority of this impact (88%) is a result of using salbutamol dry power inhalers. The Committee heard that there will be new devices and propellants produced in the near future, and therefore this budget impact would be subject to change.

In terms of reducing salbutamol overuse, data from NHS BSA from December 2020 to November 2021 demonstrated that 28,000 patients in NCL were issued six or more salbutamol devices. This correlated to a total of 159,000 salbutamol devices overprescribed. Reducing the overprescribing of these devices could reduce the estimated budget impact by £284,000 and reduce the carbon footprint by 4.2 million kg/CO_2. The Committee heard that the inhaler related indicators in the Impact and Investment Fund (IIF) would be restarted soon; both indicators could be met without the use of salbutamol dry powder inhaler devices. However, the NCL Inhaler Sustainability Group provided feedback acknowledging the high cost but stating that remains value in having the salbutamol dry powder devices available in NCL, particularly as (i) the roadmap to future practice is gradual with further changes anticipated in the future, therefore the estimated budget impact may not be reflective of the actual change; and (ii) there is a pan-London inhaler formulary in development which will include salbutamol dry powder devices, and therefore adding these now will prevent inequity of access across London.

The Committee acknowledged the fluctuating market and availability of new devices and propellants was likely to affect the actual budget impact, particularly as the shift in inhaler use would be gradual. They also acknowledged that reducing overprescribing of salbutamol would offset some of this cost in the future. The Committee were in favour of aligning priorities of the sustainability agenda across London, and supportive of adding salbutamol dry powder devices as proposed to the NCL Joint Formulary to ensure consistency with the pan-London inhaler formulary which is in production. Other amendments to the inhaler formulary (as proposed in the January JFC meeting) were also supported. The Committee agreed the focus should be on clarifying criteria, place in therapy and preferred inhaler options, rather than restricting available options.

In summary, the Committee agreed to the list of amendments to the inhalers on the NCL Joint Formulary (addition of Salbutamol Easyhaler® (for patients aged 4 onwards), addition of the triple therapy inhalers Enerzair® and Trimbow® (for use in adults with asthma), preferred use of Salamol® pMDI over Ventolin® pMDI, and restricting the use of Flutiform®). The Committee requested the NCL Inhaler Sustainability Group to finalise the inhaler formulary guidance for use and determine criteria to support safe switching of patients' therapy alongside optimisation of inhaler use.

Medicine: Salbutamol Easyhaler® (for patients aged 4 onwards); Enerzair® and Trimbow® (for use in adults with asthma); Salamol® Evohaler (used in preference to Ventolin® Evohaler)
Decision: Approved
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Trust and CCG
Fact sheet or shared care required: Deferred to the NCL Inhaler Sustainability Group to finalise the inhaler formulary guidance and determine criteria for switching patients' therapy; must be prescribed by brand

Medicine: Flutiform® - restrict initiation to respiratory specialists only when alternatives have been tried, or continued only where it is thought to be clinically inappropriate to switch
Decision: Approved
Prescribing: Secondary care initiation; primary care continuation
Tariff status: In tariff
Funding: Trust and CCG
Fact sheet or shared care required: Deferred to the NCL Inhaler Sustainability Group to finalise the inhaler formulary guidance and determine criteria for switching patients' therapy

10. Any Other Business
N/A

11. Next meeting
Thursday 21st April 2022