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Academic Health Science Partnership

NHS
North Central London
Joint Formulary Committee

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Thursday 30th July 2015
Room 6LM1, Stephenson House, 75 Hampstead Rd

Present:	Prof R MacAllister	NCL JFC Chair	**(Chair)**
	Mr P Gouldstone	NHS Enfield, Head of Medicines Management	
	Ms N Shah	NHS Camden, Head of Medicines Management	
	Dr D Bavin	Camden CCG, GP	
	Mr C Daff	NHS Barnet, Head of Medicines Management	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Dr R Breckenridge	UCLH, DTC Chair	
	Mr A Dutt	NHS Islington, Head of Medicines Management	
	Mr A Shah	RNOH, Chief Pharmacist	
	Dr R Sofat	UCLH, Consultant Clinical Pharmacologist	
	Ms W Spicer	RFH, Chief Pharmacist	
	Ms P Taylor	NHS Haringey, Head of Medicines Management	
	Mr C Daff	NHS Barnet, Head of Medicines Management	
	Mrs J Cope	GOSH, Chief Pharmacist	
	Ms B Brese	NEL CSU, Deputy Director & Chief Pharmacist	
	Dr M Kelsey	Whittington, DTC Chair	
	Ms S Drayan	NMUH, Chief Pharmacist	
In attendance:	Mr J Minshull	NCL JFC, Support Pharmacist	
	Ms I Samuel	RFH, Formulary Pharmacist	
	Mr P Bodalia	UCLH, Principal Pharmacist (Formulary and Clinical Trial)	
	Mr K Thakrar	UCLH, Medicines Management Pharmacist	
	Mr A Barron	NCL JFC, Support Pharmacist	
	Dr A David	UCLH, Consultant Foetal Medicine	
	Dr F Sedra	RNOH, Spinal Surgery Fellow	
	Prof A Nathwani	UCLH, Consultant Oncologist	
	Dr H Lachmann	RFH, Consultant Auto-inflammatory diseases	
	Dr J Read	RFH, Consultant Anaesthetist	
	Ms C Best	UCLH, Clinical Nurse Specialist	
	Mr E Hindle	MEH, Formulary Pharmacist	
	Dr F Bennett	Registrar, Clinical Pharmacology	
	Dr L Wu	UCLH, FY2	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Mr I Man	Whittington, Interim Deputy Chief Pharmacist	
	Mr B O'Farrell	RFH, Critical Care Pharmacist	
	Dr R Doherty	UCLH, FY1	
Apologies:	Prof L Smeeth	NCL JFC Vice-Chair	
	Dr R Kapoor	UCLH, Consultant Neurologist	
	Mr T James	MEH, Chief Pharmacist	
	Dr R Fox	RNOH, DTC Chair	

2. Meeting observers

Prof MacAllister welcomed the applicants and observers to the meeting.

3. Minutes of the last meeting

These were accepted as accurate.

4. Matters arising

4.1 Vitamin D Pathway

The Committee reviewed the updated Vitamin D guideline, which incorporated the recommended changes as per the May 2015 meeting, noting that the heading should also be changed to reflect it as being an NCL document. The guideline was approved subject to this revision.

4.2 Human foetal Mesenchymal Stem Cells (hfMSC) for treatment of Osteogenesis Imperfecta (Applicant: Dr A David)

Following a review of the above application and supporting data at the last meeting, the Committee deferred their final decision pending a response to their questions, specifically the importation of this Advanced Therapy Medicinal Product (ATMP) and the details of patient consent. The applicant, Dr David, was invited to attend the July meeting.

The Committee heard from Dr David that hfMSC are extracted from human foetal liver using a protocol developed by the Haematology & Regenerative Medicine Unit at the Karolinska Institute, Sweden. hfMSC are isolated using plate adhesion techniques and will be supplied to Dr Lowdell at the HTA/MHRA licensed Centre for Cell, Gene & Tissue Therapeutics at the RFH. The RFH will culture the hfMSC as an ATMP, provide the Qualified Person's release and supply this to UCLH / GOSH in response to a specific prescription as an unlicensed 'special'.

The Committee was advised that there is one patient (Patient C) who received an *in-utero* transplant under a compassionate use scheme in advance of the clinical trial and there is a view that this patient requires a booster transfusion at GOSH. There are currently no other patients who have been identified as needing an *in-utero* transplant. The Committee was informed that the trial for *in-utero* and post-natal hfMSC transfusions in severe OI was expected to recruit from December 2015. It was understood that two new patients with OI might be identified before the start of the trial, however, all patients would be encouraged to take part in the trial once the trial opens to recruitments.

Based on the additional information provided, the Committee agreed that HfMSC should be made available to 'Patient C' only for delivery at GOSH on compassions grounds. In light of the upcoming clinical trial and limited data currently available, the Committee also agreed that HfMSC treatment should not be approved for new patients identified prior to the trial opening for recruitment, or for patients who decline to participate in the trial.

4.3 Rheumatoid arthritis pathway

Ms Taylor informed the Committee that minor amendments to the Rheumatoid arthritis pathway had been requested. These amendments would be finalised outside of the Committee meeting and the approved version would be uploaded onto the JFC website.

5. Declarations of relevant conflicts of interest

None were declared

6. New Medicine Reviews

6.1 Evicel for closure of Dura Mater [APPEAL] (Applicant: Dr K Rezajooi, RFH; Presentation: Mr P Bodalia)

The Committee heard that an application for Evicel had been reviewed and not approved by the JFC in March 2013. The evidence reviewed was limited to a phase III trial and one *in-vitro* study. The phase III trial was placebo-controlled and therefore could not establish superiority over the cheaper alternative, Tisseel currently used in practice. The *in-vitro* study demonstrated higher tensile strength of fibrin clots produced by Evicel compared to Tisseel however the Committee could not ascertain whether the stronger clots were of clinical significance and therefore agreed that this should not be approved.

In January 2015 the RNOH DTC reviewed an appeal application and concluded that the higher tensile strength associated with Evicel may be beneficial in high-risk patients provided such patients could be clearly defined within a protocol. The RNOH DTC agreed to include Evicel on the RNOH Formulary under the Category of Evaluation for 20 patients with the intention that audit data should be collected and submitted to the NCL JFC after this point. The cost of Evicel for these 20 patients was borne by the RNOH.

The Committee reviewed the submitted audit data which included 20 cases of Evicel compared with 19 matched-control patients who received Tisseel. The control patients were matched by sex, age and procedure. All cases were reviewed retrospectively for presence of a post-operative cerebrospinal fluid (CSF) leak, re-operative rate (for repair of CSF leak), wound healing, pseudomeningocele formation and length of stay.

The total number of Evicel and Tisseel units used were 21 x 5ml and 41 x 2ml, respectively. There were no product related complications or post-operative complications with Evicel with a mean length of stay (LOS) of 23.3 days (range 6-52 days). For patients treated with Tisseel, there were no product related complications, however 25% had a post-operative CSF leak, 20% developed pseudomeningocele and the mean length of stay was 25.6 days (range 8-187 days). The between treatment differences for post-operative CSF leak was statistically significant (p=0.02) however differences for pseudomeningocele and mean length of stay were not significant.

In addition to the above results, Dr Sedra advised the Committee of the practical benefits of Evicel compared with Tisseel, including:

- Evicel is quicker to reconstitute than Tisseel which is advantageous for managing inadvertent CSF leaks.
- Fibrin sealant wastage may be reduced as Evicel can be used for up to 30 days once removed from the freezer however Tisseel needs to be discarded 6 hours post-reconstitution
- Although re-operation rates were documented as being zero in both patient groups, patients are transferred to NHNN / RFH for re-operation secondary to Tisseel failure. The Committee were informed that resealing a CSF leak is more complicated than the first seal, requiring insertion of a ventriculoperitoneal shunt; therefore Evicel with superior sealant properties may reduce the requirement for complex neurosurgical interventions.
- The Committee heard the price per unit of Evicel is higher than for Tisseel however fewer units per patient are required; therefore the net cost for Evicel was similar.

In summary, the Committee were satisfied that Evicel is quicker to reconstitute, incurs less wastage and is associated with a reduction in post-operative CSF leaks compared to Tisseel. The funding of fibrin sealants is already established with the commissioners. Although the cost of Evicel is higher per ml than Tisseel, fewer units per patients are required therefore the cost difference is likely to be relatively small, which would be offset by the avoidance of a hospital admission for repair of a CSF leak. The Committee therefore agreed to add Evicel for closure of Dura Mater to the NCL Joint Formulary, subject to CCG funding approval.

Action: Mr Shah to confirm funding arrangements for Evicel with Barnet CCG

6.2 Idelalisib for first-line p53 deleted chronic lymphocytic leukaemia (CLL) (Applicant: Dr K Cwynarshi, RFH and Prof A Nathwani, UCLH; Presentation: Mr K Thakrar)

The Committee reviewed an application for idelalisib as first-line treatment in patients with Chronic Lymphocytic Leukaemia (CLL) and 17p deletion or TP53 genetic mutation.

CLL is the most common leukaemia in adults with an annual incidence of 3-4 cases per 100,000. The natural history of CLL is extremely variable and survival times range from 2 years to 20 years. First-line therapy for CLL is with fludarabine + cyclophosphamide + rituximab (FCR) although there is a strong association between genetic disease profile and patient outcomes. Patients expressing the p53 gene are less likely to respond to chemo-immunotherapy, and survival times from the start of treatment are 2 to 3 years shorter. Patients with the 17p deletion also have poor outcomes; Hallek et al., 2010 showed that the proportion of patients achieving complete response with the FCR regimen in a group without the 17p deletion was 44.1%, compared to only 2.3% in a group with the 17p deletion. Patients with 17p deletion or TP53 genetic mutation are currently treated with off-label alemtuzumab in combination with high-dose oral steroids.

Idelalisib is a first-in-class phosphate-dyli-inositol 3 kinase (PI3Kσ) inhibitor. The PI3Kσ enzyme is usually overactive in CLL and is involved in the proliferation of malignant cells. Idelalisib is licensed for the treatment of CLL in combination with rituximab for patients with refractory CLL that have received at least one prior therapy (currently funded within the NHS via the Cancer Drugs Fund (CDF)), and as first-line treatment in patients with the 17p deletion or TP53 genetic mutation and who are unsuitable for chemo-immunotherapy (not funded via the CDF).

The Committee reviewed the evidence for idelalisib in CLL with 17p deletion or TP53 genetic mutation, which was limited to subgroup analyses of CLL trials. One single-arm, phase II study investigated the efficacy of idelalisib + rituximab in treatment naïve patients with CLL (n=64, abstract only). Overall 67% of patients (n=43) completed the 12 months study without any progression. Of the 43 patients, 41 entered the extension phase to continue treatment with idelalisib. The authors report progression-free survival (PFS) at 36 months was 83%. The overall survival (OS) at 36 months was 90%. Importantly, only 9 patients from the initial 64 had the 17p deletion or TP53 genetic mutation. Additionally, 4 out of these 9 patients (44%) had discontinued treatment within the first 12 months; the remaining 5 patients were in remission at 12 months.

The second study reviewed by the Committee was a multicentre, randomised, double-blinded, placebo-controlled trial which assessed the safety and efficacy of idelalisib (n=220). Eligible patients had CLL that had progressed within 24 months of their last treatment and were not able to receive any further cytotoxic agents. Patients were randomised to either rituximab + placebo or rituximab + idelalisib. The primary endpoint was PFS; secondary endpoints included OS, response rates, and safety. Approximately 40% (n=88) of the patients had either the 17p deletion or the TP53 genetic mutation. PFS at week 24 was 93% for idelalisib versus 46% for placebo; HR 0.15 (95% CI 0.08-0.28; p<0.001). The treatment effect of idelalisib was similarly favourable in all pre-specified subgroups; 17p or TP53 HR 0.12 (95% CI 0.02-0.32). OS at 12 months was 92% versus 80% in the placebo arm and overall response rate was 81% (95% CI 71-88%) versus 13% (95% CI 6-21%) for idelalisib and placebo respectively.

The Committee reviewed the evidence for off-label alemtuzumab as it is the current standard of treatment. One single-arm, open-labelled trial investigated the efficacy and safety of alemtuzumab in previously untreated and previous treated CLL patients with the 17p deletion or TP53 genetic mutation. Alemtuzumab was administered three times a week for 16 weeks. Overall 32 patients (82%) achieved an objective response; 14 patients (36%) achieved a complete response and 18 patients (46%) achieved a partial response. Six patients (15%) progressed during therapy whilst one patient (3%) had stable disease. The median PFS and OS were 11.8 months (95% CI 6.5 to 18 months) and 23 months (95% CI 16.4 months to not reached).

The Committee also reviewed the evidence for ibrutinib, which is licensed for the treatment of patients with CLL who have received at least one prior therapy, as well as for the first-line treatment in the presence of 17p deletion or TP53 genetic mutation in patients unsuitable for chemo-immunotherapy. One multi-centre, open-labelled, randomised, phase 3 trial investigated the efficacy and safety of ibrutinib versus ofatumumab in patients with relapsed or refractory CLL or SLL (small lymphocytic lymphoma). Patients were randomised to receive either oral ibrutinib or intravenous ofatumumab. The primary end point was PFS, with secondary end points including OS. Ibrutinib significantly prolonged PFS, with PFS that was not reached at a follow up at 9 months compared to 8.1 months for ofatumumab; HR = 0.22 (96% CI 0.15 to 0.32, p<0.001). Amongst patients with the 17p deletion or TP53 genetic mutation, the median PFS was again not reached in the ibrutinib arm compared to 5.8 months in the ofatumumab arm. OS at 12 months was 90% in the ibrutinib arm versus 81% in the ofatumumab arm, HR = 0.43 (95% CI 0.24 to 0.79; p = 0.005).

The Committee considered the incidence of Grade 3-4 adverse reactions for idelalisib and found that neutropenia, anaemia and pneumonia were experienced in 34%, 25% and 10% of patients respectively. Ibrutinib appeared to be associated with a lower incidence of these adverse events (16%, 5% and 7% respectively) whereas alemtuzumab had a higher incidence of neutropenia and anaemia and a high incidence of infection including CMV (64.1%, 30.8% and 51.3% respectively).

Idelalisib is administered orally twice daily in combination with 8 rituximab infusions; alemtuzumab is administered intravenously 3 times a week; and ibrutinib is administered orally once daily.

With regards to treatment costs, idelalisib and alemtuzumab are available at zero cost under a manufacturer-led compassionate access scheme with an agreement that patients commenced on treatment will be entitled to continue to receive free supply until disease progression even after the compassionate access scheme closes. Ibrutinib costs £5,150 for a four week cycle with an estimated cost of treatment per patient of £82,400.

To put the application into context, the Committee heard from Prof Nathwani that the TP53 mutation in CLL is rare, representing only 10% of the 300 patients seen at UCLH. Furthermore the population with CLL are typically over 74 years old therefore the adverse event profile and convenience in delivery of treatment is an important consideration when prescribing therapy. It was noted that ibrutinib is licensed for this indication. Prof Nathwani informed the Committee that clinical experience suggests that idelalisib and ibrutinib are equally well tolerated, however its use is restricted in patients with thrombocytopenia or who are also on anticoagulation therapy.

In consideration of the above information, although the Committee noted that idelalisib would be supplied free of charge there was uncertainty on whether the cost of rituximab and associated administration costs would be funded. NICE Technology Appraisal 174 recommends the use of rituximab as first-line treatment for people with CLL without p17 deletion/TP53 mutation in combination with fludarabine and cyclophosphamide; however it is unknown whether NHS England would fund first-line ritixumab for patients with TP53 mutation when given in combination with idelalisib.

The Committee approved the compassionate access scheme for idelalisib pending confirmation that NHS England will fund the rituximab component of the treatment regimen.
Action: Mr Thakrar to confirm that NHS England will fund rituximab infusion and drug costs for 1st line management of CLL with p17 deletion/TP53 mutation

6.3 Tocilizumab for amyloidosis (Applicant: Dr H Lachmann, RFH; Presentation: Ms I Samuels)

The Committee reviewed an application for tocilizumab as the first line treatment for AA amyloidosis and / or recurrent fever syndromes due to auto-inflammatory disease whose chronic inflammatory activity has not responded to other agents, initiated by Consultants in the National Amyloidosis Centre (NAC) at RFH only.

The Committee heard that AA amyloidosis is the most serious potential complication of disorders associated with chronic inflammation. Most patients with AA amyloidosis have amyloid deposits in the kidneys which results in progressive renal insufficiency, poor quality of life and substantial mortality. The fibrils in the amyloid deposits are formed from amyloid A protein which is derived from serum amyloid A protein (SAA) therefore the key aim of treatment is to achieve sustained suppression of SAA.

The Committee reviewed the evidence available which is currently limited to an unpublished case series from the NAC. Twenty patients with a variety of inflammatory disorders refractory to other treatment were recruited between 2010 and 2014; 70% (n=14) had developed AA amyloidosis including 4 which has undergone renal transplant and 2 on dialysis. The underlying inflammatory disorders were rheumatoid arthritis (RA, n=7), systemic juvenile idiopathic arthritis (sJIA, n=4), MKD (n=2), Castleman's (n=1), with 6 cases unclassified. All patients had received at least one previous line of treatment with an anti-cytokine therapy or disease-modifying anti-rheumatic drug (DMARD) although many patients were extensively pre-treated. Median SAA was 70mg/L (95% CI; 38-158mg/L) pre-tocilizumab; this was reduced to 4mg/L (95% CI; 3-7mg/L) after 10 days and sustained at 5mg/L (95% CI; 3-8mg/L) after 23 months (95% CI; 13-35 months). Of the 14 patients with AA amyloidosis, 12 had renal impairment; the 6 patients with native renal function showed a mean reduction in proteinuria of 3.4g/24hrs post-treatment compared to pre-treatment. Stable amyloid deposits were observed in 4 patients with AA amyloidosis and 9 showed regression of amyloid.

In terms of safety, the Committee acknowledged that tocilizumab has been available for several years for patients with RA; the most common, but manageable, adverse event observed in practice is infection.

The Committee were informed by Dr Lachmann that AA amyloidosis is a very rare disease which is becoming rarer with only 20 new cases per year within the UK. The demographic for amyloidosis shifted with the advent of biological agents for inflammatory arthritis. The better control of inflammation achieved has been responsible for a reduction in newly diagnosed cases of AA amyloidosis. Dr Lachmann

clarified that the application also includes use of tocilizumab in patients with Fever Syndromes that were at high risk of developing amyloidosis and who were not responding to first-line anti-inflammatory treatment. The Committee noted that one of the patients listed within the NAC case series was a 6 year old child. Dr Lachmann further clarified that children with amyloidosis would be eligible for treatment with tocilizumab and that treatment would be provided at GOSH under a joint care arrangement with the NAC.

With regards to cost, the Committee heard that the cost per patient per annum is approximately £9,500 and that NHS England would be asked to fund on an individual basis on the basis of rarity as described above.

In conclusion, the Committee agreed to add tocilizumab on the NCL Joint Formulary as a treatment option for AA amyloidosis and / or recurrent fever syndromes in patients whose chronic inflammatory activity has not responded to other agents, subject to individual funding being approved by NHS England.

6.4 Ropivacaine continuous infiltration via Painbuster for nephrectomy or breast surgery (Applicant: Dr J Read, RFH; Presentation: Mr B O'Farrell)

The Committee reviewed an application for continuous surgical wound infiltration (CSWI) using ropivacaine via the Painbuster Device (On-Q) for post-operative pain relief in live donor nephrectomy or patients undergoing Deep Inferior Epigastric Perforators (DIEP) flap breast reconstruction.

The Committee heard that the current management of post-operative pain includes paracetamol and intravenous opioid analgesia delivered by a patient controlled analgesia (PCA) syringe pump. The additive after-effects of the general anaesthetic and the PCA (nausea, excessive sedation, dizziness, constipation, urinary retention, respiratory depression and cognitive impairment) may delay mobilisation and prolong hospital stay. These problems are largely attributable to the amount of opioid given and can be avoided or minimised by providing adjunctive or alternative pain management techniques which reduce the opioid requirement.

The Committee were informed that the CSWI technique is an alternative approach to pain management in surgical patients, with popular use in the orthopaedic setting. It involves infiltrating the surgical wound continuously with local anaesthetic (ropivacaine 0.2%) via an elastomeric pump (PainBuster®). A loading dose of 10ml ropivacaine 0.2% is first injected by the surgeon into the wound space via two catheters and this is followed by continuous wound infiltration at a rate of 4ml/hour for up to 60 hours post-op.

The Committee heard evidence from two large systematic reviews and meta-analyses. The first publication evaluated the efficacy of CSWI in delivering local anaesthetic for postoperative analgesia for various surgeries; cardiothoracic (n=14), orthopaedics (n=12), general surgery (n=11), and gynaecology-urology (n=7). Studies were published between 1983 and 2006, including bupivacaine (n=34) and ropivacaine (n=9). Results showed that CSWI was associated with a significant decrease in visual analogue scores at rest (weighted mean difference -10mm, $p<0.001$) and visual analogue scores with activity (weighted mean difference -22mm, $p<0.001$). Patients were less likely to need opioid rescue (OR 0.15, $P<0.001$) and total daily opioid use was lower (-11mg, $p<0.001$). The length of hospital stay was reduced by one day ($p=0.04$). It was noted that the heterogeneity between studies was high, in part due to data from different procedures and different anaesthetics being combined.

The second publication reported a systematic review and meta-analysis of continuous local anaesthetic wound infiltration versus epidural analgesia for postoperative pain following abdominal surgery. The trials used levobupivacaine (n=4), bupivacaine (n=1) or ropivacaine (n=4). There were no statistically significant differences between treatments in the pain scores at rest after 24 hours (eight RCTs) or 48 hours after surgery (seven RCTs), nor for pain on movement at 24 hours (seven RCTs) or 48 hours after surgery (six RCTs); all analyses were subject to statistically significant heterogeneity.

The Committee also reviewed a prospective, double-blinded, placebo-controlled trial of 168 patients undergoing open nephrectomy. Patients were randomized to receive a CSWI infusion of either 0.5% ropivacaine or 0.9% saline delivered by an elastomeric pump (ON-Q PainBuster) through two multi-holed soaker catheters. All patients were provided with PCA morphine according to the hospital standard of care for breakthrough pain. The primary endpoint was the mean reduction in VAS at 24 and 48 hours. Pain intensity, both at rest and during coughing, was significantly decreased by the continuous infusion of

ropivacaine in the active group. Morphine consumption was also significantly reduced with mean differences of 5.8mg at 24 hours and 10.3mg at 48 hours. A cost-analysis which included costs of drugs and devices, operating theatre costs (based on a mean cost per hour), and hospital length of stay costs concluded that CSWI was cost-minimising with an overall saving of €273 (approximately £192) per patient.

With regards to safety, the Committee were informed by Dr Read that CSWI is a safe technique with no significant side effects or harm, as reported in the studies reviewed. Trial data and local experience suggests that CSWI is not associated with an increased risk of infection as catheters are inserted in a sterile surgical environment and the devices are not interfered with post-operatively.

The Committee considered whether the opiate sparing effects of CSWI were clinically significant as the main meta-analysis reported a modest median reduction of 11mg per day, also noting that the opiate sparing benefits vary according to the surgery. Dr Reid informed the Committee that DIEP flap breast reconstruction is a very painful procedure and patients often take up to 100mg morphine per day. The surgical team at RFH has completed a local audit of a local anaesthetic intermittent infusion in advance of this application (not using the Painbuster) which showed a 52% reduction in PCA opiate usage and 47% reduction in non-PCA opiate usage.

The Committee further questioned whether there was an alternative [cheaper] way of administering the local anaesthetic, such as via a syringe driver. An alternative CSWI infusion system from Baxter (PainFusor) was discussed but considered less suitable for this application as the PainFusor does not have a Y-site connection to allows one system to deliver local anaesthesia to two areas (and would thus double the cost). The Committee acknowledged that the NPSA have previously issued a safety alert against systems which have cross connectivity with IV lines, therefore a dedicated CSWI infusion system is required to meet the recommendations of this alert. The Committee also heard that the PainBuster device is small and easily portable which encourages patient mobility in keeping with the aim of an enhanced recovery experience.

Lastly, the Committee considered the choice of local anaesthesia within the device, bupivacaine or levobupivacaine being alternatives. Currently, supply problems within the UK seem to be the dominant reason for having access to all 3 preparations within the Formulary.

In conclusion, the Committee agreed that ropivacaine for CSWI via the PainBuster device was safe, reduces opiate requirements and may reduce total length of stay. The Committee therefore agreed to include this combination on the NCL Joint Formulary for the post-operative management of live donor nephrectomy and for patients undergoing Deep Inferior Epigastric Perforators (DIEP) flap breast reconstruction.

7. Midodrine for Autonomic Nervous System disorders

Mr Minshull informed the Committee that a licensed version of midodrine (2.5mg and 5mg tablets) is now commercially available in the UK. In 2013 it was agreed by the UCLH DTC that unlicensed midodrine supply would be repatriated into the Autonomic Unit at the NHNN as drug costs were substantially lower within secondary care than available via the FP10 route. With the availability of a licensed version, midodrine would now be easily available in primary care and prescribing could be repatriated to GPs.

The Committee heard that midodrine was also used at the RFH for dialysis induced hypotension however prescribing for this indication should remain at the Dialysis Unit as it was considered off-label and in-tariff.

It was queried whether prescriptions for the licensed midodrine should be prescribed by brand name to avoid the risk of the unlicensed version being dispensed. The Committee agreed that generic prescribing was important and that the issue of risk should be negligible as wholesalers are no longer permitted by the MHRA to importer unlicensed midodrine.

In summary, the Committee agreed that the Formulary status of midodrine should be updated to ‘specialist initiation’ where midodrine should be initiated in secondary care (for example by the Autonomic Unit) and considered appropriate for transfer to primary care after dose stabilisation. For

existing patients currently receiving midodrine therapy via secondary care, the Committee agreed that these patients would be eligible for repatriation to their GP.

Action: Mr Minshull to liaise with secondary care units to ensure that an appropriate handover letter is provided at point of repatriation and / or transfer

Action: CCG Heads of Medicines Management to ensure that the GP prescribing software is updated to direct prescribing to the licensed product

8. Fosfomycin for Lower Urinary Tract Infections

Mr Minshull informed the Committee that a licensed version of fosfomycin (3g granules for oral solution) is now commercially available in the UK for the management of urinary tract infection (UTI) caused by a sensitive organism.

The Committee heard that patients who are resistant to first and second-line primary care empirical treatment would have a urine sample sent by their GP to secondary care for sensitivity analysis. The microbiology service at the respective unit would test for sensitivity to all agents but release advice on sensitivities in a logical manner i.e. only list fosfomycin as a possible treatment option if the UTI is resistant to all first-line oral antibiotics and / or the patient is unable to receive certain antibiotics due to documented allergy. In the event that fosfomycin is required, practices currently refer the patient to secondary care to obtain a prescription and supply of unlicensed fosfomycin. The availability of licensed fosfomycin will enable treatment to remain with the GP.

Dr Kelsey informed the Committee that fosfomycin for UTI is given as a single dose (repeated after three days in men). The alternative management for patients with symptomatic ESBL would be inpatient admission for intravenous antibiotics.

The Committee agreed that fosfomycin should be added to the NCL Joint Formulary and may be prescribed by GPs in accordance with its Marketing Authorisation for patients with symptomatic UTI who are resistant to / unable to receive first-line oral antibiotics and have a proven sensitivity to fosfomycin.

Action: CCG Heads of Medicines Management to ensure that the GP prescribing software is updated to direct prescribing to the licensed product

9. NEL/NCL MMN ophthalmic pathways (BRVO and CRVO)

These were approved.

Action: Mr Bodalia to upload to the JFC website

10. Shared Care / Factsheet Process

As part of improving the process of patient management within NCL, the Committee discussed a revised process (further to the NCL Prescribing Guidance, Appendix 4) whereby the Medicines Optimisation Network (MON) would undertake the necessary background work and present the finalised Shared Care / Factsheets to JFC for ratification.

Action: All Committee members to email Mr Minshull with specific comments regarding the process

11. JFC Annual Report

A report of JFC activity (October 2013 to March 2015) was circulated for information. Overall, the running costs for Year 2 were lower than for Year 1, however this has come at the expense of limited development. Despite this, the number of new medicine applications reviewed in Year 2 was similar to Year 1 with the JFC continuing to take a more conservative approach to its recommendations than neighbouring Area Prescribing Committees resulting in a secondary-care cost-avoidance in the region of £440k. A new section on Planned Activities / Future Priorities is included which has been developed following feedback from CCG Committee members. Lastly, the Committee were informed that the draft report is to be updated with data from a recent cost-analysis which analysed the impact of JFC decisions on GP prescribing.

Action: Mr Bodalia to circulate the final version to the Committee members

12. Local DTC recommendations / minutes

Month	DTC site	Outcome
June 2015	WH	No new drug submissions
June 2015	RFH	NICE TAs only (Ustekinumab for PsA and Axitinib for renal cell carcinoma)
June 2015	NMUH	Sugammadex for emergency use only for patients who cannot be ventilated. Audit report requested in one year. NICE TAs (rifaximin for hepatic encephalopathy and lenalidomide for low or intermediate risk myelodysplastic syndromes)
June 2015	UCLH	Levobupivacaine to replace bupivacaine for pain management and surgical anaesthesia in adults and children. Indocyanine green for for sentinel lymph node detection in endometrial cancer. Lubion® to replace the Gestone® (for assisted reproductive technology)
July 2015	WH	Levofloxacin as second line treatment for H.Pylori eradication, Pelvic inflammatory disease (PID) and epididymo-orchitis

13. Next meeting

Thursday 27th August, 4.30pm – 6.30pm, Room 6LM1, Stephenson House, 75 Hampstead Rd.

14. Any Other Business

Ms Drayan informed the Committee that the NMUH DTC has received an application for mepacrine (management of Rheumatoid Arthritis, RA). This is a medicine which is currently available on the Formulary at other Trusts within NCL (pre-JFC). The JFC agreed that mepacrine is a very old treatment for RA and is most likely listed on local Formularies pre-DTC as part of an amnesty following their implementation. On this basis the Committee agreed that mepacrine should be available at NMUH with the method of implementation devised by the NMUH DTC. The Committee noted that such inconsistencies across the sector are likely to be identified as part of the Joint Formulary venture which is listed within the Planned Activities section of the Annual Report.