NCL Joint Formulary Committee (JFC) Meeting

Minutes from the meeting held on Thursday 20th March 2014

In Chadwick G07, Gower Street, UCL

1. Present:	Prof R MacAllister	NCL JFC Chair
	Dr R Urquhart	UCLH Chief Pharmacist
	Mr A Shah	RNOH Chief Pharmacist
	Dr D Bavin	Camden CCG, GP
	Mr A Dutt	NHS Islington, Head of Medicines Management
	Ms N Shah	NHS Camden, Head of Medicines Management
	Mr C Daff	NHS Barnet, Head of Medicines Management
	Mr T James	MEH Chief Pharmacist
	Ms P Taylor	NHS Haringey Head of Medicines Management
	Ms L Reeves	C&I Mental Health Trust
	Ms W Spicer	RFH Chief Pharmacist
	Dr R Fox	RNOH DTC Chair
	Dr H Taylor	WH Chief Pharmacist
	Dr R Sofat	Consultant Clinical Pharmacologist, UCLH
	Mr P Gouldstone	NHS Enfield, Head of Medicines Management
	Dr E Boleti	Consultant Oncologist, RFH
	Dr J Hurst	Consultant Chest Physician, RFH
	Ms S Drayan	NMUH Chief Pharmacist
	Mr TF Chan	BCF Chief Pharmacist
In attendance:	Dr J Fullerton	Specialist Registrar Clinical Pharmacology, UCLH
	Dr A Grosso	UCLP Pharmacist
	Ms S Sanghvi	UCLH Pharmacist
	Dr M George	Specialist Registrar Clinical Pharmacology, UCLH
	Dr F Bennett	Specialist Registrar Clinical Pharmacology, UCLH
	Ms I Samuels	RFH Pharmacist
	Mr E Hindle	MEH Pharmacist
	Ms R Allen	Medicines Optimisation Pharmacist, UCLH
	Ms E Kitetere	Pre-registration Pharmacist, UCLH
	Ms R Holland	UCLH Pharmacist
	Dr A Emmanuel	Consultant Colorectal Medicine, UCLH
Apologies:	Dr A Jones	Consultant Oncologist, UCLH & RFH
	Dr L Wagman	Barnet CCG
	Mr A Karr	NCL Procurement Chair
	Dr M Kelsey	Whittington DTC Chair
	Dr R Kapoor	Consultant Neurologist, UCLH
	Dr A Tufail	MEH DTC Chair
	Prof L Smeeth	NCL JFC Vice Chair
	Dr C Cooper	Islington CCG
	Dr C Stavrianakis	Haringey CCG
	Ms J Cope	GOSH Chief Pharmacist
	Ms R Dallmeyer	CSU Pharmacist
	Dr R Breckenridge	UCLH UMC Chair

2. Minutes of the last meeting

Item 1.0: It was noted that Dr Pavan Sardana, Enfield GP was present at the February meeting.

Item 2.3.3: Dr Bavin clarified that under the LMWH guidance, anticoagulation bridging should remain under secondary care, except where a GP anticoagulation service specifically includes bridging therapy.

Item 2.5.4: Ms Samuels questioned what the current position is regarding IFRs for weekly adalimumab for Crohn's pending a change to the tick-box form. The Committee agreed to contact Rebecca Dallmeyer for feedback, but that in the meantime IFRs would not be required for weekly adalimumab, as the tick-box form in its current format contravenes NICE recommendations.

Item 5.3: Ms Shah informed the Committee that the lisdexamfetamine SPC has recently been updated with black triangle monitoring and warnings regarding effects on ability to drive and operate machinery.

3. Matters arising

3.1 Lisdexamfetamine Cost Comparison

The Committee were assured that, overall, lisdexamfetamine is less expensive compared to dexamfetamine sulfate. It was therefore agreed to include lisdexamfetamine onto the Formulary. It was also agreed that lisdexamfetamine would be removed from the Formulary in the event of a price increase rendering it more expensive.

3.2 Overactive Bladder Syndrome Guideline

Dr Breckenridge had met with Mr Wood following the last meeting. Mr Wood has agreed to consider the points raised by the Committee and will discuss with colleagues locally with a view to re-submitting a revised guideline.

4. Terms of Reference

The JFC Terms of Reference (ToR) were reviewed. It was agreed that the ToR should be updated to include reference to the newly-formed London Medicines Evaluation Network and to prevent duplication of effort. It was also agreed that the JFCs remit with respect to NHS England commissioned medicines should also be included. It was suggested that the JFCs support of healthcare professional and patient education should also be added.

5. Membership

The membership of the JFC was reviewed. Prof MacAllister asked the CCG Prescribing Leads whether their CCGs wished to continue to financially support the JFC . It was agreed that Dr Grosso would send the Prescribing Leads the original business case detailing a breakdown of JFC costs and that the Prescribing Leads would raise this locally.

6. Members declarations of relevant conflicts of interest

None were declared.

7. Medicine Reviews

7.1 Omalizumab (Novartis) for atopic dermatitis (Applicant: Prof M Rustin, Presentation: Dr M George)

The Committee reviewed the clinical evidence in relation to the use of omalizumab in atopic eczema. However, the two randomized controlled trials were small and of poor quality. The JFC was unable to ascertain the role of this monoclonal antibody. Furthermore, it was noted that favorable responses to omalizumab have been reported mainly, but not exclusively, in patients suffering with concomitant asthma and in paediatric patients with acute atopic eczema of short duration. The Committee noted that the application was for adults exhibiting a chronic and long lasting course of the disease, many of whom will not be asthmatic.

The Committee considered this use as experimental and that key factors such as dosing and dosing intervals remain to be completely elucidated. Hence, this therapy was not approved by the Committee.

7.2 Linaclotide (Almirall) for constipation-associated irritable bowel disease (Applicant: Dr A Emmanuel / Dr N Zarate-Lopez; Presentation: Ms R Holland)

The Committee reviewed the evidence for linaclotide, a first-in-class, oral, guanylate-cyclase-C receptor agonist recently licensed for the treatment of moderate-to-severe Irritable Bowel Syndrome with constipation (IBS-C). The Committee agreed that linaclotide appears more effective than placebo in treating IBS-C by increasing the number of bowel movements and reducing pain. However, the Committee noted that

(a) no studies have compared linaclotide to existing treatments

(b) that the trial population differed from the refractory population detailed in the application

(c) that the applicant agreed that many of the patients' symptoms were of a psychogenic nature. Accordingly the as yet unknown long-term risks of linaclotide were a concern,

(d) diarrhoea occurred in 19.8% of patients treated with linaclotide versus 3.0% patients on placebo.

The Committee decided on the basis of a vote that linaclotide would not be approved for use.

7.3 Evicel® (Ethicon) for dural sealing (Applicant: Mr A Casey; Presentation: Ms S Sanghvi)

The Committee reviewed the evidence for using Evicel in place of the less expensive fibrin sealant Tisseel for suture support in neurosurgical dural closure. The Committee could identify only one published comparison which was an *in vitro* mechanical study by Hickerson et al which compared the strength and elasticity of fibrin clots formed with each product. The Committee could not ascertain whether the stronger clots formed by Evicel was of clinical significance. It was decided that Tisseel should remain the fibrin sealant on Formulary as it is less expensive and is also licensed for this indication.

7.4 Pregabalin (Pfizer) for Neuropathic Pain (No Application; Presentation: A Grosso)

The Committee reviewed the evidence to support the use of pregabalin in neuropathic pain, following the recent NICE guidance.

Pregabalin, like gabapentin, is an amino acid derivative of gamma-aminobutyric acid (GABA). Pregabalin is the pharmacologically active S-enantiomer of 3-aminomethyl-5-methyl-hexanoic acid, and has a similar pharmacological profile to gabapentin. Both agents modulate calcium influx through a neuronal voltage-gated calcium channel. Pregabalin has greater oral bioavailability (90% vs. 30-60%) and receptor binding affinity (3- to 10-fold) when compared to the parent compound, gabapentin. However, the JFC understood that differences in potency alone do not amount to a significant advantage unless they are associated with greater clinical efficacy, or reduced toxicity. Pregabalin expenditure far exceeds that of all other agents available for use in neuropathic pain.

The NICE guideline (November 2013) suggests that patients should be offered a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment. If the response to the first choice was unsatisfactory, one of the remaining three drugs would then be used, and consider switching again if the second and third drugs tried are also not effective or not tolerated.

The Committee noted that the pooled efficacy and pooled safety parameters included in the NICE health economic asessment cited almost identical probabilitues for both domains between gabapentin and pregabalin. The Committed noted that pregabalin is licensed for twice daily dosing whereas gabapentin is licensed for thrice daily dosing despite the half-life of the two agents being very similar: 6 hours [pregabalin] vs. 5-7 hours [gabapentin]. The Committed noted pregabalin to be almost 7-fold the cost of gabapentin (£47 vs

£322 per patient per month on average). Amitriptyline and duloxetine cost about £8 and £250 per month respectively.

The Committee noted that the NICE Guidelines Development Group (GDG) "*suggested [that pregabalin was] poor value for money in comparison with gabapentin and amitriptyline*". Cost-effectiveness calculations resultant from the NICE modelling suggest that pregabalin is not a cost-effective treatment option when compared to other treatments according to conventional QALY thresholds. For these reasons, the GDG felt it would not be possible to support recommendations that suggested pregabalin as an initial treatment for neuropathic pain. However, the GDG also stated that "*when compared with placebo alone both drugs appeared to be viable options from a health economic point of view*". As a result, the GDG considered it appropriate to recommend these treatments in a context where other options were contraindicated, have been tried and proved ineffective, or not tolerated.

The GDG assumed that the most cost-effective sequence of treatments would be to try the options in order of their individual probability of cost effectiveness (probability of highest net monetary benefit) i.e.

Amitriptyline (13%)
Gabapentin (10%)
Duloxetine (1.3%)
Pregabalin (1.0%)

The Committee noted that this ordering was subsequently dropped by NICE in its final (short version) guidance and that the four agents are now merely listed alphabetically. This arose out of a reluctance to recommend an unlicensed drug (amitryptyline) in preference to licensed alternatives.

The JFC took the view that the prescribing hierarchy should be enforced. Given the similarity of pregabalin to gabapentin, the JFC though it unlikely that pregabalin would be effective where gabapentin was ineffective or poorly tolerated. The JFC though it pharmacologically irrational to expose patients to pregabalin when gabapentin had been ineffective or poorly tolerated. The JFC voted whether pregabalin should be made available as a last-line option. The members voted 12:3 in favour of removing pregabalin from the Formulary for treatment of neuropathic pain. It was agreed that patients already on therapy should not be switched. In essence, the Committee agreed that amitriptyline should be the treatment of first choice. If a patient responded to amitriptyline but suffered intolerable anticholinergic adverse events then a change to duloxetine should be considered. Gabapentin is to remain on Formulary as the GABA analogue treatment option. The Committee suggested that a FAQ document might be useful in helping clinicians understand the rationale for these changes.

8. Local DTC recommendations

8.1. **Desogestrel for Contraception:** Approved at RFH. This decision was ratified by the JFC.

8.2 **Vital 1.5kcal as a sip feed:** Approved at RFH. This decision was ratified by the JFC.

8.3 **Zoledronic acid to replace pamidronate:** Approved at RFH. This decision was ratified by the JFC.

9. Date of next meeting: 24th April 2014

10. Any other business

Ms Spicer suggested that the issue of using Avastin for wet AMD should be discussed at the JFC in light of recent legal precedents in Europe. The Committee asked Ms Spicer to forward these details to Dr Grosso.