NCL Joint Formulary Committee (JFC) Meeting

Minutes from the meeting held on Thursday 26th February 2015

Room 6LM1, Stephenson House, 75 Hampstead Rd

Present:	Prof R MacAllister	NCL JFC Chair	**(Chair)**
	Dr R Sofat	Consultant Clinical Pharmacologist, UCLH	
	Dr R Breckenridge	UCLH UMC Chair	
	Dr D Bavin	Camden CCG, GP	
	Dr M Kelsey	Whittington DTC Chair	
	Dr R Urquhart	UCLH Chief Pharmacist	
	Ms W Spicer	RFH Chief Pharmacist	
	Dr H Taylor	Whittington Chief Pharmacist	
	Mr T James	MEH Chief Pharmacist	
	Mr A Shah	RNOH Chief Pharmacist	
	Ms L Reeves	C&I Mental Health Trust Chief Pharmacist	
	Mr A Dutt	NHS Islington, Head of Medicines Management	
	Ms N Shah	NHS Camden, Head of Medicines Management	
	Mr P Gouldstone	NHS Enfield, Head of Medicines Management	
	Mr TF Chan	BCF Chief Pharmacist	
	Ms P Taylor	NHS Haringey Head of Medicines Management	
	Dr A Tufail	MEH DTC Chair	
In attendance:	Dr T Wagner	Nuclear Medicine Consultant, RFH	
	Dr R Mizoguchi	Consultant Geriatrician, RFH	
	Dr J Summerfield	Consultant Psychiatrist, C&I Mental Health Trust	
	Dr R Henderson	Consultant Ophthalmologist, MEH & GOSH	
	Mr E Hindle	MEH Pharmacist	
	Mr M Wyke-Joseph	NMUH Pharmacist	
	Ms I Samuels	RFH Pharmacist	
	Ms S Sanghvi	UCLH Pharmacist	
	Mr P Bodalia	UCLH Pharmacist	
	Ms F Bennett	Clinical Pharmacology Registrar, UCLH	
Apologies:	Prof L Smeeth	NCL JFC Vice-Chair	
	Dr E Boleti	Consultant Oncologist, RFH	
	Dr J Hurst	Consultant Chest Physician, RFH	
	Dr R Fox	DTC Chair, RNOH	
	Dr R Kapoor	Consultant Neurologist, UCLH	
	Mr J Paszkiewicz	Prescribing Advisor, NCL/NEL CSU	
	Dr L Wagman	Barnet CCG, GP	
	Dr V Thiagarasah	Enfield CCG, GP	
	Dr C Stavrianakis	Haringey CCG, GP	
	Mr C Daff	NHS Barnet, Head of Medicines Management	
	Ms S Drayan	NMUH Chief Pharmacist	
	Mr A Karr	NCL Procurement Consortia Chair	
	Dr P Ancliff	GOSH DTC Chair	
	Ms J Cope	GOSH Chief Pharmacist	

2. Minutes of the last meeting

Ms N Shah sought clarification regarding the Camden DMARD guideline decision from October 2014. At that meeting the Committee approved use of the document pending changes in accordance with clinicians' comments but agreed that it would be helpful to have a more specific shared care document across NCL. Until this is in place it was agreed to approve both the generic Camden guideline across NCL and consider other shared care protocols to support specific conditions. Since this meeting a separate UCLH shared care guideline for IBD has been approved for use between UCLH and Camden only.

Ms N Shah questioned the wording 'pain patent' under item 7 (generic pregabalin). The Committee agreed that although the licensed indication for pregabalin is 'neuropathic pain', the patent is 'pain' and therefore the minutes are correct.

3. Matters arising

3.1 Amyvid for diagnostic testing of Alzheimer's disease (Applicants: Dr T Wagman & Dr R Mizoguchi)

The Committee discussed the appeal letter submitted by the applicants. Prof MacAllister noted that in the paper by Frisoni et al the likelihood ratio of 9.4 for amyloid imaging was for patients with established diagnosis, whereas for those without a confirmed diagnosis the likelihood ratio was 1.7. Dr Mizoguchi reassured the Committee that Amyvid would not be the sole decision making tool but would be used in conjunction with MDT discussion, the clinical picture and neuropsychometric tests to establish a likely diagnosis. The applicants outlined that the role of Amyvid scanning would be limited to a small number of cases, primarily in frontotemporal dementias and primary progressive aphasia. The applicants acknowledged that there is no specific data on the use of Amyvid to differentiate between diagnoses of Alzheimer's disease and these indications, but highlighted data from other similar amyloid tracers.

The Committee raised concerns that the availability of Amyvid would spread to routine use. After detailed discussion it was agreed that use would be restricted to patients under 80 years old with suspected frontotemporal dementia or primary progressive aphasia. It was estimated that there would be at most 10 patients per annum receiving Amyvid. The Committee noted that a new application to the JFC would be required before use would be permitted in other areas, as new evidence is published.

On the basis of these discussions, the Committee agreed to include Amyvid onto the NCL Joint Formulary under Category of Evaluation, restricted to the RFH site only in line with the above criteria, and requested data to be presented after use in 10 patients.

4. Declarations of relevant conflicts of interest

None were declared.

5. New Medicine Reviews

5.1 Aripiprazole MR injection for Schizophrenia (Applicant: Dr J Summerfield; Presentation: Ms L Reeves)

The Committee reviewed an application for prolonged release aripiprazole injection to be used as maintenance treatment of schizophrenia in adults whose condition had been stabilised with oral aripiprazole. The Committee considered the evidence summarised by NICE (Evidence Summary: New Medicine 39) which reported that there are no published head-to-head trials comparing one antipsychotic depot injection with another. Prof MacAllister reminded the Committee that oral aripiprazole was previously rejected at JFC for use in children with autistic spectrum disorder due to the lack of data showing any advantage over risperidone. Ms Reeves informed the Committee that aripiprazole is anecdotally reported as being better tolerated compared with risperidone in some patients due to a lower incidence of weight gain and reduction in prolactin stimulation. Prof MacAllister highlighted that a study by Ghanizadeh et al previously reviewed by the JFC showed no difference between the two agents in terms of safety or tolerability outcomes. Although oral aripiprazole is not on the NCL formulary, it has historically been on the formulary at Camden & Islington Mental Health Trust. The Committee acknowledged the difficulties in switching patients established on oral aripiprazole to an alternative depot injection and on that basis agreed to include aripiprazole prolonged-release injection onto the NCL Joint Formulary, restricted to the Camden & Islington Mental Health site only and restricted to patients already stabilised and responding to oral aripiprazole.

5.2 Intravitreal Bevacizumab for Retinopathy of Prematurity (Applicant: Dr R Henderson; Presentation: Mr E Hindle)

The Committee reviewed an application and protocol for the use of intravitreal bevacizumab in premature infants with stage 3 retinopathy of prematurity (ROP) who are either not suitable for conventional laser therapy treatment or have failed previous laser treatment.

The evidence for efficacy of bevacizumab in ROP is limited to one large RCT and several case series and reports. The BEAT-ROP study (n=150) was a prospective, randomised, controlled, multicentre trial assessing intravitreal bevacizumab monotherapy for zone 1 or zone 2 posterior stage 3 ROP. Inclusion criteria were infants with a birth weight of ≤1500g and a gestational age of 30 weeks or less. Infants were randomly assigned to receive either intravitreal bevacizumab or conventional laser therapy (current standard of care) delivered bilaterally. The primary ocular outcome was recurrence of ROP in one or both eyes requiring retreatment before 54 weeks postmenstrual age. 143 infants survived to 54 weeks' postmenstrual age. The 7 infants who died were not included in the primary-outcome analysis. ROP recurred in 4 infants in the bevacizumab group (6 of 140 eyes [4%]) and 19 infants in the laser-therapy group (32 of 146 eyes [22%], P=0.002). A significant treatment effect was found for zone 1 ROP (P=0.003) but not for zone 2 disease (P=0.27).

The Committee found that the case reports were heterogeneous in nature and mostly without comparator; however, a positive effect on ROP disease with intravitreal bevacizumab was described in all reports.

With regards to determining the safety profile of this treatment, the Committee noted that the BEAT-ROP study was too small to assess safety and adverse effects were not reported. A small case series (n=11) by Sato T et al indicated that bevacizumab can escape from the human eye into the systemic circulation and reduce serum VEGF. In adults the incidence of serious systemic adverse effects are rare with both intravitreal bevacizumab and ranibizumab. The large head-to-head clinical trials in adults showed no statistical difference in serious atherothrombotic events or all-cause-death between bevacizumab and ranibizumab. Case reports describe sporadic local ocular adverse events. Although no systemic adverse events have been described in the literature, the Committee acknowledged that the data discussed are too short-term to highlight any long term ocular or systemic adverse effects.

Dr Henderson informed the Committee that ranibizumab is associated with less systemic exposure compared to bevacizumab. However there are fewer data of its use in ROP and it is considerably more expensive. He will be participating in an upcoming trial of ranibizumab for ROP but on balance of risk and cost, will use bevacizumab until further data is gathered. Dr Henderson also informed the Committee that he has a contract at GOSH and in the previous year has treated two patients at GOSH with intravitreal bevacizumab. The Committee noted that intravitreal bevacizumab is available as a pre-filled syringe (unlicensed product) from two manufacturers at a similar cost.

Overall the Committee agreed to include intravitreal bevacizumab onto the NCL Joint Formulary (in accordance with the submitted protocol as above), restricted to MEH and the neonatal unit at GOSH (which operates in support with MEH).

6 Simeprevir for Genotype 1 Chronic Hepatitis C

This item was referred to local DTCs for implementation due to the recent publication of a NICE technology appraisal.

7 Shared Care: Midodrine for Orthostatic Hypotension

The Committee received an application and shared care protocol from the Whittington Hospital regarding use of midodrine for the management of orthostatic hypotension. The Committee noted that midodrine is currently on the formulary for this indication at RFH and UCLH (pre-JFC). Following review of the published data (which was originally considered at the UCLH DTC), the Committee agreed to extend this decision across NCL. Midodrine was accepted onto the NCL formulary as a second-line option for symptomatic orthostatic hypotension (following inadequate response to first-line fludrocortisone). Dr Urquhart informed the Committee that as midodrine is an unlicensed product, the cost of obtaining this is significantly more expensive in primary care compared to secondary care and on that basis patients within NHS Camden have recently been repatriated to UCLH as part of an NHS cost-efficiency scheme. The Committee therefore agreed that a shared care protocol would not be appropriate, and prescribing should remain with secondary care.

8 NICE Guidance for Diabetes

The Committee discussed the draft NICE guidance for Type 2 Diabetes in adults which is currently under consultation. Mr Gouldstone raised the following concerns:

- Choice of repaglinide as second-line oral option (not currently on NCL formulary)
- Choice of pioglitazone as third-line oral option, taking into account bladder cancer and heart failure risks
- Lower HbA1C targets and lack of target setting in the elderly
- SGLT2 inhibitors not included within the guidance
- Lack of emphasis on use of NPH insulin over analogues

The Committee agreed to forward any further comments to Mr Gouldstone, for submission to NICE on behalf of NCL JFC.

9 Local DTC Recommendations

RFH

- **Z-Mab for Ebola Virus Infection –** Approved for RFH only.
- **Z-Mapp (MIL-77) for Ebola Virus Infection –** Approved for RFH only.
- **Riociguat for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension –** Interim approval for RFH only (free of charge for continuation after end of study).

UCLH

- **Nindetanib for Idiopathic Pulmonary Fibrosis –** Not approved
- **Infliximab biosimilar –** Dr Breckenridge outlined the UMC discussion regarding infliximab biosimilar and potential savings. The UMC agreed that the published data, statements from EMA and NICE and estimated savings supported a 100% switch from Remicade® to infliximab biosimilar, but recognised that patient consultation would be vital for implementation. Dr Breckenridge informed the Committee that UCLH are working on patient information and an FAQ document which would be used in clinics and available online. Once finalised this could be shared across NCL. The UMC are currently in consultation with relevant clinicians to finalise an implementation plan.

10 Next Meeting: 26th March 2015, Room 6LM1, Stephenson House, 75 Hampstead Rd

11 Any other business

Nil