NCL Joint Formulary Committee (JFC) Meeting

Minutes from the meeting held on Thursday 23rd January 2014

In Foster Court, Room 132, Gower St, UCL

1. Present:	Prof R MacAllister	NCL JFC Chair
	Prof L Smeeth	NCL JFC Vice Chair
	Ms W Spicer	RFH Chief Pharmacist
	Dr R Urquhart	UCLH Chief Pharmacist
	Mr P Gouldstone	NHS Enfield, Head of Medicines Management
	Mr T James	MEH Chief Pharmacist
	Mr A Shah	RNOH Chief Pharmacist
	Dr R Fox	RNOH DTC Chair
	Mr TF Chan	BCF Chief Pharmacist
	Ms R Dallmeyer	CSU Pharmacist
	Dr R Kapoor	Consultant Neurologist, UCLH
	Mr A Dutt	NHS Islington, Head of Medicines Management
	Ms R Clark	NHS Camden, Deputy Head of Medicines Management
	Mr C Daff	NHS Barnet, Head of Medicines Management
	Ms E Mortty	NHS Haringey, Prescribing Advisor
In attendance:	Dr A Grosso	UCLP Pharmacist
	Ms S Sanghvi	UCLH Pharmacist
	Ms R Holland	UCLH Pharmacist
	Mr K Thakrar	UCLH Pharmacist
	Ms I Samuels	RFH Pharmacist
	Mr E Hindle	MEH Pharmacist
	Dr S McCartney	UCLH Colorectal Consultant
	Ms M Kaur Singh	CSU Pharmacist, NELCSU
	Mr M Wyke-Joseph	NMUH Pharmacist
	Mr D Wood	Consultant Urologist, UCLH
	Mr N Marshall	RFH Pharmacist
Apologies:	Dr A Jones	Consultant Oncologist, UCLH & RFH
	Dr L Wagman	Barnet CCG
	Mr A Karr	NCL Procurement Chair
	Dr D Bavin	Camden CCG
	Dr M Kelsey	Whittington DTC Chair
	Dr H Taylor	WH Chief Pharmacist
	Dr R Sofat	Consultant Clinical Pharmacologist, UCLH
	Ms L Reeves	C&I Mental Health Trust
	Dr E Boleti	Consultant Oncologist, RFH
	Dr R Breckenridge	UCLH UMC Chair
	Ms N Shah	NHS Camden, Head of Medicines Management
	Dr A Tufail	MEH DTC Chair
	Ms S Drayan	NMUH Chief Pharmacist
	Ms P Taylor	NHS Haringey Head of Medicines Management
	Dr C Cooper	Islington CCG
	Dr C Stavrianakis	Haringey CCG
	Dr J Hurst	Consultant Chest Physician, RFH
	Ms J Cope	GOSH Chief Pharmacist

2. Minutes of the last meeting

The minutes were accepted as accurate.

3. Matters arising

3.1 Degarelix for Prostate Cancer

The Committee reviewed draft guidance from NICE for degarelix in advanced, hormone-dependent prostate cancer. The preliminary recommendations from NICE were broadly consistent with the Committee's previous decisions except that NICE have recommended use of degarelix in patients at risk of impending spinal cord compression. NICE did not recommend antagonist therapy for patients intolerant to agonist treatment. The Committee could find no evidence to support the impending spinal cord compression indication. It was therefore agreed that NICE should be contacted formally with these concerns via the consultation gateway. Degarelix will remain non-formulary in the meantime.

3.2 Strontium Ranelate for Osteoporosis

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended that strontium ranelate should no longer be used to treat osteoporosis in light of cardiovascular safety concerns. The Committee agreed that strontium should be withdrawn from all NCL formularies with immediate effect.

3.3 Low Molecular Weight Heparin Guidance

The Committee reviewed the amended guidance for low molecular weight heparins following the recent consultation process. Concerns were again raised from CCG members regarding capability of GPs to calculate creatinine clearance with the Cockcroft & Gault equation, confidence in communication of transfer of prescribing and that all anticoagulant bridging should be managed in secondary care. However, the Committee agreed that these points were all sufficiently addressed by the updated guidance, and it was therefore approved for use.

3.4 Overactive Bladder Syndrome Prescribing Guidance

Overactive bladder syndrome [draft] prescribing guidance was sent out to stakeholders in NCL for consultation, with the aim to provide an overarching evidence-based treatment pathway. The Committee reviewed the written comments received and heard from Mr Dan Wood, Consultant Urological Surgeon at UCLH, outlining feedback from UCLH Urology, Urogynaecology and Care of the Elderly colleagues.

Mr Wood agreed that oxybutynin immediate-release should be considered first-line but that solifenacin and fesoterodine should also be available prior to considering mirabegron as mono- or dual-therapy. The Committee challenged the choice of solifenacin over [less expensive] generic tolterodine considering their similar efficacy and safety profiles. Fesoterodine was reviewed by the Committee in 2012 and was not approved based on insufficient evidence demonstrating an advantage over pharmacologically-similar tolterodine. The Committee also challenged the evidence-base purporting an advantage in using more expensive modified-release formulations. In addition the Committee noted that other stakeholders had requested use of trospium for patients with cognitive impairment and darifenacin as it is the next anticholinergic to lose market exclusivity.

Prof MacAllister requested that the clinical teams provide evidence to further support their arguments but noted that anecdotal data would not be persuasive.

4. Members declarations of relevant conflicts of interest

None were declared.

5. CCG-Related Medicine Applications and Reviews

5.1 Dolutegravir (ViiV) for HIV-1 infection without integrase resistance (Applicant: Dr M Johnson; Presentation: Mr N Marshall)

The Committee reviewed an application for dolutegravir for HIV-1 treatment-naïve and treatment-experienced patients without integrase resistance. Dolutegravir is a HIV integrase strand transferase inhibitor and does not require boosting with a pharmacokinetic enhancer.

Mr Marshall explained that the application was prompted by a patient at RFH with a complex treatment history. The patient is currently on enfuvirtide but does not have sufficient body mass to continue injecting and the team are reluctant to give raltegravir due to association with multi-drug resistance. The Committee heard that dolutegravir has only just received a UK Marketing Authorisation and that the NHS Price is currently being negotiated by the HIV Clinical Reference Group. It was therefore agreed to defer full consideration of the evidence and application to the NCL formulary until the NHS costs were determined. However the Committee agreed that dolutegravir could be used for the single patient at RFH due to exceptional circumstances.

5.2 Dapoxetine (A Menarini FI SRL) for premature ejaculation (Applicant: Dr M King)

This item was deferred until the next meeting.

5.3 Maintenance anti-TNF therapy for Ulcerative Colitis (Applicant: Dr S McCartney; Presentation: Mr K Thakrar)

The Committee reviewed maintenance anti-TNF therapy with infliximab or adalimumab for ulcerative colitis (UC), on the background of multiple individual funding requested (IFRs) being submitted to the CCGs for this indication. The Committee heard that patients with moderate to severe UC who relapse despite optimal oral treatment are initially given intravenous steroids. Patients who do not respond to steroids are then offered ciclosporin and/or considered for surgery. NICE TA 163 recommends the use of three doses of infliximab for patients in whom ciclosporin is contraindicated or not clinically appropriate. This guidance only relates to the induction course, after which the patient should revert back to maintenance treatment with azathioprine or aminosalicylates if in remission, or to surgery if they fail to respond to anti-TNF.

Dr McCartney explained that for patients who respond to induction infliximab and have been refractory to oral therapy including immunosuppressants, continuation of infliximab with regular review and strict stopping criteria would potentially prevent colectomies or allow patients time to prepare for surgery. This was felt to be particularly important for newly diagnosed patients who are often young and for whom the delay/avoidance of colectomy allows completion of activities such as exams and time to adjust to the disease and implications of surgery on their lifestyle.

The Committee reviewed data from the ACT 1 and ACT 2 studies (n=728 in total); which were randomised, double-blind studies comparing the efficacy and safety of maintenance infliximab to placebo in patients with moderate to severe active UC. Patients were randomised to receive either infliximab 5mg/kg or 10mg/kg or placebo at weeks 0, 2 and 6 and then every 8 weeks through to week 22 (for ACT 2) or week 46 (for ACT 1). The results demonstrated that infliximab was superior to placebo in both the clinical response and clinical remission rates at week 8, and throughout the study, with clinical remission rates of 35% versus 17% at week 54 in the ACT 1 study. There was no significant difference between the infliximab 5mg/kg and 10mg/kg doses.

The Committee further reviewed the ACT 1 and ACT 2 open-labelled extension studies by Reinisch et al. Patients on infliximab were eligible to enter the extension study after completing the main study; however patients discontinued placebo treatment. The primary endpoint was disease activity measured using the Physician's Global Assessment (PGA); quality of life was assessed with the Inflammatory Bowel Disease Questionnaire (IBDQ). The results showed that continued treatment with infliximab was effective in maintaining PGA scores indicative of either no disease or mild disease activity. At week 52, there were 18 patients (8%) that still had no disease or mild disease activity from the initial 229 patients. In terms of health-related quality of life, the mean IBDQ at baseline was 182 and ranged from 192 to 199 throughout the study.

A *post hoc* analysis by Sandborn et al (n=630), investigated whether the remission rates observed in the initial studies led to a reduction in colectomy and hospitalisation rates. The proportion of patients undergoing colectomy at 54 weeks was 14.7% (36) for placebo versus 11.6% (28) for infliximab 5mg/kg and 7.4% (18) for infliximab 10mg/kg. The Committee noted that the difference was only statistically significant for the infliximab 10mg/kg {HR 0.47; 95% CI 0.20 to 0.62: p = 0.007} and not for 5mg/kg infliximab {HR 0.71; 95% CI 0.48 to 1.16: p = 0.166}. The proportion of patients who were hospitalised was 25% (60) in the placebo arm versus 16% (39) in the infliximab 5mg/kg arm and 15% (37) in the infliximab 10mg/kg arm. There were also a smaller number of patients requiring UC-related surgeries/procedures in the infliximab arms during the 54-week analysis (19% versus 14% and 12% respectively).

The Committee reviewed the randomised, double-blind, placebo controlled trial (Sandborn et al; ULTRA 2) in 494 patients to evaluate the efficacy of adalimumab as induction and maintenance in moderate to severe UC. The results showed that clinical remission at week 53 was 17.3% for adalimumab versus 8.5% for placebo. The long-term outcomes of colectomy and hospitalisation rates for adalimumab are yet to be reported.

The Committee heard that commonly reported serious adverse events with infliximab include infections, hypersensitivity and infusion-related reactions, elevation of liver enzymes, and worsening of heart failure. In long-term safety follow-up of clinical studies with infliximab of up to 5 years, representing 6,234 patient-years (3,210 patients), 5 cases of lymphoma and 38 cases of non-lymphoma malignancies have been reported. Long-term safety analyses from the ACT-1 and ACT-2 extension studies (n=230 for infliximab) showed 21.3% of patients in the infliximab arm experienced serious adverse events, including UC flare (4.8%), pneumonia (2.2%), GI bleed (1.7%), haemorrhagic gastritis, nausea, bone fracture, abdominal pain, intestinal obstruction and fever. Five malignancies were reported during the extension studies for infliximab patients. Infusion reactions occurred in 36 of 230 patients (16%) who received an infliximab infusion, with three patients experiencing a serious infusion reaction.

The Committee heard that NICE TA 140 reported a cost per QALY gained of £53,000 and thus maintenance infliximab was not endorsed by NICE. This was obtained using data from the ACT 1 and ACT 2 trials that primarily enrolled a higher number of patients with moderate disease. A manufacturer-funded economic model by Tsai *et al* evaluated the cost-effectiveness of maintenance treatment with infliximab 5mg/kg in moderate-severe UC patients based on data from the ACT I and II studies. This model differed from the original NICE economic evaluation; patient body weight was lower (more appropriate to the typical UK patient weight of 73kg) and the model also incorporated a vial sharing scheme. With these amendments the incremental cost-effectiveness ratio (ICER) for infliximab was reduced to under £20,000 in the remission strategy at 10 years. An unpublished analysis from the manufacturers using the current pan London contract price (average weight of 73kg without vial sharing) revealed a cost per QALY of £24,000.

The Committee heard that approximately 70 patients across NCL would be expected to be suitable for maintenance therapy with anti-TNF, and the choice between infliximab and adalimumab would be based on patient preference and lifestyle. The Committee agreed that continuation of treatment for patients who had responded to induction anti-TNF therapy with either infliximab or adalimumab appears reasonable, but requested a treatment protocol with clear monitoring and stopping criteria. In addition it was noted that funding would need to be confirmed via a single pan-NCL business case, administered via the CSU.

5.4 High-dose anti-TNF therapy for Crohn's Disease

The Committee heard that currently multiple IFRs are being put forward by NCL Trusts for higher dose anti-TNF therapy for Crohn's disease; (1) weekly adalimumab 40mg, (2) infliximab 10mg/kg and (3) six/four weekly infliximab 5mg/kg. However, the Committee noted that NICE TA 187 supports dose-escalation as an option for people whose disease has stopped responding. The current pan-London tick-box forms places an arbitrary time-limit of 12 weeks for this escalated treatment (regardless of response), after which clinicians have been submitting IFRs to continue therapy for responders with varying success. The NICE TA recommends that patients should be reviewed at 12 weeks and that therapy in patients who are not responding should be stopped.

The Committee could not find the basis for the time limits placed on the tick-box form, and agreed that the form was divergent from NICE guidance. It was therefore agreed that IFRs should no longer be required for patients who were responding to higher dose anti-TNF therapy for Crohn's disease and continued to fulfil the NICE criteria. Ms Dallmeyer agreed to investigate amending the NCL tick-box form.

5.5 Subcutaneous Trastuzumab

The Committee discussed a recommendation from NHS England to implement subcutaneous trastuzumab following a financial modelling project. It was agreed to defer this item and contact relevant consultants to submit an application form for review to determine its exact place in therapy and implications of the traztuzumab biosimilar.

6. Local DTC Recommendations

6.1 UCLH

Alicaforsen for Pouchitis: Not Approved at UCLH DTC. This decision was ratified by the JFC.

7. NCL-MMC Minutes

These were made available for information.

8. NCL Prescribing Guidance

The Committee reviewed the updated version of NCL Prescribing Guidance. This was approved pending clarification of Appendix 4 to clearly state that only medicines rarely prescribed in primary care would be considered unsuitable for shared care but that this should not extend to all newly launched medicines.

9. JFC First Year Report

A summary of JFC activity for 2012-13 was included for information.

10. JFC Terms of Reference (CCGs, NHSE, NEL, Commissioning Cycles)

This item was deferred until the next meeting.

11. Meeting Dates and Venues

These were circulated for information.