North Central London
Joint Formulary Committee

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Thursday 29th October 2015
Room 6LM1, Stephenson House, 75 Hampstead Rd

Present:	Prof R MacAllister	NCL JFC Chair	**(Chair)**
	Mr A Dutt	NHS Islington, Head of Medicines Management	
	Ms N Shah	NHS Camden, Director of Quality & Clinical Effectiveness	
	Mr B Sandhu	NEL CSU, Assistant Director Acute Services	
	Mr C Daff	NHS Barnet, Head of Medicines Management	
	Dr E Boleti	RFH, Consultant Medical Oncologist	
	Ms P Taylor	NHS Haringey, Head of Medicines Management	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Mr T James	MEH, Chief Pharmacist	
	Dr R Sofat	UCLH, Consultant Clinical Pharmacologist	
In attendance:	Mr J Minshull	NCL JFC, Support Pharmacist	
	Ms I Samuel	RFH, Formulary Pharmacist	
	Mr P Bodalia	UCLH, Principal Pharmacist	
	Mr A Barron	NCL JFC, Support Pharmacist	
	Mr E Hindle	MEH, Formulary Pharmacist	
	Ms S Sanghvi	UCLH, Formulary Pharmacist	
	Ms H Amer	UCLH, Registrar, Clinical Pharmacology	
	Dr A Shah	UCLH, Registrar, Clinical Pharmacology	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Ms H Mehta	NMUH, Formulary Pharmacist	
	Dr F Bennett	UCLH, Registrar, Clinical Pharmacology	
	Ms E Ng	NHS Islington, Prescribing Adviser	
	Dr D Patel	RFH, Consultant Diabetologist	
	Dr S Naik	UCLH, Consultant Diabetologist	
	Ms S Naidu	Camden Diabetes IPU, Consultant Nurse	
Apologies:	Dr R Breckenridge	UCLH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Dr R Fox	RNOH, DTC Chair	
	Dr M Kelsey	Whittington Hospital, DTC Chair	
	Dr R Kapoor	UCLH, Consultant Neurologist	
	Dr V Thiagarasah	NHS Enfield, GP	
	Dr A Stuart	NHS Camden, GP Lead Medicines Management	
	Ms W Spicer	RFH, Chief Pharmacist	

2. Meeting observers

Prof MacAllister welcomed the applicants and observers to the meeting.

3. Minutes of the last meeting

It was noted that Mr A Dutt was present at the meeting; the minutes were updated to reflect this.

Methotrexate and tiotropium in asthma were both approved for initiation by the Severe Asthma Service only; the minutes were updated to reflect this restriction.

The minutes were otherwise accepted as an accurate record of the meeting.

4. Matters arising

Prof Robinson queried who will take responsibility for the off-label use of tiotropium HandiHaler® in severe asthma, which was approved for use by the Committee at the last meeting. The applicant had been asked specifically during the meeting whether he would be willing to prescribe the HandiHaler device for his severe asthma patients and had agreed to using this device, therefore the prescriber will take responsibility in line with standard prescribing practice.

4.1 NCL Guidelines for Insulin for Type 1 diabetes

Feedback from applicant

The Committee discussed two emails from Dr Rosenthal that commented on the Committees conduct during the insulin items heard on 24th September 2015 (items 4.3, 7, 7.1 and 7.2). The emails raised the following issues:

- Physician centred view of diabetes management
- Lack of consideration of a health economics paper which was submitted as part of the degludec appeal (cost of hypoglycaemia)
- Comments from the Committee that open-labelled studies are intentionally biased, a view which is disrespectful to patients who participate in studies investigating new treatments for Type 1 diabetes
- Discussion of EMA data that had not been circulated prior to the meeting and was too small for the applicant to see
- The discussions and questioning process at the meeting was less collaborative and co-operative than anticipated
- Lack of understanding about the relationship between HbA1c targets and hypoglycaemia

The Committee disagreed that its approach was physician rather than patient-focused. The Committee consists of a number of individuals who are involved in looking after patients with diabetes. Moreover, even if these individuals do not have the expertise of the diabetology teams, the paramount issue is the evidence and its consideration, which is what the Committee is very well versed in. It was however acknowledged that the patients' perspective was valuable and finding a replacement Patient Representative was a priority for the JFC Support Staff.

The Committee confirmed that excluding the health economic paper was appropriate as the key inputs of the deterministic cost-model were populated using a non-systematic literature search. The hypoglycaemia rates were the largest drivers of the 'cost of hypoglycaemia' and these rates were taken from a single study (2007 UK Hypoglycaemia Study Group) with a very small sample of T1DM patients (n=75+52). It was acknowledged that severe and problematic hypoglycaemia was a significant problem in T1DM with costs commonly falling outside of prescribing budgets, however the Committee were not satisfied that the paper accurately quantified this cost due to the fundamental methodological weaknesses.

The Committee upheld their criticism of open-label studies. In contrast to studies of double-blind design, open-label studies are known to introduce risk of assessment bias (from the investigator) and detection or reporting bias (from the subject). The likelihood of introducing bias is higher with subjective endpoints (e.g. hypoglycaemia) than with objective endpoints (e.g. HbA1c or mortality). The Committee criticised those involved with designing insulin trials, clarifying that the investigators and research teams were being criticised and not the subjects. The Committee therefore rejected the accusation that they were disrespectful to patients.

Regarding the EMA data which had not been circulated to the applicants prior to the meeting, the Committee agreed that wherever possible, data would be circulated in advance of the meeting. It was acknowledged that this may not always be possible as members frequently undertake a personal review of applications shortly before the meeting. It was agreed that the onus should be on the applicant to know the available data prior to submitting an application, rather than expecting the Committee to provide applicants with the data underpinning their application.

The Committee were regretful that Dr Rosenthal and Dr Naik felt that the discussions were dismissive and unanimously agreed that a collaborative and evidence-based approach between JFC, Commissioners and Diabetes specialists would result in the best treatment outcomes for patients.

The Committee acknowledge that the relationship between HbA1c targets and hypoglycaemia risk was complex and agreed to discuss the issue with the Diabetologists attending for agenda item 9.

Insulin degludec for T1DM – final appeal process

The Committee heard the NCL Diabetologists had expressed an interest in submitting a final appeal for insulin degludec in adults with an HbA1c >8.5% or problematic hypoglycaemia *or* frequent admissions for diabetic ketoacidosis. The final appeals process involves referring the case to the South East London APC for consideration. It was noted that SEL had already approved insulin degludec for adults with T1DM where psychosocial or other factors indicated the need for longer duration insulin to facilitate continued treatment, *and* insulin degludec is expected to avoid decompensation, *and* patient has had frequent emergency hospital admissions attributed to poorly controlled diabetes, *and* all other therapies have failed. In SEL, degludec is initiated in secondary care and dispensed by hospital pharmacies upon receipt of a signed screening form (which confirms eligibility). Transfer of care to GPs is permitted after a minimum 3 month stabilisation period and positive assessment of benefit. It seems likely that the SEL APC will make a similar decision on degludec where we to refer it to them.

Based on issue data, although approved in SEL, the strict APC approval criteria appears to have prevented widespread use of insulin degludec and the current spend per capita on insulin degludec in SEL is approximately equivalent to NCL (although NCL prescribing varies greatly with greatest prescribing in Barnet CCG). It was noted that Barnet and Chase Farm are typically high users of newer diabetic agents and there were concerns about other Trusts levelling up to this usage. An audit of degludec outcome data was imminent in SEL and the Committee requested that the data be reviewed by JFC and NCL Diabetologists. It was agreed that a close working relationship between JFC and NCL Diabetologists was essential and it was hoped that this relationship would yield substantial savings through encouraging biosimilar glargine. It was suggested that a small working group of the JFC work with NCL Diabetologists to identify the group of patients who would derive the largest benefit from insulin degludec. The NCL and SEL Diabetologists should share experiences and discuss the differences between the different proposed indications. Once the proposed indication for NCL has been refined, the request should be brought back to JFC where a 1-year evaluation period would be considered.

4.2 Melatonin for sleep disorders (visual disturbances) (Applicant: Dr R Quinlivan)

Following a review of the above application in May 2015, the Committee deferred their final decision pending a response to their questions, particularly around the monitoring and stopping criteria that will be used. The applicant, Dr Quinlivan, was invited to provide answers to these questions.

As Dr Quinlivan was unable to attend the meeting, responses per provided in advance via email.

- Approximately 5 patients per annum are transferred from GOSH to NHNN who are receiving melatonin for sleep disorders associated with visual disturbance. These patients come from different areas of England.
- Melatonin is not currently available on the UCLH formulary, treatment cannot be continued.
- Melatonin is preferred to benzodiazepines and Z-drugs as these are associated with hangover effects.
- If melatonin were approved for this indication, Dr Quinlivan would continue to review these patients approximately every six months, and consider a melatonin treatment holiday every eighteen months to determine ongoing efficacy of treatment (based on patient and carer reports of sleep and resultant behaviour).
- The preferred agent is Circadin® 2 mg modified-release tablets (licensed UK medicine) used off-label. The dose is usually 4 mg to 6 mg daily, occasionally increased to 10 mg.

In summary, the Committee agreed that melatonin 2 mg modified-release tablets should be added to the NCL Joint Formulary for use by the NHNN Centre for Neuromuscular Diseases for the management of sleep disorders caused by visual impairment. It was agreed that this would be appropriate for GPs to continue prescribing.

5. Declarations of relevant conflicts of interest

Mr Andrew Barron declared that he has worked with Novartis on Entresto®, mentioned under item 10.
No other conflicts of interests were declared.

6. Local DRT recommendations / minutes

Month	DTC site	Drug and indication	JFC outcome
January 2015	WH	Nebido – Testosterone replacement therapy for male hypogonadism	See item 8.1
June 2015	RFH	Sonovue – Diagnostic agent characterization of liver lesions	Approved for RFH use only
August 2015	RFH	Riociguat (RIOC) – Chronic Thromboembolic Pulmonary Hypertension	Approved for RFH use only
August 2015	RFH	Everolimus (compassionate use) – Advanced or metastatic Pancreatic Neuroendocrine Tumors	Approved for RFH use only
August 2015	RFH	Thalidomide – Arteriovenous malformations	Approved for RFH use only
August 2015	MEH	Simbrinza – Reduction of IOP in adults with Chronic Open-angle Glaucoma / ocular hypertension	See item 7.1

6.1 Glaucoma Prescribing Guidelines

The Committee reviewed an updated guideline for glaucoma that included Simbrinza (brinzolamide/brimonidine). The guideline was approved.
Action: Mr Barron to add the Moorfields glaucoma guideline to the JFC website

7. Rapid Tranquilization in Paediatrics (Applicant: Dr Groszmann, UCLH, RFH, WH; Presentation: Ms Sanghvi)

A rapid tranquilization algorithm for Children and Young People was presented to the Committee to standardise practice across hospitals in NCL. The algorithm is currently in use in at RFH and WH and is primarily designed for adolescents (12 to 18 years) with appropriate doses, and also forms the framework for younger children provided dosing advice from the specialist consultant is sought. The algorithm will only be used by child psychiatry and paediatric senior trainees or consultants and will be supported by a wider guideline which is currently being written. The rationale for including a range of oral, orodispersible and intramuscular preparations that are not licensed for use in children was discussed. It was agreed that orodispersible tablets may have a role in supporting swallowing of the tablet and to avoid IM injections, but it was noted that they are no more rapidly absorbed systemically than other tablet formulations.

The Committee recommended the following amendments be made to the algorithm:

- Include a comment that if the maximum dose of lorazepam has been administered by any route (i.e. including a combination of oral and IM doses), an alternative drug must be used if further treatment is required
- A maximum dose of 5mg IM midazolam has been suggested by the UCLH lead paediatric pharmacist
- The oral risperidone range is at the higher end. This should be adjusted to 0.5 mg to 6 mg to allow the physician to administer smaller doses
- ECG monitoring is recommended where possible with haloperidol
- The time to wait before treatment escalation should be included for all stages and routes of drugs should also be consistently included. For flumazenil the recommended route is IV.

A national audit of the use of psychotropic medicines in children with learning difficulties is scheduled for next year, which may impact on this algorithm, which the JFC will need to remain aware of.

It was agreed that olanzapine orodispersible tablets and risperidone orodispersible tablets should be added to the NCL Joint Formulary for use in rapid tranquilisation of children and adolescents only. The algorithm was approved pending minor amendments as above. The full guideline should be brought back to JFC for NCL wide ratification.

8. New Medicine Reviews

8.1 Nebido (testosterone undecanoate) for hypogonadism (Applicant: Dr Eleftheriou, UCLH, NMUH; Presentation: Mr Barron)

An application was heard for the use of testosterone undecanoate (Nebido) for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests. The Committee were informed that testosterone undecanoate is approved at RFH and WH for thalassaemia, and at UCLH for female-to-male transsexuals aged 16 to 18 transitioning from full dose Sustanon. Nebido is commonly prescribed in NCL with approximately 73% of patients who require intramuscular testosterone already treated with Nebido; of these, 90% of prescriptions are in primary care. The Committee was satisfied that testosterone undecanoate was an established treatment in both primary and secondary care and agreed to add testosterone undecanoate to the NCL Joint Formulary for haematology and for adolescent endocrinology.

8.2 Melatonin for sleep disorders (adults) (Applicant: Dr Eriksson, UCLH; Presentation: Mr Minshull)

An application was heard for the inclusion of melatonin as a treatment option for three sleep-related indications in adults: insomnia in adults aged ≥ 55 years (licensed indication), REM Sleep Behaviour Disorders (unlicensed) and Circadian Rhythm Disorders (unlicensed).

REM Sleep Behaviour Disorder (RBD) is a rare condition characterised by disruptive behaviours emerging during REM sleep, resulting in injuries to the patient and their bed partners. Due to the rarity of the condition, evidence for the efficacy is limited to three prospective studies and one retrospective review. Melatonin treatment reduced the percentage of REM sleep without atonia and sleep onset latency compared to baseline, though the effect was not statistically significant when compared to placebo. The Clinician's Global Impressions score for patients receiving melatonin was statistically significantly reduced compared to placebo treatment. Melatonin treatment had no impact on other sleep variables. The reduction in amount of sleep with atonia was supported by the open-label studies; the retrospective review reported improvements in "control of their RBD" for 12 of 14 patients treated.

Circadian Rhythm Disorders (CRD) describes a range of different sleep conditions caused by intrinsic errors affecting the body's regulating clock. A systematic review and meta-analysis of 5 RCTS including adults treated with melatonin in delayed sleep phase disorder (a type of CRD) was discussed. Melatonin treated patients saw an improvement in time to dim-light melatonin onset and sleep-onset. Impact on wake-up time, sleep-onset latency and total sleep time were not statistically significantly impacted by treatment with melatonin. Two small, single-blind, placebo controlled trials, showed that treatment with melatonin allowed nine of fourteen blind patients with Free Running Disorder (another form of CRD) to synchronise to a normal sleep cycle.

Efficacy of melatonin in primary insomnia was established in three placebo controlled RCTs (1,315 patients in total) and 1 open-label study. Treatment with melatonin demonstrated an improvement in quality of sleep, morning alertness and behaviour following waking compared to placebo [improvement of sleep with melatonin OR 1.97 (95% CI: 1.14 – 3.41)], though it was noted that placebo responders were excluded from the melatonin insomnia studies following a placebo run-in period, which represented a limitation of these studies.

The adverse effects reported for patients taking more than 9 mg melatonin at night (including delusions, hallucinations, headache and morning sleepiness) were raised as a concern by the Committee. It was noted that the most common adverse events experienced during melatonin trials were headache, pharyngitis, back pain, and asthenias, which occurred in both treatment and placebo arms and were not necessarily due to melatonin.

Dr Eriksson explained that patient numbers in trials for RBD are low, but this reflects the reality of the condition, which is very rare. RBD and CRD patients will be seen initially in the Sleep Disorder Service, where they will be monitored regularly for response to treatment with melatonin. Doses in RBD may need to be escalated to achieve an efficacious dose, but this can be done rapidly and it will be possible for the Consultant to stop treatment within a couple of weeks if the patient isn't responding.

The benefit of melatonin over Z-drugs and benzodiazepines in insomnia comes from the lack of hangover effect and less concern about abuse. Medicines used to treat insomnia are usually recommended to be given for a very short period (usually between 2 to 4 weeks), therefore recommending continued prescribing of a medication that can be used for up to 13 weeks sends a different signal about how insomnia should be managed, therefore the Committee recommend that prescriptions should remain in secondary care.

In summary, the Committee was satisfied that melatonin is safe and has a beneficial effect in the treatment of patients with RBD, CRD and insomnia and should be added to the NCL Joint Formulary for initiation in the Sleep Disorders Service. Prescribing of melatonin in RBD and CRD should be initiated by the Sleep Disorder Service and can be transferred to primary care once patients have been stabilised. For insomnia, it was agreed that melatonin should be used second line for up to 13 weeks, after zopiclone, zolpidem, or a benzodiazepine, and prescribing should not be transferred to primary care to avoid a change in practice of this common condition.

9. Review of insulin for Type II diabetes

The Committee reviewed a guideline for insulin in Type 2 diabetes. The guideline was developed jointly by the Camden IPU and JFC support pharmacists, and had been sent to all provider Trusts in NCL for comment. The Camden IPU is a value based commissioned service that provides integrated working between general practice, community diabetes services and hospital services. Dr Dipesh Patel (RFH), Dr Sarita Naik (UCLH) and Ms Shantell Naidu (Camden IPU) attended on behalf of the diabetology clinical team.

Basal insulin

Once-daily Neutral Protamine Hagedorn (NPH) insulin is the first-line agent for the majority of T2DM patients with an HbA1c <9% at baseline. There are three NPH insulins on the market; Insuman Basal, Insulatard and Humulin I with no RCT evidence indicating any differences between them. The guideline therefore recommends Insuman Basal SoloStar as the first-line NPH insulin due to the lowest acquisition cost. For patients with dexterity or visual impairment, Insulatard Innolet is preferred due to the larger dial. It was discussed that although clinicians in NCL have extensive experience of Humulin I KwikPen, the most expensive NPH insulin, the clinical experts acknowledged that the difference in price between Humulin I and Insuman basal was approximately 10% and therefore agreed to prescribe Insuman basal for new patients.

Patients with significant co-morbidities, who are at risk of falling, or have impaired awareness of hypoglycaemia should be considered for a more relaxed HbA1c target and first-line basal analogue, rather than NPH. It was noted that the baseline risk of hypoglycaemia in insulin naïve patients is an important consideration; in accordance with the DARTS Collaboration, the elderly (potentially confusion/dementia and also delayed hormonal response to hypoglycaemia) and those with renal impairment are at highest risk. Tight HbA1c targets are not recommended for these patients, however despite this, hypoglycaemia can still manifest. HbA1c is known to be a poor predictor of hypoglycaemia as it ignores glucose variability. The choice of insulin contributes to glucose variability; NPH is a suspension therefore may absorb at a variable rate (on a day to day basis) whereas glargine forms a depot provides a more predicable profile.

Basal analogues are also considered in patients in line with NICE TA53 (patients with problematic hypoglycaemia on NPH and patients who would require dose escalation to twice-daily NPH insulin). With regards to the choice of analogue insulin; Abasaglar (biosimilar glargine) is the preferred agent. Patients stable on Lantus can be considered for Abasaglar only following patient consultation and demonstration of the new device. The advantages of once-daily analogues over twice-daily NPH are patient convenience, improving concordance to therapy (a twice-daily regimen can be a barrier to treatment intensification) and reduced blood glucose testing. Whilst the Committee were not convinced about the convenience argument, they acknowledged that this had become standard practice following NICE TA53.

The guideline explicitly does not recommend once and twice-daily insulin detemir. The potential benefit of detemir in preventing weight gain was considered when developing the guideline however it was determined that the certain incremental cost was not justified by the potential benefit in this population.

Overall, it was agreed that NCL Diabetologists would gain experience with Insuman Basal. The place in therapy for basal analogue was agreed (in line with NICE TA53 and for patients with significant co-morbidities) and Abasaglar was the preferred analogue agent.

Biphasic insulin

Biphasic insulins are recommended for insulin naïve patients with an HbA1c >9%, patients already on once-daily NPH insulin who experience significant postprandial hyperglycaemia and patients failing to achieve adequate control on once-daily glargine. Biphasic human insulins should be used first-line, however, biphasic analogues were recommended for patients with significant co-morbidities, prefer to inject with meal, and who experience problematic hypoglycaemia or post prandial hyperglycaemia on biphasic human insulin.

The guidelines recommended Humulin M3 or NovoMix 30 however the Committee heard that patients frequently needed more prandial insulin (switching to a Insuman Comb 50 or Humalog Mix50), therefore it was logical to starting these patients on Insuman Comb 25 or Humalog Mix25.

The Committee agreed the proposed place in therapy for human and analogues biphasics and that the preferred agents should be Insuman Comb (25 and 50) and Humalog Mix (25 and 50).

Basal-bolus

It was agreed that the small population with T2DM who require bolus insulin should be treated with rapid-acting analogues to facilitate compliance to therapy.

9.1 Toujeo (insulin glargine 300iU/mL) for Type II diabetes

The guideline proposed Toujeo® for three different populations; those who would otherwise need to split their glargine dose (≥60 units per dose), *or* experience unacceptable variation in blood glucose control secondary to poor-compliance with fixed timed dosing with once-daily biosimilar glargine *or* experience multiple episodes of nocturnal hypoglycaemia whilst using basal insulin analogues.

Large injection volume

There are no maximum doses of Lantus or Abasaglar; the Lantus SoloStar and Abasaglar KwikPen can administer up to 80 units and 60 units per injection, respectively, and doses above this should be divided among two or more injection sites. It was discussed that many patients on Lantus (control arm) in the Toujeo studies were splitting the dose therefore it was accepted that splitting Lantus dose across two sites provides similar outcomes to a single-site Toujeo dose. The Committee were in agreement that injecting doses ≥60 units at a single site was inappropriate therefore discussed the remaining benefits of single-injection site Toujeo vs two-injection site Lantus/Abasaglar.

The Committee heard from the clinical experts that patients on large glargine doses frequently get superior outcomes when they split their dose across two sites however the additional injection can be a barrier for some patients. Switching patients to Toujeo therefore would retain the convenience of single injection dosing whilst reducing the overall injection volume and improving overall insulin absorption. There may be an additional benefit of reducing lipodystrophy although this was not specifically discussed in the clinical trials papers.

It was estimated that 50 patients in Camden are already on high dose glargine and would be eligible for Toujeo. If extrapolated to approximately 250 patients in NCL (5 CCGs), the budget impact of Abasaglar vs equivalent of Toujeo (£185 per person per annum) is approximately £46,000 per annum (Lantus vs Toujeo is £7,600). It was noted that the incremental cost is primarily due to the greater waste expected from giving a higher dose from a single injection.

The Committee raised concerns about the potential for prescribing, dispensing and administration errors with high strength glargine; patients stabilised on Toujeo who are accidentally switched back to Lantus/Abasaglar could develop hypoglycaemia due to differences in bioavailability. The Committee were also unclear as to the population being treated and whether the value of the drug was simply convenience or whether there were other benefits. On balance, the Committee were minded that a potential incremental cost of £46,000 was too much to justify reducing the number of injections sites by 1 per day.

Variation in blood glucose control secondary to poor-compliance with fixed timed dosing with once-daily biosimilar glargine

With regards to Toujeo providing superior glycaemic control for patients who have poor-compliance to a fixed time dosing regimen with once-daily Lantus/Abasaglar, the Committee noted that Toujeo has a slightly protracted duration of action and the SPC allows for dosing ±3hr from the usual time. Evidence to

support this indication originates from Toujeo extension studies where participants were asked to deviate from the usual time of injection at least 2 times per week by 3 hours. This lead to small but potentially significant worsening of HbA1c between flexible and fixed dosing intervals (HbA1c treatment difference in sub-study from EDITION 2 (basal only, was +0.13% [95% CI: -0.152 to 0.415]). Whilst the guideline acknowledges that fixed timed dosing is preferable, it was hypothesised that patients who cannot comply, might do better on Toujeo as there is evidence that flexible-dosing Toujeo is only slightly worse that fixed-dosing Toujeo. The Committee considered the inclusion and exclusion criteria for EDITION 2 and concluded that the population in EDITION 2 was unrepresentative of the proposed population. This was significant as the very small treatment effect observed in EDITION 2 may be even smaller in clinical practice, and the harms may be greater. This was particularly relevant as the clinical trial data had created the proposed indication.

The clinical experts informed the Committee that variation in blood glucose control is not necessarily a compliance problem and it was agreed that this indication could be removed from the guideline. The Committee therefore did not recommend adding Toujeo to the NCL formulary for this indication.

Nocturnal hypoglycaemia whilst using basal insulin analogues

The Committee reviewed the evidence from EDITION 2 and the EDITION 2 extension study. EDITION 2 was a 26-wk, multinational, randomized, open-label, parallel-group, treat-to-target non-inferiority trial investigating the safety and efficacy of Toujeo and Lantus in insulin-dependent T2DM. Baseline characteristics were HbA1c 8.2%, BMI 34.8kg/m2, previous basal insulin dose 64 units/day with approximately 80% taking Lantus before randomisation. Results demonstrated comparable HbA1c between groups (mean difference -0.01%, 95% CI; -0.14-0.12). Confirmed hypoglycaemia (PG<3.9mmol/L or severe) was statistically lower with Toujeo (rate ratio=0.77 [95% CI: 0.63-0.96]) however it was noted that main driver for result was from the large difference in the initial 8 weeks of the study (titration period). Severe hypoglycaemia was comparable between groups however superiority was demonstrated for nocturnal hypoglycaemia (rate ratio=0.52 [95% CI; 0.35-0.77]). In the extension study, HbA1c, confirmed hypoglycaemia, severe hypoglycaemia were all comparable between groups however nocturnal hypoglycaemia remained statistically superior (ratio rate=0.63 [95% CI: 0.42-0.96]).

The Committee discussed that the EDITION trial programme were open-label studies for which there was no justifiable reason. The clinical experts informed the Committee that patients with severe hypoglycaemia were most costly to the health economy however the Committee emphasised that there was no statistical difference between Lantus and Toujeo with regards to severe hypoglycaemia.

The Committee concluded that the treatment effect for nocturnal hypoglycaemia was uncertain due to the open-label trial design and the lack of robust data that Toujeo would reduce the incidence of severe hypoglycaemia. The Committee therefore did not recommend adding Toujeo to the NCL Joint formulary for patients who are experiencing nocturnal hypoglycaemia on Lantus/Abasaglar.

10. New drug submission flow-diagram

The Committee reviewed the process by which new drug applications are reviewed across NCL. It was discussed that a less prescriptive approach was needed for applications submitted in advance of a NICE TA. It was suggested that the diagram be amended to allow the Committee to identify important pre-NICE submissions. The flow-diagram was approved subject to this amend.

11. Process for NHS England Commissioning Policies

This item was deferred to the October 2015 meeting.

12. JFC Action Tracker

This item was deferred to the October 2015 meeting.

13. Next meeting

Thursday 26th November, Room 6LM1, Stephenson House, 75 Hampstead Rd.

14. Any Other Business

Mr A Dutt advised that the layperson member for Islington CCG Medicines Management Committee is interested in joining the JFC. The Committee agreed that an invitation should be sent for attendance at the next JFC as an observer.