AREA PRESCRIBING COMMITTEE MEETING
Birmingham, Sandwell, Solihull and environs
Minutes of the meeting held on
Thursday 14th September 2017
Venue – Birmingham Chamber of Commerce
75 Harborne Rd, Birmingham, B15 3DH

PRESENT:

Dr Paul Dudley	Birmingham CrossCity CCG (Chair)
Dr Lisa Brownell	BSMHFT
Prof Mark DasGupta	Birmingham CrossCity CCG
Satnaam Singh Nandra	Birmingham CrossCity CCG
Hannah Peach	Sandwell & West Birmingham CCG
Kate Arnold	Solihull CCG
Prof Jamie Coleman	UHB NHS FT
Dr Emma Suggett	UHB NHS FT
Tania Carruthers	HoE NHS FT
Katy Davies	HoE NHS FT
Nigel Barnes	BSMHFT
Dr Neil Bugg	Birmingham Women's & Children's Hospitals NHS FT
Dr Sangeeta Ambegaokar	Birmingham Women's & Children's Hospitals NHS FT
Yusuf Asif	Birmingham Women's & Children's Hospitals NHS FT
Melanie Dowden	Birmingham Community Healthcare NHS FT
Ravinder Kalkat	Midlands & Lancashire CSU
Isabelle Hipkiss	Midlands & Lancashire CSU

IN ATTENDANCE:

Mr D. Costello for item 0917/05	UHB NHS FT
Dr S. Samarasekera for item 0917/06	UHB NHS FT

No.	Item	Action

0917/01 Apologies for absence were received from:

Prof Robin Ferner, Sandwell & West Birmingham Hospitals NHST
Inderjit Singh, UHB NHS FT, deputy attended
Dr Timothy Priest, HoE NHS FT, deputy attended
Maureen Milligan, The ROH NHS FT
Elizabeth Walker, Sandwell & West Birmingham CCG, deputy attended
Mary Johnson, South East Staffordshire & Seisdon Peninsula CCG
Jonathan Horgan, MLCSU

The chair informed the members that Alima Batchelor from Birmingham South Central CCG is no longer in post and that representation for this CCG will be picked up by Prof Mark DasGupta and Kate Arnold.

It was confirmed that the meeting was quorate.

0917/02 Items of business not on agenda (to be discussed under AOB)

- Flash glucose monitoring
- Oral methylprednisolone for relapsing multiple sclerosis
- Ethinylestradiol tablets
- Gonadorelin analogues in female patients
- NHS England national consultation on items less suitable for prescribing in Primary Care
- Carteolol eye drops 1% discontinued

0917/03 Declaration of Interest (DoI)

It was confirmed that the APC secretary has only recently requested the committee members to complete their annual declaration of interests. There are some outstanding and members were reminded to submit these at the earliest opportunity. It was also confirmed that all clinicians attending the meeting had completed a DoI.
There were no other interests to declare relating to items on the agenda.

0917/04 Welcome and Introductions

The Chair welcomed everyone to the meeting today. Introductions around the table were carried out for the benefit of new attendees.

The Chair reminded members, that the meeting is digitally recorded for the purpose of accurate minute taking and once the minutes are approved, the recording is deleted by the APC secretary.

0917/05 Gardasil ® injection for recurrent respiratory papillomatosis - New Drug Application

The Chair welcomed Mr Declan Costello, Consultant ENT Surgeon at UHB NHS FT to the meeting and invited him to present the application for Gardasil ® vaccine.

Mr Costello began by stating that he specialises in voice disorders and has a cohort of patients with recurrent respiratory papillomatosis (RRP). This condition is characterised by crops of wart-like growths on the vocal chords.

Historically RRP is treated by surgical debridement with lasers but the issue is that these lesions are recurrent and patients need repeated surgical interventions to keep the airway clear. Some patients require operations every year or two; in some patients this can be every six weeks. RRP tends to be a lifelong condition but can sometimes go into spontaneous remission.

Some papers published over the last few years have suggested that Gardasil®, which is a quadrivalent human papillomavirus (HPV) vaccine against types 6, 11, 16 and 18, may be useful in treating RRP which is known to be caused by HPV types 6 and 11. It appears that the frequency of operations is reduced following use of Gardasil® or that, as in some case reports, the papilloma is completely eliminated.

The mode of action is not entirely clear; however it is possible that there is an immunomodulatory mechanism in which the presentation of the HPV systemically is allowing the papilloma to be cleared.

Increasing the intervals between surgical interventions in this group of patients would not only improve their quality of life but also reduce the cost to the NHS as each operation under general anaesthetic can cost £1,000 to £1,500.

Gardasil® is already given to adolescent girls to prevent cervical cancer; it has recently gone through an evaluation process for it to be given to adolescent boys. The ENT community has been pushing very heavily for boys to be vaccinated as well. However it seems unlikely that this will happen at a national level.

In terms of safety, there is no issue as it is given to all adolescent girls in the national vaccination programme. The biological plausibility for it to work is there. At a cost of £260 for 3 inoculations over 6 months, there is also a cost benefit argument even if a small number of patients were to have longer intervals between operations or even be cleared of their disease.

The Chair invited questions and comments from members. Discussion points/concerns raised included:

- A member asked Mr Costello about the number of patients he sees with this condition, bearing in mind that he has referrals from a much wider area than the APC's geographical footprint. Mr Costello confirmed that, as this is a rare condition, he would expect to have a dozen patients in a year through his clinic.
- It was stated that in the event Primary Care commissioners did not support this application, the alternative would be for the patient to attend three separate out-patient clinics to have the vaccine administered.
- It was confirmed that NHS England was not the responsible commissioner for this condition, as it was estimated that every voice clinic in the country would have a similar cohort of patients as Mr Costello which would add up to more than 1,000 patients.
- A representative went on to discuss the evidence submitted with the application; one paper included 2 case studies and the other paper was a case series and asked the presenting clinician if there was any more robust clinical evidence to support its effectiveness in RRP. The case series appears to show some statistically significant improvements, but in some cases the interval between interventions actually went down. Mr Costello confirmed that there isn't any more robust evidence in RRP; the manufacturers may not consider it worthwhile carrying out trials in this use.

- It was suggested that it may be worth approaching the company to ask about the prospect of funding a trial in these patients.
- A member asked at what age this condition occurred. The clinician stated that it could either be in very early childhood as a result of HPV being picked up through the birth canal, or in early to mid-adulthood. This led to the hypothesis that the current cohort of teenage girls receiving this vaccine would not be expected to develop this condition; unfortunately this could not be said for their male peers.
- It was stated that it would take a couple of decades before any of the geographical epidemiology data coming through could confirm this hypothesis.
- A member asked about the frequency of out-patient reviews by the ENT clinician to ascertain if this corresponded to the dosing schedule of the vaccine. Mr Costello tends to review patients as often as needed, but typically every 4 to 6 months. However if the last surgical intervention was 3 years ago for example, the patient would only be seen every year or 18 months. This very much depends on how aggressive the disease is and varies considerably between patients.
- A member asked why the application stated that this product would not be suitable for immunocompromised patients, as this was not a live vaccine and not contra-indicated in these patients. It was suggested that this was because an immunomodulatory response to the vaccine was required for it to have an effect, and this may be diminished in immunocompromised patients.
- A member asked if the clinician intended to use this vaccine in these patients regardless of the outcome of this application or APC decision. Mr Costello confirmed that he would very much like to carry on using it in patients with RRP.
- A member explained that CCGs have a collaborative commissioning policy on experimental and unproven treatments which stipulates that, except for those circumstances set out in the policy, treatments which are judged to be experimental or not to be of proven effectiveness will not routinely be funded. The exceptions are that treatment will be funded in the context of a clinical trial or in the context of an individual funding request (IFR). An IFR implies a very small cohort of patients, usually not bigger than one.
- The cohort of patients that would benefit from Gardasil® is clearly defined in the application but unfortunately this appears to fall between the experimental and unproven categories.
- Mr Costello agreed that using Gardasil® in RRP could best be described as unproven, rather than experimental as this implied no prior knowledge of how it would work or possible side effects. He went on to say that the evidence for its effectiveness is gathering, albeit not in the form of large RCTs, but acknowledged that it was not robust.

The Chair thanked Mr Costello for attending the meeting, for answering all the questions from the APC members and advised him that the decision would be relayed within 5 working days, in line with APC policy.

Further discussion points raised in the absence of the clinician included:

- The Children's Hospital already use this vaccine in a cohort of children under their care (10 patients) but it is currently restricted to those with tracheal papillomatosis rather than laryngeal disease.

- A member commented that with the current national immunisation campaign in teenage girls, there should come a time when clinicians would

stop seeing this disease in female patients. Unfortunately, as boys were not currently included in the vaccination campaign, one would not get the herd immunity one gets with other vaccinated diseases. Herd immunity is a form of indirect protection from infectious disease that occurs when a large percentage of a population has become immune to an infection, thereby providing a measure of protection for individuals who are not.

- A Trust representative stated that an ENT consultant had requested this vaccine for one patient.
- A member commented that the APC needs to be seen to be consistent with the level of evidence it accepts when reaching a decision, and that any decision has to be taken with a population view as opposed to individual patients.
- The member went on to say that implementing this in Primary Care would not be an insignificant piece of work as this immunisation is not currently remunerated under the GMC contract, nor is there a patient group direction (PGD) in place to support the administration by practice nurses.
- Although the members were sympathetic to the clinician's clinical argument, there is a clear collaborative commissioning policy in place which was adopted by the 7 CCGs in the Midlands and notified to the local Trusts. However, the proposed use of Gardasil® was not covered by the criteria for exception discussed earlier.
- It was acknowledged that the number of patients potentially referred to primary care in the BSSE footprint for subsequent doses of Gardasil® will be very small, and that this would be an off-label use of a licensed product.
- It was also pointed out that school nurses currently administer the vaccine in teenage girls in the national immunisation program, and therefore GPs or practice nurses may not be that familiar with it.

The Chair directed the members to the Decision Support Tool for completion:

Patient Safety: No issues regarding safety; already being used in teenage girls in national immunisation campaign for prevention of cervical cancer. However safety of Gardasil® in children below 9 years of age has not been established.

Clinical effectiveness: Licensed product but off-label use for this indication. Efficacy of Gardasil® in children below 9 years of age has not been established. Clinical effectiveness based on biological plausibility.

Strength of evidence: Relatively weak; 2 case studies involving small numbers of patients.

Cost-effectiveness or resource impact: Opportunity cost of £260 per course, however resource impact is unknown due to variability in interval between surgical interventions.

Place of therapy relative to available treatments: Adjuvant therapy to surgical resection of laryngeal lesions.

National guidance and priorities: None

Local health priorities: Primary Care not supportive; covered by Collaborative Commissioning Policy on Experimental and Unproven Treatments.

Equity of access: N/A

Stakeholder views: N/A

Implementation requirements: Depends on final RAG status.

Decision Summary: Approved as RED- for ENT specialists only, for recurrent respiratory papillomatosis (RRP)

ACTIONS:

- **Relay decision to Mr Costello by Thursday 21st Sept.** **APC Sec**
- **Add Gardasil® to APC formulary as Red- For use by ENT Specialists only in recurrent respiratory papillomatosis (RRP)** **APC Sec**

0917/06 Brivaracetam- New Drug Application-

The Chair welcomed Dr Shanika Samarasekera, Neurology Consultant at UHB NHS FT and invited her to present the application for brivaracetam.

Dr Samarasekera began by clarifying that this application was not for patients who failed on levetiracetam but for patients with severe refractory epilepsy warranting specialist input. These patients have generally tried three or more antiepileptic drugs (AEDs) and brivaracetam would replace an existing AED.

The clinician is not trying to achieve seizure freedom in this cohort of patients as it is documented that after patients have tried 2 AEDs, the probability of seizure freedom is below 10%. The aim is to contain the number of seizures, to avoid recurrent A&E attendances and to prevent them dying in the context of a seizure.

The group that causes the most difficult problems in terms of prescribing includes patients with severe traumatic brain injury, those with refractory epilepsy and neuropsychiatric disorders e.g. on the autistic spectrum of behavioural problems with or without learning disability.

This drug would be a useful addition to the clinicians' armamentarium for this niche group of patients.

In terms of cost, the specialists aim to keep patients on three AEDs maximally. Usually the first one would be a carbamazepine / valproate derivative; the second might be a "newer" agent such as lamotrigine or topiramate; the third drug would be lacosamide or perampanel.
The proposal would be to switch the third agent when it isn't working to brivaracetam if it was available on the formulary.

The Chair invited questions and comments from members. Discussion points/concerns raised included:

- A member asked the clinician to run through the evidence for its clinical effectiveness. Dr Samarasekera quoted the outcome of three placebo-controlled RCTs which demonstrated a 50% seizure reduction. When it is directly compared to levetiracetam, it is comparable in terms of seizure freedom; however as it is not intended to be used as a first line agent, the data is not available in a higher refractory population. A large meta-analysis which included over 8000 patients confirmed that it is comparable in efficacy in terms of 50% seizure reduction compared to levetiracetam; it is tolerated better than perampanel and lacosamide. There is also limited

data on 2000 patients which indicates that neuropsychiatric side effects such as anxiety and depression are half of those with the commonly used AEDs. The commonest drug causing this problem is levetiracetam; however this could be because so much of it is used.

- Dr Samarasekera confirmed that it has a similar mode of action to levetiracetam; it works on the same synaptic vesicle pathway allegedly with greater affinity than levetiracetam. The reason the clinician stated that it was not for levetiracetam failures at the beginning of her presentation was because the specialists would not start a patient with refractory epilepsy on a brand new drug but would use the established agents instead. The clinician used her 1000 patients on refractory follow-up in Hereford as the most comparable population; fewer than 10 of these were on perampanel.
- The specialist confirmed that this drug would be used third line as adjunctive therapy. The standard definition of refractory is that patients have tried at least two drugs to the maximum tolerated dose but the patients Dr Samarasekera sees are refractory on polytherapy already. The aim is to limit to 3 agents maximum.
- A member was interested to find out how the specialists decide on which drug to use as a third line agent as there is a range of these available. The consultant outlined the usual approach:
    - 1st line: levetiracetam, carbamazepine or sodium valproate. Although NICE include gabapentin in their recommendation, it is not used as such. Lamotrigine does not tend to be used first line as it takes much longer to act.
    - 2nd line: lamotrigine, topiramate or gabapentin
    - 3rd line: lacosamide, perampanel or eslicarbazepine. Clinicians might revert back to previous combinations or start using phenobarbital. This is the tier where the clinicians see the emerging neuro-oncology patients, difficult to manage patients and those with traumatic brain injury/ learning disability. This is also where brivaracetam would fit.
- The decision making process around the choice of third tier agent was described as:
    - In a patient with obvious mood disturbances issues or behavioural issues, the specialist would avoid perampanel.
    - If a patient has had a problem with a sodium channel blocker previously, the specialist cannot use eslicarbazepine. This leaves lacosamide or brivaracetam.
    - Lacosamide also acts on sodium channels and although some patients tolerate it better than carbamazepine/ eslicarbazepine, it can still cause problems.
    - If brivaracetam is not available on the formulary, the clinician would have to add in clobazam and the patient ends up on long term benzodiazepines which are inherent of their own problems or advise the patient to tolerate the severe side effects.
    - If patients have clear neuropsychiatric issues, levetiracetam would not be used first line and therefore would not be used at all. Perampanel and zonisamide would also be avoided in these patients.
- A member commented that previous specialists making the case for a new AED to be added to the formulary were very persuasive with regards to the need for alternatives to existing therapies. Although the member acknowledges that epilepsy is a very difficult condition to manage and that a tiered approach is appropriate, the question was put to the consultant as to how many AEDs were needed on the formulary. There are currently

around 15 agents on the anti-epilepsy formulary, compared to the standard 2 or 3 in other sections of the formulary, and these newer agents have relatively limited evidence.

- Dr Samarasekera tried to address this question by stating that the issue with epilepsy is that it has been labelled as idiopathic for a long time and grouped under idiopathic generalized epilepsies. However with the genetic studies undertaken, clinicians are able to make more refined diagnoses and identifying and better understand genetic syndromes and this is where these niche drugs have a place in therapy. The clinicians now have much better targeted therapy and are able to reduce a patient from 200 seizures a day to 50, which is a significant improvement for that patient. There are some patients with frontal lobe seizures with 200 seizures a day who respond very well to eslicarbazepine or lacosamide or a combination of these, but these are just a handful of patients across the region.
- A member asked where the clinician would position brivaracetam against levetiracetam if it wasn't going to be used in levetiracetam failures as stated at the beginning of her presentation. Dr Samarasekera explained that co-morbidities would be a deciding factor in choosing brivaracetam over levetiracetam; these were severe refractory epilepsy patients with coexisting neuropsychiatric disorder, autistic spectrum disorder or learning disability. The evidence is there to confirm that brivaracetam is as efficacious as levetiracetam in the refractory seizure cohort; however there is no specific data for the traumatic brain injury cohort or solely neuropsychiatric disorder cohort.
- The issue with levetiracetam is not its efficacy, but more its tolerability. The pooled analysis of 25 studies involving 8,500 patients published in Seizure early 2017 has shown that the probability of neuropsychiatric side effects (e.g. anxiety, depression) experienced with brivaracetam is half that of levetiracetam. This meta-analysis also demonstrated that it is better tolerated than perampanel and lacosamide.
- A member asked if this was an opportunity to remove drugs in this section of the formulary in an effort to rationalise the options. The clinician stated that tiagabine was not used much.
- Dr Samarasekera summarised by saying that having a range of AEDs on the formulary enabled the tertiary centre clinicians to target therapies better as a result of more refined diagnosis and to tailor to individual patients' lifestyle more appropriately.

The chair thanked Dr Samarasekera for attending the APC meeting and for answering the members' questions.

Further discussion points raised in the absence of the clinician included:

- A member commented that brivaracetam and levetiracetam were manufactured by the same company before levetiracetam became available as a generic drug with a significantly lower acquisition cost. Brivaracetam has a similar mode of action and is comparable in efficacy and could be classed in the same group of agents as levetiracetam.
- A very clear cohort of patients and place in therapy would need to be defined if it was to be accepted on the formulary.
- This drug was first presented by the neuropsychiatry epilepsy team at BSMHFT DTC in April 2016 and the clinicians were requested to define the cohort of patients this drug would be used in and to present the evidence that brivaracetam was better tolerated in this defined group. Unfortunately this has not been provided as yet.

- It was noted that the European Medicines Agency' assessment report concluded that brivaracetam is less effective than levetiracetam, although noted that many of the patients may have failed on levetiracetam.
- The application form makes reference to neutropenia being reported in 0.5% of the brivaracetam patients (6/1099) in the trials, but that none of the six cases were severe or required any specific treatment or led to discontinuation of brivaracetam and none had associated infections.
- Feedback from HoE NHS FT MMAG was that a clearly defined cohort of patients would need to be identified and that any initiation would be carried out by a tertiary centre epilepsy specialist.
- Some members were still unclear as to the sequence these AEDs would be used in, and queried if there is in fact an unmet need that only this drug can fill. At best this drug would offer another option.
- The All Wales Therapeutics and Toxicology Centre assessment report on brivaracetam, which was circulated with the application, concluded that there is uncertainty in whether brivaracetam is more effective than the chosen comparators (lacosamide, perampanel, eslicarbazepine and zonisamide). However it acknowledged that it has a favourable tolerability profile and does not need to be up-titrated to the minimal therapeutic doses and has a low interaction potential. It also suggested that it might be a cost-effective option to perampanel and zonisamide.

The Chair directed the members to the Decision Support Tool for completion:

Patient Safety: Comparable with other anti-epileptic drugs (AEDs). The most common adverse events with brivaracetam were somnolence, dizziness, headache and fatigue. Low potential for neuropsychiatric side effects. Neutropenia has been reported in 0.5% of brivaracetam patients- needs monitoring. Low interaction potential. No requirement for up-titration to reach therapeutic dose.

Clinical effectiveness: Some evidence in placebo-controlled trials but no superiority to other agents. No additional benefit to levetiracetam.

Strength of evidence: Three RCTs versus placebo, but no trials against active comparators. Results from a Network Meta-Analysis (NMA), which included studies with brivaracetam, eslicarbazepine, perampanel, lacosamide and zonisamide, estimated that the probability of achieving seizure freedom was greater for brivaracetam than for the comparators, but the difference was not statistically significant. Brivaracetam treatment also gave the highest probability of achieving a 50% response rate, but the difference between brivaracetam and the comparators was not statistically significant.

Cost-effectiveness or resource impact: Cost neutral compared to other 3rd-4th line agents, but vastly more expensive than generic levetiracetam (£129 per month vs £5 per month).

Place of therapy relative to available treatments: 3rd- 4th line

National guidance and priorities: MTRAC July 2016, NICE Clinical Guideline 137 Epilepsies: diagnosis and management (2012), predates availability of brivaracetam. SMC accepted for restricted (July 2016). All these documents state that it must be initiated by specialist.

Local health priorities: CCGs supportive if used as described in application (3rd line), and if rationale for choosing this agent in preference of other AEDs is clearly outlined to GPs if transfer to Primary Care deemed appropriate.

Equity of access: N/A

Stakeholder views: N/A

Implementation requirements: Oral formulations would require ESCA if accepted, but need to include a section to outline rationale as mentioned above. RICaD not appropriate for this agent.

Decision Summary: Oral formulations are approved as Amber with ESCA-Initiation by Tertiary Epilepsy Consultant only. ESCA needs to include a section to outline rationale for choosing this agent in preference of other 3rd line AEDs. Injection formulation- approved as Red- hospital only.

ACTIONS:

- **Relay decision to Dr Samarasekera by Thursday 21st Sept.** **APC Sec**
- **Write first draft of ESCA for brivaracetam** **Epilepsy Specialists**

0917/07 Emollin ® 50:50 spray – Abbreviated application form

The abbreviated application form has been submitted by Dr Helen Goodyear, Consultant Paediatrician at Heart of England NHS FT (HoE NHS FT). This was discussed at the Trust's Medicines Management Advisory Group (MMAG) in June 2017. MMAG support the use of Emollin® on the recommendation of Dermatologists for paediatric use in patients requiring emollient treatment during the school day. HoE NHS FT does not feel it necessary for the applicant to attend the APC.

The chair summarised the information included in the application form: this product is a 50:50 combination of white soft paraffin and liquid paraffin, presented as a spray. The proposed indication is for children with severe atopic eczema for use at school; the teachers do not need to touch the child to apply this emollient. The administration schedule is noted as 1 or 2 applications per school day.

The clinician states that tubs of emollient are returned unused and the child has sore, extremely dry skin at the end of the school day.

The application form included a cost comparison with Cetraben® cream (£3.98 for 150g); Emollin® spray £4.00 for 150ml, £6.39 for 240ml.
The clinician proposed that prescribing would be under specialist advice only and not as a first line emollient.

The Chair invited questions and comments from members. Discussion points/concerns raised included:

- Members were very concerned that once teachers/ parents were aware of an emollient spray available on the formulary, there would be undue pressure for GPs to prescribe this formulation instead of the standard creams, ointments or lotions, and the use would be much wider than intended by the clinician. So there is significant potential for creep.
- It is acknowledged that there are severe cases where the action of rubbing a cream in can traumatise the skin but these are rare.

- With regards to clinician's remark about unused tubs, GPs would prescribe pump dispensers rather than tubs to minimise risk of cross-contamination.
- Members questioned whether this spray was flammable as this would be a concern for schools. The manufacturer's description on their website is: "*The paraffins are dissolved in a volatile silicone which quickly evaporates leaving only the pure emollient on the skin*." Another website confirms it is flammable and should be kept away from sources of ignition. It was also noted that users should avoid the spray getting onto hard floors as this makes them slippery. All these factors raise significant health and safety risks.
- The members discussed the fact that as this is a long term condition, parents would teach their child to self-apply emollient at an early age.
- A lengthy discussion followed on what teachers were allowed/ not allowed to do with regards to safeguarding; this may depend on individual school policies and age of child.
- APC representatives from the applicant's Trust confirmed that the clinician's proposal was that this would be used on dermatologist recommendation only, in addition to the child's emollients for use at home, for a small spray to be taken to school for application during the school day to avoid extremely dry skin, when teachers are not allowed to touch the child.
- A comment was made that some formularies do include a spray emollient, with restrictions i.e. fragile skin.
- The only other spray emollient is Dermamist® which costs £5.97 for 250ml.
- A member asked how many applications the Emollin® spray would provide and how the cost compared dose for dose. The manufacturer would need to be contacted to confirm this.
- It was confirmed that 500g of WSP 50%/LP 50% ointment costs £4.57 for 500g. It was acknowledged that weight for weight the spray was not as cost effective as the ointment.
- It was agreed that the decision has to be deferred once a number of issues have been clarified:
    - How many doses/applications does the spray deliver?
    - Does the child need to be moisturised during the school day?
    - Can the child apply emollient itself?
    - Are teachers allowed to touch the child to apply emollients?
    - If it involves removal of clothing, will the teachers still be allowed to administer the spray emollient?
    - Does policy vary between schools and nurseries?
    - Do Schools' medicines policies insist on the medication being prescribed and not bought over the counter.

Actions:

- **Inform clinician of deferred decision and rationale** **APC sec**
- **Seek clarification of issues raised by members** **APC sec**

0917/08 Toujeo®- insulin glargine 300 units/mL – draft RICaD for ratification

The APC secretary reminded the members that the committee had approved Toujeo® insulin glargine 300 units/mL as Amber with RICaD following resubmission of the application in April 2017.

The draft RICaD which has been written by colleagues at HoE NHS FT and approved by the Diabetes network was circulated to APC members in July 2017 for consultation and comments; none have been received to date.

A member commented that the section for "reasons why insulin Toujeo® 300 units/mL has been chosen in preference to drugs without formulary restrictions" included patients being at high risk for nocturnal hypoglycaemia; however this was not replicated in the Initiation criteria section for the specialist to tick. The criteria for its use approved in April 2017 did not include "high risk" of nocturnal hypoglycaemias and stipulated that the specialists need to demonstrate a reduction in nocturnal hypos before transferring care to the GP.

Another comment was made that the links to the risk assessment tool were missing. These will be added once this tool is finalised and published on the APC website.

The members agreed to ratify this RICaD subject to changes made as noted.

ACTIONS:

- **Clarify with DMMAG reason for including high risk of nocturnal hypos in section under "reasons why" as this was not included in agreed indication.** **APC sec**
- **Obtain final copy of risk assessment tool to upload to APC website.** **APC sec**
- **Add links to this tool to RICaD** **APC sec**
- **Publish on APC website.** **APC sec**

0917/09 Drugs for dementia ESCA- for ratification

The APC secretary reminded the members that drugs for dementia are currently Red on the APC formulary with the following annotation "The APC's view is that on clinical grounds, the status of these drugs for dementia should be amber, with a framework in place in primary care before transfer.
HOWEVER, until the commissioning arrangements have been agreed to allow safe transfer of patient care, the status will remain RED."

The ESCA for discussion today has been developed by a number of individuals from Birmingham commissioners, a Solihull GP, Birmingham GP and BSMHFT including a consultant psychiatrist. It has been approved by the BSMHFT PTC.

It was circulated for consultation on 1st June 2017; a couple of comments from a consultant in Elderly Care (UHB NHS FT) have been received by the secretary:

1. "Does the ESCA apply to clinicians in Geriatric Medicine as well as CMHT as stated in the document?" It was confirmed that it had been agreed to replace CMHT with Specialist throughout the ESCA. This would then include Consultants and Non-Medical Prescribers.
2. "Can the ESCA include "for use in Parkinson's disease (PD) dementia as well as Alzheimer's disease, in line with NICE guidelines?" It was stated that this ESCA was brought to the APC to support a pilot in 4 GPs practices across Birmingham and Solihull CCGs only. The pilot currently excludes any patient with PD dementia or complicating factors associated with dementia.

It therefore needs to be clarified that this ESCA is to support the pilot practices only working with BSMHFT, and not for general use. The pilot aims to determine whether GPs would be comfortable picking up prescribing of these agents which will then inform the commissioning discussion.

The main resistance from Primary Care is around the access to the additional support that is available such as admiral nurses, memory clinics etc., not just taking on the ongoing prescribing. It was confirmed that this support would still be available once GPs prescribe these drugs.
A comment was also made that secondary care/ community-based clinicians would have more time to deliver this additional support once ongoing prescribing was no longer their responsibility.

The members agreed that this ESCA would not be published on the website at the present time.

ACTIONS:

- **Replace CMHT with Specialist throughout the document.** **APC sec**
- **Forward finalised document to BSMHFT and CCGs involved in pilot only.** **APC sec**

0917/10 Oral antipsychotic drugs ESCA- queries/ feedback from practices

The ESCA for oral antipsychotics was approved and published on the APC in June 2016. The APC secretary has received a number of queries/ feedback from general practices seeking clarification.

- The ESCA has 2 options for the 3 month review (Mental Health or GP), but it doesn't give guidance as to who ought to be doing the monitoring. It was confirmed that the testing would be done by whoever is prescribing at 3 months. The transfer to primary care is once the patient is stable which may vary between patients, hence the options provided in the ESCA.

- Will Mental Health (MH) retain these patients in the long term? An ESCA would imply that MH would retain these patients, however point 10 under specialist responsibilities stipulates that "Review the patient at least once a year until the patient is discharged from specialist mental health services where this is possible." This was included at the commissioners' request as they were keen for stable patients with psychosis to be discharged from MH back to Primary Care. So the ESCA does not stipulate that the patient will be discharged nor does it prevent discharge as there are patients who are completely well, working and symptom free and it would seem inappropriate for these to continue to have out-patient appointments with specialists.

- What about patients that have been on antipsychotics for a long time, before the ESCA was available and have not seen a psychiatrist recently? It was confirmed that the ESCA was put in place for new initiations only. The GP may refer to the ESCA for guidance if required.

- Some GPs feel that it is unreasonable to expect them to look at the SPC to identify which drugs require an ECG to be done annually. They feel a list should be included in the ESCA. The MH representatives confirmed that in practical terms this would only apply to haloperidol; pimozide is rarely used and not included in ESCA and sertindole is not on the formulary as longer licensed. It was agreed to bring this back with a summary of monitoring from the Maudsley guidelines which includes a list of drugs requiring ECG.

- It was suggested that as the ESCA was going to be reviewed to incorporate a list of drugs requiring ECG, it may be worth detailing the symptoms of hyperprolactinemia as this had been requested by a practice as well. The advice from MH is that the GP should test prolactin levels if they suspect there is a problem.

- It was pointed out that these queries may have arisen following an audit of antipsychotics undertaken by practices.

- One practice in Birmingham South Central CCG is having a particular issue with ESCAs not being sent with new initiations of antipsychotics and is repeatedly sending decline to prescribe forms with no effect. The APC representatives for the MH Trust are aware of this internal communication issue with one particular team from their Trust. The Clinical Director has been asked to go back to this team to address this and a meeting is also scheduled for week commencing 25th September to put a plan in place.

ACTIONS:

- **Guidelines for monitoring developed by CrossCity CCG to support the audit to be brought to APC with a view to add as an appendix to the ESCA for oral antipsychotics.** **CCG**
- **Add symptoms of hyperprolactinemia to ESCA** **APC Sec**

0917/11 Midlands and East Regional Medicines Optimisation Committee (RMOC)
Feedback following first meeting

The feedback from the 3 BSSE APC members who were appointed to the Midlands and East RMOC was very positive following the first meeting on 31st August.
It was an encouraging start with a good mix of 30 representatives from across this vast region. This included 2 clinical pharmacologists, representatives from Mental Health, pharmacists from secondary care, primary care and community services, 2 patient representatives, 4 GPs with experience of working on APCs.
There are 4 RMOCs across the country and, as this was the first meeting, each RMOC discussed the same agenda. This included biosimilars, antimicrobial stewardship and polypharmacy.
The conclusion was that there is a huge spread of good practices across the country and one of the key roles of the RMOCs is to ensure that everyone is aware of these examples of good practice and facilitate their sharing.

There is a joint meeting of the 4 RMOCs planned for October, and the next meeting for Midlands and East RMOC is scheduled for December.

ACTION:

- **Put back on agenda for January 2018 APC meeting** **APC sec**

0917/12 Minutes of the meeting held on Thursday 13th July 2017 – for ratification

The minutes of the meeting held on Thursday 13th July 2017 were discussed for accuracy.

- Page 3, bullet point 4: change wording to read “Dr Pucci agreed that there is not enough high quality evidence”.

It was confirmed that subject to the above amendment, the minutes are approved, can be uploaded to the APC website and the recording deleted.

0917/13 Matters Arising

The Chair moved onto the action table for comments and updates:
(See separate document attachment for updated version). Consider actions closed if not discussed.
The outstanding actions include:

- 0717/05: Feedback from Prof Martin re clarification on patient group nebivolol would be used in. Update: Dr Martin has asked for this to be reported to next month.
- 0717/07: make agreed changes to atomoxetine and dexamfetamine ESCA documents. Update: Ongoing. APC secretary waiting for authors to update these.
- 0617/09: Collate comments and feedback from consultation on DMARD ESCA format. Update: the APC secretary stated that late responses were received during August. The delay in deciding on the format was delaying work on other ESCAs. It was agreed that if sufficient responses were received, a decision would be made by email.

ACTION: **Circulate results of consultation on DMARD ESCAS to APC members to reach decision on future format by email.** **APC sec**

- Minutes of the management development meeting held in August 2017 were circulated for information. The APC secretary stated that this had been a very productive meeting with representation from commissioners and secondary care. The main aim was to review the policy as the Committee has been in operation for 3 years and new developments such as RMOCs need to be covered. It also offered the opportunity to review the appeal policy following the learning from the number of appeals lodged to date.
  Unless the secretary receives any other comments, the revised APC policy will be added to the October agenda for ratification.

ACTION: Bring revised APC policy with amendments discussed at the August management development meeting to the October meeting for ratification. **APC sec**

0917/14 Summary of decline to prescribe forms- for information

Summaries from ROH, BCHC and BCH were circulated with the papers. The secretary will circulate UHB and Sandwell & West Birmingham Hospitals' with the draft minutes.

The APC secretary noted that a recurring item on the decline to prescribe forms submitted to the Children's Hospital was sodium chloride 1mmol/mL oral solution. This is currently Red on the APC formulary, however a licensed product (Syrisal®) was discussed at the May 2017 meeting where it was agreed that if a Trust wants the APC to review the RAG status in light of this licensed product, an abbreviated application will need to be submitted in order to understand the licensing in the paediatric patient group as it is not clear from the manufacturer's letter.

ACTIONS:

- **Circulate/ upload to Office 365 UHB NHSFT and SWB Hospitals summaries with draft minutes.** **APC sec**
- **Remind Trust of abbreviated application form for sodium chloride oral solution 1mmol/mL as described in action table (0517/09)** **APC sec**

0917/15 Trust Chairs non-Formulary approvals – For information

Summaries from BSMHFT, UHB and BCH were circulated with the papers for this meeting.

0917/16 NICE Technology Appraisals (TAs)

In the absence of an APC meeting in August, the APC secretary summarised the NICE TAs published in July and August 2017.

In July, there were 10 TAs published; of these 3 were terminated, 4 are NHSE commissioned and 3 are CCG commissioned. See below:

- Collagenase clostridium histolyticum for treating Dupuytren's contracture (TA459) - This technology is commissioned by clinical commissioning groups. Providers are NHS hospital trusts. RED status agreed.
- Adalimumab and dexamethasone for treating non-infectious uveitis (TA460) - Dexamethasone is commissioned by clinical commissioning groups, adalimumab is commissioned by NHS England. Providers are NHS hospital trusts. RED status agreed.
- Roflumilast for treating chronic obstructive pulmonary disease (TA461) - This technology is commissioned by clinical commissioning groups. Providers are NHS hospital trusts. This guidance replaces TA244.
  Currently listed as GREY status until place in therapy confirmed. Dr Alice Turner (Consultant in Respiratory Medicine) suggested that this should be an Amber drug with a RICaD as this is an oral preparation and does not need hospital attendance to be administered.

In August 2017, there were 11 TAs published; of these 3 were terminated, 5 are NHSE commissioned and 3 are CCG commissioned. See below:

- Bisphosphonates for treating osteoporosis (TA464) - The technologies are commissioned by clinical commissioning groups. Providers are NHS hospital trusts and primary care. It was agreed to retain the current RAG statuses, respectively.
- Baricitinib for moderate to severe rheumatoid arthritis (TA466) - This technology is commissioned by clinical commissioning groups. Providers are NHS hospital trusts. RED status agreed.
- Eluxadoline for treating irritable bowel syndrome with diarrhoea (TA471) - This technology is commissioned by clinical commissioning groups. Providers are NHS trusts. It was confirmed this is an oral preparation. A proposal of Amber with RICaD was put forward and agreed; the technology states that it is started in secondary care, and to stop eluxadoline at 4 weeks if there is inadequate relief of the symptoms of irritable bowel syndrome with diarrhoea. This would need a specialist's review.

The APC secretary informed the members that a Highly Specialised Technology (Asfotase alfa for treating paediatric-onset hypophosphatasia (HST6)) was also published in August 2017. It was confirmed by NICE that

these are mandatory as TAs, and therefore need to be included in this summary. As the highly specialised name suggests, these are commissioned by NHS England and will be listed as Red on the APC formulary.

ACTION:

- **Update APC formulary with decisions on NICE TAs.** **APC sec**
- **Request Respiratory clinician to draft RICaD for roflumilast.** **Resp Team**
- **Draft a RICaD for eluxadoline for IBS with diarrhoea** **GI team**

Any other business:

1. **Flash glucose monitoring (fgm):** one of the members brought this new technology to the attention of the APC members. The CCGs currently spend a significant amount of their prescribing budgets on blood glucose testing strips (BGTS) and associated consumables. On average this costs £50-£60 a year per diabetic patient. This new technology (flash glucose monitoring) measures glucose levels in interstitial fluid in the muscle tissue rather than blood and involves a sensor on/under the skin to remain in situ and replaced every two weeks. A wireless meter can be brought into proximity to the sensor, through clothing, and the glucose level data viewed. This would remove some of the reliance on BGTS and finger pricking.
   The reason for bringing this to the APC is that the secretary of state has approved for these sensors to be included in the Drug Tariff from November 2017 and will therefore be prescribable on the NHS. This will cause a significant cost pressure: the sensors currently cost £60 each and have to be changed every 2 weeks, which would cost £1500 per patient per year. In comparison the BGT strips cost £15 per 50 strips.
   It has been roughly estimated that if every patient on BGTS moved to fgm, it would cost £20 million for this health economy alone.

   It was also noted that a finger-prick test using a blood glucose meter is still required during times of rapidly changing glucose levels when interstitial fluid glucose levels may not accurately reflect blood glucose levels (i.e. acute illness such as Influenza, diarrhoea and vomiting), if hypoglycaemia or impending hypoglycaemia is reported, or the symptoms do not match the system readings. Fgm users will still need to perform finger-prick blood tests prior to and during driving to meet current DVLA requirements.

   It was proposed that the APC issues a commissioning statement saying that it is not currently supported as CCGs do not fund in year developments unless they have been considered and approved.
   Flash glucose monitoring will need to be considered by APC, and it expects and welcomes a submission via the Diabetic Medicines Management Advisory Group (DMMAG). The members would particularly value their view on the cohorts of patients who are likely to obtain most benefit from this considerable investment, remembering that there is no new money to fund this, so investment in this technology will mean that another healthcare intervention will need to be stopped. In fact, it would be very helpful if DMMAG could provide a list of cohorts with those most likely to benefit first, and working through other patients who may benefit. It would be extremely helpful if this list could consider both adult and paediatric patients.
   Given the size of the investment, it is likely that the recommendation of

APC will need to be taken forward to CCG decision making bodies.
The members present supported this approach.

ACTIONS:

- **Draft an APC interim position statement with regards to flash glucose monitoring.** **APC sec**
- **Ask DMMAG for their views and plans for this technology.** **APC sec**
- **Submit an application which clearly defines patient cohort**. **DMMAG**

2. **Oral methylprednisolone in relapsing Multiple Sclerosis (MS)**
   It was agreed to review the current non-formulary status of methylprednisolone tablets; these were removed from the formulary during the harmonisation of chapter 6 due to low use. However following a recent hospital admission of a patient with relapsing MS which required oral methylprednisolone as recommended in the NICE Clinical Guideline 186 on management of MS, it was identified that this needed to be reviewed. This is an oral preparation which requires specialist input. The Trust would supply the full 5 day course.

   ACTION:

- **Change RAG status of methylprednisolone tablets from Black to Red, in line with NICE CG186** **APC sec**

3. **Ethinylestradiol tablets for induction of puberty**
   A member Trust has queried the formulary status of ethinylestradiol tablets as it had been requested by the Women's Hospital and UHB to remain on the formulary during the harmonisation of the oestrogen and HRT section, specifically for induction of puberty in girls and women. The clinicians use the unlicensed 2 microgram tablets to initiate treatment and would ask GPs to pick up prescribing once they reach a dose of 10 micrograms, which are licensed tablets.
   It was also noted that SWB CCG formulary lists this drug as an Amber RAG status for menopausal and osteoporosis prophylaxis (with progestogen for 12-14 days of the cycle in women with an intact uterus) if other drugs cannot be used and for treatment of female hypogonadism (on advice of specialist) and menstrual disorders, which are the licensed indication.
   It was agreed to defer any decision and obtain further clarification on the different formulary status between SWB CCG and APC.

4. **Gonadorelin analogues for use in female patient**s
   These agents are currently included in the formulary in section 6.7.4 for endometriosis or breast cancer; however it does not specify specialist initiation or recommendation. This was queried recently by a GP. The NICE Clinical Knowledge Summary (CKS) guideline on management of confirmed endometriosis does clearly state that these drugs should be initiated by a specialist than transferred to Primary Care if appropriate.
   It was agreed to add the annotation "Specialist initiation" to the 3 drugs currently listed in this section.

   ACTION:

- **Add "Specialist initiation" to formulary entries for goserelin, leuprorelin and triptorelin in section 6.7.4** **APC sec**

5. **NHS England National consultation on items which should not routinely be prescribed in primary care.**
   A member brought this national consultation to the attention of the APC members; NHSE and NHS Clinical Commissioners are consulting on a list of 18 items which they recommend should not be routinely prescribed in Primary Care.
   Most of these drugs are Red on the APC formulary, but it was felt that the members should have the opportunity to look at this consultation and would be encouraged to respond to it.

   ACTION:
- **Circulate link to online NHSE/NHSCC consultation with draft minutes** **APC sec**

6. **Carteolol eye drops 1% discontinued**
   A member commented that carteolol eye drops 1% (Teoptic®) have been discontinued by the manufacturer and no generic alternative is available. The 2% eye drops remain available.

   ACTION:
- **Update APC formulary** **APC sec**

The Chair thanked the members for their input today. The meeting closed at 17:15

Date of next meeting: Thursday 12th October 2017 14:00 – 16:45
Birmingham Research Park