NewTherapiesSubgroup

19th July 2016 Minutes

12:30 - 2:30 pm
Pharmacy Dept. CMFT

GMMMG Greater Manchester Medicines Management Group

NHS

Present:

Elizabeth Adcock (EA) Medicines Information Pharmacist, PAHT
Elizabeth Arkell (EAr) Medicines Management Lead, UHSM
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Makrand Goré (MG) Medicines Management Pharmacist, Bolton CCG
Rachael Fallon (RF) Deputy Director of Pharmacy and Medicines Governance, CMFT
Dr Peter Selby (PS) Consultant Physician and Honorary Clinical Professor of Metabolic Bone Disease, CMFT.
Zoe Trumper (ZT) Medicines Management Pharmacist, Wigan Borough CCG

Support:
Andrew Martin (AM) Strategic Medicines Optimisation Pharmacist, GM CSU.
Bhavana Reddy (BR) Head of Prescribing Support, RDTC *(Professional Secretary)*

Apologies received: HS.

Declarations of Interest:
A declaration was made regarding ulipristal and safinamide by two people. Both were excluded from taking part in discussions regarding the relevant agenda items.

1) Minutes of the meeting on May 2016.

The minutes were accepted as a true and accurate record.

ACTION: To be sent to GMMMG then to be published on website.

2 Matters Arising:

The group were updated on the matters arising document. There was nothing new to report.

Review Dates on recommendations

AM raised the issue of review dates again to clarify arrangements regarding archiving old recommendations. BR stated that no old recommendations had been archived and these wouldn't be archived until the information had been updated within the GMMMG formulary. This was being done alongside current work so may take some time but it was also necessary with the impending merging of the two GMMMG subgroups.

ACTION: BR to liaise with professional secretary of Formulary Subgroup to ensure that archived NTS recommendations are incorporated into the formulary where applicable.

2a) Ulipristal intermittent use recommendation and treatment protocol.

BR stated that as per previous discussions the details around use of other treatment options had been included within the recommendation and statement had been made on when they could be used i.e. *in patients with fibroids less than 3 cm in diameter* as per the NICE clinical guideline. The group are now happy with the recommendation and associated treatment protocol and approved it as final. It was noted that ulipristal was already included within the GMMMG formulary however a RAG status for this particular indication may be required. It was noted that SRFT had put in a

request to use ulipristal for this indication in all patients. A copy of the draft recommendation had been shared with SRFT for comments.

ACTION: BR to take to next GMMMG meeting for sign off.

2b) Ticagrelor for MI (license extension)

The group reviewed the negative NTS recommendation on ticagrelor. The group was happy with this recommendation and approved it. There was however discussion relating to the potential imminent publication of the NICE TA for this new indication. The group felt that the safety aspects should be highlighted to prescribers and therefore they opted to go ahead and get GMMMG approval in the meantime.

ACTION: BR to take to next GMMMG meeting for sign off.

2c) Lesinurad (Zurampic®) for the treatment of Gout.

The group discussed the draft NTS recommendation which stated that '*lesinurad should not be recommended for routine use however it may be prescribed by specialists for a niche group of patients who are symptomatic despite other therapies where the benefits outweigh any risks.'* The group queried when NICE would look at this but it wasn't clear when a recommendation was likely. The group approved the draft recommendation and asked that it be sent for GMMMG approval.

ACTION: BR to take to next GMMMG meeting for sign off.

2d) Brivaracetam (Briviact®) for epilepsy.

The group discussed the specialists response to the queries raised. The group was still not convinced of the benefit of using this drug and queried why another agent couldn't be used in those patients with side effects to levetiracetam. The clinical trials for brivaracetam are short in duration (16 weeks) and are placebo controlled so there is no evidence that use of brivaracetam would be any better or even equivalent to other treatment options. The group requested that BR contact specialists for further information.

ACTION: BR to contact specialists with response above.

Post meeting note:

Following various discussions with specialists, the group agreed via email to update the recommendation as follows: **'**The group does not recommend the routine use of brivaracetam. It may however be considered for refractory patients in whom first line and adjunctive AED options as outlined in NICE CG 137: appendix E: Pharmalogical treatments have failed. i.e. as an option in the third column titled 'Other AEDs that may be considered on referral to tertiary care' and for initiation by specialist epileptologists only.' It was agreed that brivaracetam can only be initiated by tertiary specialists for refractory patients. The group agreed that use should be audited in 12 months' time so more real world information on brivaracetam can be gained.

ACTION: BR to take to GMMMG for sign off.

2e) Safinamide

The group discussed safinamide again now that it had been launched and a price was available. Safinamide had only been given a marketing authorisation for mid to late stage Parkinson's disease. In its assessment report, the EU CHMP considered that the benefits of safinamide in the early PD setting were not robustly shown, and did not outweigh the risks. It is understood that the Applicant did not pursue the indication in early PD any further. Safinamide is licensed as adjunct therapy only and at a cost of £839.50 per patient per year. The costs for existing treatments are £922 for rasagiline and £115 per year for selegiline (generic). The group agreed that it did have a role and may keep patients off Apomorphine. It was felt that it should be available for specialist use after all first line options as per the NICE clinical Guideline had been exhausted. The group agreed that specialists should be consulted prior to finalising the recommendation.

ACTION: BR to draft recommendation as above.

3) Gabapentin and Pregabalin for the treatment of cough <u>(unlicensed indication)</u>

The group had been asked to review the evidence base for use of pregabalin for the treatment of chronic cough as GP's had been asked to prescribe this by the UHSM specialist cough clinic.

The group reviewed the evaluation document and noted the following points:

- Cough which remains despite optimal therapy of any identified triggers is known as refractory cough; and NICE recommends referral to a respiratory specialist in these circumstances.
- Gabapentin and pregabalin have been proposed as potential treatments for chronic refractory cough, since there may be a neuropathic element to disease in some patients. Neither drug is licensed for this indication. There is very limited evidence of efficacy.
- Studies did not generally seek to definitively establish the presence of neuropathy. Instead, patients were required to have persistent cough despite treatment for other possible causes (e.g. GORD, COPD).
- One small randomised trial (n=62) and several small observational studies found that gabapentin is helpful for improving the symptoms of chronic cough, improving symptom scores and quality of life.
- One randomised trial (n=40) found that pregabalin plus speech therapy was more effective than speech therapy alone, although both treatment groups saw improvement over baseline cough severity scores. A case series also found that pregabalin improved symptom scores.
- The adverse events reported for both drugs appeared to be in line with the respective known safety profiles. Common adverse effects included gastrointestinal effects (e.g. nausea) and neurological effects (e.g. dizziness, fatigue, and somnolence).
- There are currently no standardised treatment pathways for patients with chronic cough. Potential underlying causes should be identified and treated, and further management is empirical.
- The incidence of chronic cough is not possible to estimate, and it is not clear how many patients will require management in the Greater Manchester area. Gabapentin currently costs approximately £70 per year, while pregabalin costs £840-1,260 per year

The group also discussed the UHSM protocol which listed low dose morphine as the first line treatment. It was noted that in their clinic experience approximately 50% patients with otherwise refractory chronic cough respond to low dose morphine. Additional side effects are commonly mild (constipation) and the therapy can be easily stopped and started as required.
Gabapentin/pregabalin is reserved for second line use, as they find in their experience that these treatments are less well tolerated than low dose morphine with many patients experiencing side effects of dizziness and drowsiness even at low doses, causing the treatment to be discontinued. Patients need to be titrated up gradually. There is a perception that pregabalin is better tolerated than gabapentin which could be why it appears to be used over gabapentin. The group were keen to dispel this perception as there is no evidence to suggest that pregabalin is better tolerated. Both have similar side effects although there are differences in potency and doses. The group agreed that for chronic cough patients in whom low dose morphine is not suitable the gabapentin may be tired however due to the current high cost per patient, the limited evidence base and greater abuse potential pregabalin is not recommended. It was noted that amitriptyline and citalopram had also been tried for this indication in the US.

ACTION: BR to draft recommendation as above.

4) Birch Bark Extract wound dressing

Birch bark extract (Episalvan®) is indicated for the treatment of partial thickness wounds in adults. It is a cutaneous gel. The active ingredient is dried birch bark extract, which largely comprises a pro-inflammatory compound called betulin. Birch bark appears to have been used traditionally in some cultures to promote the healing of wounds. Betulin appears to aid wound healing via up regulation of the inflammatory mediators' cyclooxygenase-2 (COX-2) and interleukin 6 (IL-6).

Episalvan is a sterile cutaneous gel containing 100 mg/gram dry birch bark extract, equivalent to betulin 72-88 mg/gram. The only excipient is sunflower oil; there are no preservatives or fragrances. The gel is intended to be applied to the surface of partial thickness wounds in a layer 1 mm thick, then covered with a sterile dressing. Gel should be re-applied each time the wound dressings are changed for a period of up to 4 weeks. Episalvan is considered to be a herbal medicinal product. The recommended maximum duration of use is 4 weeks.

There are several completed trials of Episalvan. No phase III studies have been published in the literature, but details are available from the regulatory documents. Clinical trials all involved treatment of skin graft donor sites or burns. Two open-label phase III randomised controlled trials (RCTs) compared Episalvan to non-adhesive wound dressing alone ("standard care"). Patients were recruited from centres in Eastern and Western Europe, with no UK participants. Patients were adults with a graft donor site measuring at least 15 cm^2 and at least 3 cm wide. All patients had to be willing and able to attend for dressing changes at the trial centre, and to return for follow-up at 3 & 12 months. Patients with chronic skin disorders or other diseases which could affect the study were excluded. Both trials used an intra-individual control method, whereby half of the graft donor site received standard care while the other half was treated with Episalvan. Treatment allocation of the two wound halves was randomised. Treatment was open-label, but wound assessment was carried out by blinded investigators. Episalvan was applied at every dressing change, which in practice meant every 3-4 days, for a maximum of 28 days. Episalvan was applied to the same half of the wound at every dressing change until the wound had fully closed or for 28 days, whichever was shorter.

The group reviewed the clinical trial data for the two phase III trials and made the observations below:

- In patients with skin graft donor site wounds, wound halves treated with Episalvan healed roughly one day sooner than wound halves treated with non-adhesive dressings alone ($p<0.0001$).
- In patients with partial-thickness burns, wound halves treated with Episalvan healed roughly one day sooner than wound halves treated with Octenilin Wound Gel ($p<0.0001$).
- The EMA considered these differences clinically relevant, since healing of partial thickness wounds influences duration of hospital stays and need for additional surgery.
- The available evidence is restricted to treatment of skin graft donor sites and burn injuries. Graft donor sites are very clean, uniform wounds and it is not clear that the benefits observed in these trials would translate to other types of partial-thickness wound.
- Safety data are limited but reassuring. Most adverse events were minor or moderate in severity. The most common events were pain, infection, pruritus and pyrexia.
- There is no price or launch data currently available.
- The EMA considered that since healing of partial thickness wounds influences the length of hospital stays and requirement for additional surgical procedures, even these small differences should be considered clinically relevant. However, it is not clear what proportion of patients enrolled in the clinical trial programme were hospital inpatients, if any. Any extrapolation of these results to that population should therefore be made with caution.
- The place in therapy remains unclear due to limited comparative evidence and uncertainty surrounding the clinical importance of the trial findings

The group agreed that specialists should be contacted and a cost obtained prior to a definite recommendation being made.

ACTION: BR to contact specialists and await price for product.

5) Colchicine for the treatment of pericarditis (unlicensed indication)

The group had been asked to review the evidence behind the use of colchicine for pericarditis as although this was common practice in GM there were no recommendations or guidelines looking at risk vs benefits of colchicine for this unlicensed indication.

The group reviewed the evidence in the evaluation report and noted the points below:

Acute pericarditis is either idiopathic in nature or results from a viral infection. Acute pericarditis is not usually life threatening and is normally treated medically on an outpatient basis with NSAIDs, and steroids in severe cases or where NSAIDs are contraindicated. Recurrence is the most common serious complication and is characterised by the return of severe pericardial pain after recovery from acute pericarditis. Recurrence can occur in 15% to 32% of cases and the cause is usually unknown, although in some cases it may be due to viral infection or may be a consequence of coronary artery bypass grafting. Two types of recurrent pericarditis have been identified, intermittent or incessant. In the incessant type, discontinuation of NSAIDs usually causes a relapse in less than six weeks. In the intermittent type, people have varying symptom-free intervals, usually longer than six weeks, without therapy. Colchicine is a drug with anti-inflammatory properties which has been used for a long time to treat gout. Since 1987 colchicine has been used to prevent recurrences of acute pericarditis. The exact mechanism by which colchicine prevents recurrences of pericarditis is still not fully understood.

A Cochrane review of colchicine for pericarditis in 2014 analysed the data from four trials and concluded that *colchicine, as adjunctive therapy to NSAIDs, is effective in reducing the number of pericarditis recurrences in patients with recurrent pericarditis or acute pericarditis. However, evidence is based on a limited number of small trials. Patients with multiple resistant recurrences were not represented in any published or on-going trials, and it is these patients that are in the most need for treatment.*

From the clinical data we can conclude that every 4 patients with recurrent pericarditis treated with colchicine and for every 10 patients with acute pericarditis treated with colchicine, one further episode of pericarditis may be avoided over 18 months. There was also no significant difference in adverse events between the colchicine and control group. However, people taking colchicine were twice as likely to withdraw from treatment. The optimal duration of therapy also requires more evaluation in clinical trials. The group agreed that there was some trial evidence for use and that use is supported by an international body: the 2015 European Society of Cardiology Guidelines for the diagnosis and management of pericardial diseases. The group therefore recommended use as per the European clinical guidelines.

ACTION: BR to draft recommendation as above.

6) Horizon Scanning and Work plan

The group discussed the horizon scanning document and noted that there wasn't much that needed to be added to the workplan. There had been some requests for the group to review the following:

Enstilar® - it was agreed that this should progress through the formulary subgroup as it is not a new drug but a new combination product that would need to be reviewed in line with other treatment options already included within the formulary.

Ferric Maltol – The group agreed that this should be added to work plan.
DUAVIVE® - a new product was also added to the work plan.

It was agreed that the group would review the following in the September meeting:

- Ixekizumab for psoriasis
- Ferric maltol
- Free Style Libre
- Opicapone for PD

ACTION: BR to update work plan as above.

7) Update on other groups
Formulary Subgroup
The group was updated on the last formulary subgroup meeting.
GMMMG
The group was updated on the agenda for the next GMMMG meeting which is on Thursday.

Interface Subgroup
The group was updated on the interface subgroup meeting

9) AOB
No other issues were raised under any other business.

10) *Date of Next Meeting: 20th September 2016, 12.30-2.30pm, CMFT*