NewTherapiesSubgroup

Minutes

17th February 2015, 12:30 - 2:30 pm
Pharmacy Dept. CMFT

GMMMG Greater Manchester Medicines Management Group

NHS

Present:

Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Elizabeth Craig (EC) Medicines Information Pharmacist, PAHT
Makrand Goré (MG) Medicines Management Pharmacist, Bolton CCG
Jane Law (JL) Deputy Director of Pharmacy and Medicines Governance, CMFT
Andrew Martin (AM) Strategic Medicines Optimisation Pharmacist, GM CSU.
Keith Pearson (KP) Head of Medicines Management, Heywood Middleton and Rochdale CCG
Bhavana Reddy (BR) Head of Prescribing Support, RDTC *(Professional Secretary)*
Dr Hina Siddiqi (HS) General Practitioner, Trafford CCG

Apologies received: JB, EA, ZT, RW and HS.

Declarations of Interest
No declarations of interest were made relating to the agenda.

1) Minutes of the meeting on January 2015.

The minutes were accepted as a true and accurate record.

ACTION RDTC to publish as final.

2a) Matters Arising:

Nabilone and Sativex® for pain (unlicensed uses)

The group felt that the mechanism for use in exceptional circumstances should be updated as it needed further clarification. It was agreed that both recommendations should be updated to state: *'the specialist should have an initial discussion with the local medicines management or prescribing lead before applying to a local effective use of resources panel for funding'*

Post Meeting Note: GMMMG felt on reflection that this addition regarding exceptional use was not necessary as this was the normal process, so asked that the above sentence be removed.

ACTION: BR to update recommendations as above and highlight changes to GMMMG

2b) Matters arising –Duaklir® Genuair® Combination Inhaler draft recommendation.

The group discussed the draft Duaklir® recommendation and felt that a minor adjustment was needed and that the word 'where' should be replaced with 'only when' within the following statement: *the group recommends the combination aclidinium/formoterol inhaler as an option where a separate LABA and LAMA inhaler would be prescribed*. The group then approved the recommendation as final.

ACTION: BR to update recommendation as above then take to GMMMG

2c) Matters arising – draft naloxegol recommendation.

The group discussed the draft recommendation and following a minor typo it was approved as final.

ACTION: BR to update recommendations and take to GMMMG for sign off.

2d) Tiotropium draft recommendation

The group reviewed the information provided regarding tiotropium use in asthma and noted the following points:

- Two similar RCTS analysed together found that tiotropium produced small changes in lung function and increased time to first severe exacerbation in people with poorly controlled asthma, compared with placebo.
- However the clinical trials did not show any clinically important improvements in asthma control or quality of life.
- Whilst people diagnosed with COPD and those who had a smoking history of 10 pack years or more or who had smoked in the year before the studies were excluded, participants had to show persistent airflow limitation. This was defined as FEV_1/FVC ratio of 0.7 or less and FEV_1 80% predicted or less (mean=62.2% predicted) Therefore although trial participants had asthma they had spirometer characteristics similar to those with moderate (stage 2) COPD.
- Specialist opinion shows that there is a growing recognition of an overlap between asthma and COPD and that those with longstanding severe, uncontrolled asthma (even in non-smokers) may result in airways remodeling and fixed airflow obstruction.
- It would therefore seem sensible that if a LAMA is going to be of benefit in asthma it is most likely to be in those with more severe disease and a pattern of illness and physiology more similar to that seen in COPD.

The New Therapies Subgroup of the GMMMG considered the use of tiotropium (Spiriva® Respimat®) inhaler for add-on maintenance treatment in adults with asthma already treated with inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting β2 agonists and who experienced one or more severe exacerbations in the previous year.

The group recommends the use of tiotropium as an option only in patients with poorly controlled asthma who have persistent airflow limitation at step 4 of the BTS guidelines.

Tiotropium was found to produce small changes in lung function and increased the time to first severe exacerbation in people with poorly controlled asthma compared to placebo. It did not however produce clinically important improvements in asthma control or quality of life.
The Spiriva® Respimat® inhaler is currently more expensive than montelukast or aminophylline tablets but is cheaper than salbutamol tablets.
According to set criteria tiotropium was found to be a medium priority for funding in the specific patient group identified

ACTION: BR to draft recommendation as above.

2e) Indacaterol/glycopyrronium (Ultibro® Breezehaler) combination inhaler for COPD review

The group re-reviewed the Ultibro® recommendation and agreed that it should be updated as per other LAMA/LABA inhalers. After discussions it was agreed that the priority for funding for all LABA/LAMA combination inhalers should be medium priority: *'i.e. should be considered for funding but depends on local priorities and affordability'.* The group agreed that all three combination inhalers should be included within the formulary. The choice of inhaler would be affected by various factors such as initial prescription, ease of use of inhaler device and patient preference.

The New Therapies Subgroup of the GMMMG considered the use of indacaterol plus glycopyrronium (Ultibro®) inhaler for the for the maintenance bronchodilator treatment of chronic obstructive pulmonary disease.
The group recommends the combination glycopyrronium/indacaterol inhaler as an option only when a separate LABA and LAMA inhaler would be prescribed.
Ultibro® has been shown to reduce the rate of moderate to severe COPD exacerbations when

compared to glycopyrronium alone.
Ultibro® breezehaler costs £ £447.48 per patient per year[1]. Whilst this is cheaper than the cost of separate LAMA and LABA inhalers and may help with adherence for some patients; it is more expensive than other LAMA/LABA inhalers by £53.15 per patient.
According to set criteria for the above indication Ultibro® breezehaler was deemed to be a medium priority for funding

ACTION: BR to draft recommendation as above and to feed formulary status back to the formulary subgroup

2f) Evaluation of Devices.

The group considered the decision making criteria for reviewing prescribable devices and approved the paper presented. The group agreed to use the criteria listed to evaluate the Cystistat® recommendation which is now due for review.

- **Cystistat® re-review**

The group discussed the limited evidence base available for the use of Cystistat® (sodium hyaluronate) solution for the management of pain due to interstitial cystitis. The group noted that painful bladder syndrome/interstitial cystitis (PBS/IC) are clinically challenging conditions to manage in patients however no new evidence is available since Cystistat® was last reviewed, six months ago. The evidence available is summarised below.

There have only been 3 Randomised Controlled trials:

- None are published in peer reviewed journals
- One was abandoned.
- One included 138 patients: both Cystistat® and placebo cohorts reported more than >50% of patients with satisfactory response: no statistical difference.
- One included 130 patients in 5 yr. study: 60% in hyaluronic acid cohort reported overall symptoms improvement compared to 80% in placebo cohort.

The two RCTs show placebo to be as/more effective. The majority of data available are non-RCTs and these show mixed results. There are no studies comparing Cystistat® with alternative treatments and there is no evidence of cost effectiveness.

The group considered the above information in light of the criteria document and agreed that Cystistat® did not show any measurable benefits to patients over existing therapies. The group therefore agreed that it could not be recommended for use. According to the table the group identified that Cystistat® had not met the case for adoption but that the technology may have the potential to provide patient benefits but that further data was required before a recommendation could be made. A recommendation for use within a research context was suggested.

The group agreed that the recommendation should be updated as below:

The New Therapies Subgroup of the GMMMG considered the use of Cystistat® bladder instillations (sodium hyaluronate) for the management of pain due to interstitial cystitis.

The group does not recommend the use of Cystistat® bladder instillations other than in a research context.

The case for adoption was not supported as the group was concerned about paucity and quality of the clinical trial data available with most trials being non-randomised and non-controlled. It was however noted that as a medical device the usual standards for licensing did not apply. It was also noted that most treatment options for this indication have limited evidence base. Due to the limited clinical evidence available it was felt that Cystistat® was best used in a research setting.

According to set criteria Cystistat® was deemed to be a low priority for funding.

ACTION: BR to draft recommendation

3) Safinamide for the treatment of mid to late stage Parkinson's disease.

The group reviewed the clinical data for the use of Safinamide of the treatment of mid to late Parkinson's disease (PD). Safinamide is an oral, once-daily adjunctive therapy for the treatment of PD. It is the first new chemical entity in ten years to receive a positive opinion from CHMP for the treatment of PD patients. There is an unmet need for treatments that improve both the motor and non-motor symptoms associated with PD. As some of these symptoms appear to be mediated by non-dopaminergic mechanisms, agents with a mechanism of action 'beyond dopamine' may be beneficial in the treatment of PD. Safinamide has a novel dual mechanism of action that modulates both dopaminergic and glutamatergic neurotransmission. The group noted that evidence for use in early Parkinson's disease had also been presented but that the CHMP had concluded that the medical need for additional medication for early stage patients, together with the magnitude of the benefit seen with Safinamide in this patient group did not provide compelling grounds for approval for this use in Europe. The group therefore concentrated on the mid to late stage data and noted the following points from the clinical trials:

- The approved indication is for the treatment of adult patients with idiopathic PD as add-on therapy to a stable dose of Levodopa (L-dopa) alone or in combination with other PD medicinal products in mid-to late-stage fluctuating patients.
- The manufacturer intends to launch safinamide in Q2 2015.
- The efficacy and safety of Safinamide as add on treatment in mid-late stage PD patients with motor fluctuations, currently receiving L-dopa alone or in combination with other PD medications, was evaluated in four double-blind, placebo-controlled studies. Only two of these have been published in full.
- Results from these trials show that the addition of safinamide 50 or 100 mg/day to levodopa significantly increased 'ON' time without troublesome dyskinesia, and improves motor function in the 'ON' state. An extension study showed that the benefits in 'ON' time and motor function were maintained for up to two years.
- However, the change in mean DRS (Disease Rating Scale) scores which was the primary outcome was not significantly different in the safinamide vs. placebo groups despite a notable decrease with safinamide compared to an almost unchanged score with placebo.
- In the SETTLE study safinamide 50-100 mg/day significantly improved the primary outcome of change in 'ON' time vs. placebo ($p<0.01$) in patients on stabilised on standard therapy.
- In clinical trials involving patients with early or mid-to-late stage PD, safinamide was generally well tolerated, with an adverse event profile similar to that of placebo The most commonly reported adverse events included nausea, headache, abdominal pain, vomiting, pyrexia, hypertension, insomnia, blurred vision, gastritis, dizziness, and back pain. The majority of these effects were mild or moderate in severity and are likely to be related to increased dopaminergic activity.
- The cost of safinamide is not yet available, but it may be conservatively assumed that it will be in the range of other currently marketed branded PD drugs. As a further treatment option it will be additional to current costs.

The group felt that although the increase in 'ON' time with safinamide is relatively modest, its tolerability, adverse effect profile, and reduced incidence of troublesome dyskinesia offers a valuable new treatment option in this patient group. It was agreed however that specialist feedback should be sought before a definite recommendation was made.

ACTION: BR to contact specialist for feedback

4) Naltrexone/bupropion (Mysimba® for obesity.

Naltrexone/bupropion 8mg/90mg (Mysimba®) is a fixed-dose combination of the opioid antagonist naltrexone and the dopamine reuptake inhibitor, bupropion that is due to be licensed for weight management, in combination with a reduced-calorie diet and physical activity, for people with a

body mass index (BMI $\geq$ 30Kg/m^2, or a BMI $\geq$ 27Kg/m^2 and at least one weight-related complication (type 2 diabetes, hypertension or dyslipidaemia).

The group noted the following data from the clinical trials:

- The effects of naltrexone/bupropion on weight loss have been studied over 28 to 56 weeks in four double-blind, placebo-controlled phase III trials with the same co-primary endpoints (percentage change in bodyweight and proportion achieving at least 5% reduction).
- Three trials enrolled patients with a BMI 30-45kg/m^2 or 27-45kg/m^2 with hypertension, dyslipidaemia or both. A fourth enrolled patients with BMI 27-45Kg/m^2 and type 2 diabetes, with or without hypertension or dyslipidaemia.
- All participants in one trial received intensive group-based multidisciplinary support for behaviour modification, with individualised energy intake goals and an exercise regimen. Participants in the other three trials received regular instructions to reduce calorie intake by 500Kcal/day and increase physical activity, with further behaviour modification advice.
- The majority of participants in the trials were white women between 40 and 50 years old.
- People with history of angina, myocardial infarction, severe psychiatric illness, seizures or other serious medical conditions, and those treated with any of a range of potentially interacting medications, including any opioid, were excluded. Very severely obese people (BMI $\geq$45Kg/m2) were also excluded from trials.
- Across all four trials, mean weight loss was greater and a larger proportion of patients achieved at least a 5% reduction in bodyweight with the licensed dose of naltrexone/bupropion than with placebo ($p<0.01$ for all comparisons)
- However EMA guidelines on evaluation of medicines for weight control state that a 10% reduction in bodyweight that is also 5% greater than that associated with placebo can be regarded as both clinically significant and a valid primary efficacy criterion.
- The most frequent adverse events leading to discontinuation of naltrexone/bupropion were nausea (6.3%), headache (1.7%) and vomiting (1.1%).
- The NHS price for Mysimba® is not yet available.
- It has not yet been established whether initial weight loss advantages that might be gained from combining naltrexone/bupropion with other measures can be sustained.
- Safety and efficacy data are currently limited to 56 weeks and there are outstanding concerns about potential psychiatric and cardiovascular adverse effects.

The group agreed that further data on longer-term efficacy and cardiovascular safety is required before Mysimba® can be recommended. Until such data are available, alternative approaches to weight loss are preferred.

The New Therapies Subgroup of the GMMMG considered the use of Naltrexone/bupropion 8mg/90mg (Mysimba®) in combination with a reduced-calorie diet and physical activity, for people with a body mass index (BMI $\geq$ 30Kg/m^2, or a BMI $\geq$ 27Kg/m^2 and at least one weight-related complication.

The group does not recommend the use of Mysimba® for the above indication.

Whilst data from clinical trials shows a 5% reduction in bodyweight with the licensed dose of Mysimba®, against placebo, the group noted that the EMA guidelines stipulate that a clinically significant reduction in body weight would be at least a 10% reduction in body weight. It has also not been established whether the initial weight loss advantages seen can be sustained over the long term. Further longer term safety and efficacy data is required before Mysimba® can be recommended for use. According to set criteria Mysimba® was deemed to be a low priority for funding.

ACTION: BR to draft recommendation as above

5) Re-reviews of old recommendations.

The group noted the list of expired recommendations that needed re-review. A search had been carried out to highlight any new guidance, reviews or key clinical trials that had been published since the date of the original NTS recommendation. The group discussed the expired recommendations with corresponding new evidence and made the following decisions:

- Racecadotril - no new evidence; next review date set to 2018
- Linaclotide – no new evidence and in line with NICE IBS guideline; next review date set to 2018
- Inhaled loxapine – no new evidence. NICE TA was terminated so a recommendation is still required; next review date set to 2018.
- Lixisenatide – the group requested that this recommendation be amalgamated with the other GLP-1 mimetics and a generic recommendation be published. To be drafted for next meeting.

ACTION BR to update recommendations as above.

6) Current work plans & new submissions received since January & Horizon Scanning
The group noted the current work plan and agreed that the two new drugs for psoriasis should be considered at the next meeting as part of an update to the pathway. Dulaglutide had now been launched so the group may need to consider this in the generic '*GLP-1 mimetics'* recommendation.

It was agreed that the biosimilar insulins could be considered at the May meeting following feedback from GMMMG.

ACTION: BR to update work plan as above

7) Updates from other groups.

Formulary Subgroup
The group was updated on the last formulary subgroup meeting.
GMMMG
There had been no GMMMG meeting since the last update.
Interface Subgroup
The group was updated on the interface subgroup meeting.

8) AOB

It was agreed that the March meeting would be cancelled as there would be no GP representation and the meeting would therefore not be quorate.

No other business was raised.

9) *Date of Next Meeting: 21st April 2015, 12.30-2.30pm, CMFT*