NewTherapiesSubgroup

Minutes

January 19th 2016, 12:30 - 2:30 pm
Pharmacy Dept. CMFT

Present:

Elizabeth Adcock (EA) Medicines Information Pharmacist, PAHT
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Rachael Fallon (RF) Deputy Director of Pharmacy and Medicines Governance, CMFT
Keith Pearson (KP) (Chair) Head of Medicines Management, Heywood Middleton and Rochdale CCG
Zoe Trumper (ZT) Medicines Management Pharmacist, Wigan Borough CCG
Dr Hina Siddiqi (HSa) General Practitioner, Trafford CCG

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

Apologies received: PB, LA and MG.
It was noted that RW had tendered his resignation from the group. The group thanked him for his involvement so far. It was agreed that another consultant would be sought. RF agreed to contact PS at CMFT.

As PB had sent apologies KP chaired this meeting.

Declarations of Interest:

KP declared that he had attended an advisory board relating to agenda item 7. He requested that someone else chair this section of the meeting as he would not take part in the discussions; JB agreed to take on the chairmanship for agenda item 7 only.

1) Minutes of the meeting on November 2015.

Following some minor updates 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. It was noted that the GLP1 recommendation had not been approved by formulary however further information had been sent to them to review and they were expected to approve it this month. Both Ulipristal and Dymista® were on the main agenda.

2a) Anal Irrigation Systems

Following a few minor corrections the draft recommendation was approved. The group agreed that this should be sent to GMMMG for sign off.

ACTION: BR to take to GMMMG for sign off in February as January meeting had been cancelled.

2b) Capsaicin patches (Qutenza®)

The group approved the draft recommendation and agreed that all prescribing for capsaicin patches should remain under the care of a specialist. The group noted that most of the available data related to post herpetic neuralgia so use was restricted to this indication.

ACTION: BR to take to GMMMG for sign off.

2c) Alirocumab or Evolocumab for the treatment of primary hypercholesterolaemia and mixed dyslipidaemia.

The group discussed the above draft recommendation. It was noted that NICE were due to issue another appraisal consultation document for evolocumab and it was felt that the NTS recommendation should therefore be brought back following the NICE guidance. Whilst the group had approved use in a restricted subset of patients it was felt that waiting for NICE would clarify the position as they may be looking at a slightly wider indication. Specialists had indicated that NICE may publish an updated recommendation by February. The group agreed to discuss this again at the March meeting.

ACTION: BR to bring back to March meeting

3) Sacubitril-Valsartan for heart failure

The group had been asked to review the above combination product for heart failure however an appraisal consultation document (ACD) from NICE had been issued after the last meeting. The ACD states that sacubitril-valsartan is recommended as an option for treating people with heart failure with reduced ejection fraction only in people with NYHA Class II to III chronic heart failure and if they are already taking a stable dose of ACE inhibitors or angiotensin II receptor blockers and with a left ventricular ejection fraction of 35% or less. It was noted that sacubitril valsartan was statistically significantly more clinically effective than enalapril at improving both overall mortality and cardiovascular mortality and in reducing hospital admissions. The group noted the high cost of treatment however it was envisioned that treatment costs would be offset by a reduction in hospitalisations. It was also noted that sacubitril valsartan represented a small step change in the management of heart failure and was innovative compared to existing treatments. As a NICE TA is due imminently it was agreed an addition NTS recommendation was not necessary. However the group agreed that it would be useful for the formulary group to define its place in therapy in conjunction with specialists.

ACTION: Await publication of NICE TA

4) Guanfacine for the treatment of attention deficit hyperactivity disorder

The group reviewed the new treatment for ADHD – Guanfacine. They noted the following points from the clinical evidence review:

- Guanfacine is a selective alpha 2a adrenergic receptor agonist licensed for the treatment of ADHD in children and adolescents of 6-17 years old, for whom stimulants are not suitable, not tolerated or have been ineffective.
- It is available as prolonged release tablets which should be taken once daily in either the morning or evening. The starting dose is 1 mg daily, followed by careful dose titration according to individual response.
- The efficacy of guanfacine was assessed in one meta-analysis of seven randomised placebo controlled trials. A total of 1752 children and adolescents (ages 6 to 17) with an ADHD diagnosis according to DSM-IV-TR criteria were included across the trials. Six of the included studies investigated the prolonged release presentation (GXR), whilst the remaining study assessed immediate release guanfacine (GIR). Doses ranged from 1 mg to

7 mg daily in either a dose optimisation schedule (five trials) or a fixed dose schedule (two trials). Treatment duration ranged from 6 to 13 weeks.

- The meta-analysis primary outcome was treatment response, defined as a Clinical Global Impression of Improvement (CGI-I) score of ≤2, which equates to either "much improved" or "very much improved" symptoms. Treatment response occurred in 59% of participants in the guanfacine group compared to 33% in the placebo group (odds ratio 3.18, 95% CI 2.44 – 4.13). The number needed to treat (NNT) was 3.9 (95% CI 3.3 – 4.8).

- One phase III randomised, double-blind trial compared the effects of dose optimised GXR or atomoxetine with placebo. The primary outcome was change in ADHD-RS-IV score from baseline to visit 15. Patients in the GXR group experienced greater decreases (-23.9, SD 12.41) compared to atomoxetine (-18.6, SD 11.91) and placebo (-15.0, SD 13.07). However the active controlled trial was adequately powered to detect differences between placebo and the active treatment arms, but not to detect differences between the active groups.

- No trials directly comparing guanfacine with other medications used for ADHD have been published.

- The trials used various rating scales, notably ADHD-RS-IV and CGI-I as their main endpoints. The use of such scales in investigating ADHD treatments is commonplace, though their usefulness may be limited. It has been postulated that a difference of 10 to 15 points on the ADHD-RS-IV scale may be clinically significant, though the robustness of this link remains unclear.

- In a pooled analysis of both the licensed population and healthy volunteers, rates of treatment emergent adverse events (TEAEs) were higher in guanfacine-treated patients compared to atomoxetine or placebo (84.9% vs 67.9 or 63.7% respectively).

- An increase in mean BMI percentile from 52.3% to 62.4% over 24 months was reported in a long term trial of guanfacine treatment. BMI increases occurred in 2.9% of patients. Given the long term nature of treatment, this may result in serious weight gain.

- Guanfacine has not been sufficiently compared to other drug treatment options such as methylphenidate and atomoxetine, so its place in therapy remains unclear.

- Longer term trials are required to establish its safety and efficacy. It may provide a licensed option for patients in whom unlicensed clonidine would otherwise be used, but it is not currently licensed as an adjunctive treatment.

The group agreed that Guanfacine should not be recommended for routine use but may be a useful fourth line option.

The New Therapies Subgroup of the GMMMG considered the use of Guanfacine for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents of 6-17 years old, for whom stimulants are not suitable, not tolerated, or have been ineffective.

The group recommends the restricted use of guanfacine for those patients in whom stimulants <u>and atomoxetine</u> are not suitable, not tolerated or have been ineffective. i.e. when stimulant trials (methylphenidate and lisdexamfetamine) and atomoxetine have been ineffective or not tolerated, alternatively it may also be considered as a second line option for use in patients in whom the use of stimulants is contra-indicated and atomoxetine has been ineffective or not tolerated.

Treatment must be initiated and prescribed by a specialist until the patient is stable and the dose has been adequately titrated.

The efficacy of guanfacine was assessed in one meta-analysis of seven randomised placebo controlled trials. Guanfacine has not been sufficiently compared to other drug treatment options such as methylphenidate and atomoxetine, so its place in therapy remains unclear however it may be a useful licensed option for those patients in whom unlicensed clonidine would otherwise be used, but to note it is not currently licensed as an adjunctive treatment.

According to set criteria guanfacine was deemed to be a low priority for funding

ACTION: BR to contact mental health trusts for feedback and draft recommendation as above.

5) E-Voke® electronic inhalers

- An e-cigarette consists of three components: a battery, an atomiser and a cartridge or 'tank' containing the nicotine liquid called e-liquid or e-juice. The liquid nicotine is suspended in propylene glycol or glycerine and water. The level of nicotine in the cartridges may vary and some also contain flavourings. When a user sucks on the device, a sensor detects air flow and the battery heats the liquid through a small heating element in the cartridge causing it to evaporate. This vapour then delivers the nicotine and flavours to the user.

- The e-Voke® device is the first electronic cigarette in the UK to seek regulatory approval as a medicine. The marketing authorisation is held by Nicovations Ltd, which is part of Nicoventures, a division of British American Tobacco.

- The e-Voke device consists of a stainless steel vaporiser and battery unit which are screwed together by the patient before first use. The battery is rechargeable, and must be unscrewed from the vaporiser in order to be charged. The device is supplied with a USB charging adaptor. The battery is designed to last roughly 130 inhalations before needing to be recharged, and charging takes 2-3 hours.

- One clinical study was submitted to support the marketing authorisation application for e-Voke. This was a pharmacokinetic study with a crossover design, comparing the bioavailability of nicotine when delivered by: e-Voke 10 mg or 15 mg cartridges with Nicorette® 15 mg Inhalator or smoking a cigarette (Benson & Hedges Gold). Plasma nicotine levels were higher with e-Voke 10 mg and 15 mg than the Nicorette 15 mg inhalator at all-time points. Nicotine levels associated with cigarette smoking were considerably higher than all other methods. The conclusion was that e-Voke electronic inhalers are at least comparable with the reference product (Nicorette) and as safe (in terms of nicotine consumption) as cigarettes. No new safety concerns were highlighted.

- There are currently no published clinical trial data showing a reduction in harms related to smoking due to the use of e-Voke or an increase in the numbers of quit rates compared to other stop smoking therapies.

- Emerging data shows that e-cigarettes are increasingly being used for harm reduction purposes rather than stop smoking aids. This may lead to longer use than current nicotine replacement therapies. However the NICE guidance on Tobacco Harm Reduction, recommends that quitting all forms of nicotine use is the best option for smokers.

- The long-term effects of nicotine include addiction, increased risk of heart diseases, and decline in insulin levels, cancer and premature aging.

- The group agreed that more rigorous data showing the benefits of e-Voke® as a stop smoking aid must be available prior to e-cigarettes being approved for use.

- E-Voke is thought to cost £20 for the kit plus £10 for a cartridge. One cartridge contains roughly 130 inhalations depending on the depth and length or user inhalations. The maximum dose is 5 cartridges per day.

The New Therapies Subgroup of the GMMMG considered the use of e-Voke electronic inhaler to relieve and or prevent withdrawal symptoms and reduce the cravings associated with tobacco dependence.

The group does not recommend the use of e-Voke on the NHS. Further data is required evaluating the use of e-Voke® as a <u>stop</u> smoking aid and comparing use to other nicotine replacement therapies (NRT) prior to its use within the Greater Manchester region.

Depending on the number of inhalations per day the e-Voke may be more costly than NRT. Current data available does not evaluate the benefit of e-Voke as a stop smoking aid. The NICE guidance on Tobacco Harm Reduction recommends that quitting all forms of nicotine use is the best option for smokers due to the long term risks associated with nicotine use.

E-Voke® is a GSL medicine and is still available for purchase by patients.

According to set criteria e-Voke® was deemed to be a very low priority for funding

ACTION: BR to draft recommendation as above.

6) Dymista® re-review

The group reviewed the application from the specialists regarding the use of Dymista®, the SMC advice and the previous NTS recommendation.

The group noted that the price of Dymista® had now been reduced and it was now cheaper than the two constituent components. It was also noted that the specialists were proposing it as a third line treatment option if an intranasal antihistamine or glucocorticoid is not considered sufficient. The NW allergy specialist group had offered to produce some formal guidelines for the use of Dymista® to sit alongside the recommendation and the group was happy to take them up on this. It had been proposed that Dymista® could be trialed prior to referral to specialists and that this step is currently missed resulting in an early referral. It was felt a change in recommendation and the development of a treatment pathway would aid primary care with this.

The group agreed that the old NTS recommendation should be updated to allow use third line as recommended.

ACTION: BR to draft recommendation as above and contact specialists taking them up on the offer to develop a pathway.

7) Ulipristal – new indication (application from specialists)

JB chaired this agenda item.

The group noted that an application had been received by specialists asking for approval for the new indication of intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. A formulary submission support pack was also received which has been produced by the manufacturer.

The new indication for ulipristal means that this is the only licensed product for the long term management of uterine fibroids. It is now indicated for the intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women. Efficacy has been proven in the Pearl III and IV studies. The trials also showed an improvement in quality of life scores and can avoid the need for hysterectomy in some patients.

The dosage is 5mg once daily for treatment courses of up to 3 months each. To date, repeated intermittent treatment has been studied for up to 4 intermittent courses only. The first course is started during the first week of menstruation; re-treatment courses should start, at the earliest, during the first week of the second menstruation following the previous treatment course completion.

The specialist application refers only to pre-menopausal women aged 46-50 as this was the age group studied in the clinical trial. The application anticipates that approximately 25% of women within this age range could be managed with Ulipristal instead of going forward for surgery. This is estimated to equal ~112 patients across the Greater Manchester region. [Based on HES data 13/14 showing a total of 450 patients (aged 46-50) referred for diagnosis and treatment of uterine fibroids per annum]. Ulipristal costs £114.13 for a 28 day pack. Costs for a 90 day supply (3 month course) = £366.85 per patient. To treat 112 patients this would be £41,087 per treatment course. In comparison a hysterectomy costs £3322 per procedure so there would be some cost savings associated with medically managing these patients. The group agreed that there is sufficient data to recommend use of Ulipristal for this new indication. It was agreed that treatment courses should be limited to the four courses studied and for the age range specified.

The New Therapies Subgroup of the GMMMG considered the use of ulipristal (Esmya®) 5mg tablets for the intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women.

The group recommends use as per the licensed indication in women of reproductive age, for up to four treatment courses.

The efficacy of repeated treatment courses of ulipristal 5mg once daily was evaluated in two phase III studies (PEARL III and PEARL IV) assessing up to four courses of intermittent 3-month treatment, with heavy menstrual bleeding and other symptoms associated with uterine fibroids. The pivotal PEARL IV study demonstrated that 73% of patients on the licensed dose of ulipristal achieved the secondary outcome of controlled bleeding and approximately 50% of patients were in amenorrhoea after the fourth treatment course. Intermittent treatment with ulipristal has the potential to avoid surgery/other invasive procedures or to delay them or allow less invasive procedures. This could be beneficial for many patients with symptomatic fibroids e.g. younger patients who wish to preserve their fertility, peri-menopausal women and those who are not fit enough to undergo surgery.

Ulipristal costs £366.85 per patient for a three month supply (90 days/one treatment course). Managing appropriate patients with ulipristal may avoid the need for a hysterectomy in some patients and therefore there may be some potential cost savings associated with this. The cost of one hysterectomy (national tariff cost) is ~£3322 per patient per procedure.

According to set criteria ulipristal 5mg tablets was deemed to be high priority for funding in the patient group described

ACTION: BR to draft recommendation as above.

8) Horizon Scanning and Work plan

The group reviewed the monthly horizon scanning document and agreed the following should be added to the agenda for the March meeting:

- Idarucizumab (reversal agent for dabigatran)
- Etanercept biosimilar (if launched)
- Sufentanil s/l tablets for post-operative pain

The group also agreed to add the following new drugs/indications to the work plan: new licensed indications for ticagrelor, birch bark extract gel and Lesinurad (gout).

It was also agreed that the group would need to keep an eye on the new anti-interleukin therapy for asthma that was currently being evaluated in clinical trials.

ACTION: BR to update work plan as above.

8) 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: 15th March 2016, 12.30-2.30pm, CMFT*