NewTherapiesSubgroup

Draft Minutes

15th September 2015, 12:30 - 2:30 pm
Pharmacy Dept. CMFT

GMMMG Greater Manchester Medicines Management Group

NHS

Present:

Elizabeth Adcock (EA) Medicines Information Pharmacist, PAHT
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Rachael Fallon (RF) Deputy Director of Pharmacy and Medicines Governance, CMFT
Keith Pearson (KP) Head of Medicines Management, Heywood Middleton and Rochdale CCG
Zoe Trumper (ZT) Medicines Management Pharmacist, Wigan Borough CCG
Dr Hina Siddiqi (HS) General Practitioner, Trafford CCG
Dr Richard Warren (RW) NIHR Senior Clinical Lecturer and Consultant Dermatologist, Salford Royal Foundation Trust.

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

Apologies received: MG, EA and HSo.

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

1) Minutes of the meeting on July 2015.

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 launch of albiglutide had been delayed. The formulary review for GLP1 receptor agonists was still outstanding.

2a) Linaclotide re-review

The group discussed the letter and paperwork received from Almirall, the company marketing linaclotide in Europe. The group had a robust discussion regarding the NICE guidance for IBS which recommends linaclotide in a similar place to the NTS recommendation i.e. in patients who have not responded to other therapies. It was noted that the NICE document stated that '*the Committee decided that a weak recommendation would be appropriate for this drug'* based on the clinical trial data, however the committee felt that there was an unmet need, which formed the basis of the NICE recommendation. The group then discussed the current NTS recommendation and noted that it was the recommendation that '*linaclotide should not be initiated by primary care'* that the company was particularly unhappy with, however this recommendation is in line with recommendations made by other regions. This is mainly due to the fact that many areas do not have access to primary care testing for diagnosis of IBS, which therefore means that the patient would need to be referred to secondary care. The current recommendation is therefore in line with the currently commissioned patient pathway. The group did however agree that access to primary care diagnosis tools would be beneficial. The group also noted that the current RAG status was Green – following specialist initiation. This is in line with other similar drugs. The group agreed that they would update the NTS recommendation to state that primary care initiation is only acceptable if

there is a robust pathway in place which includes the appropriate tools to allow a primary care diagnosis.

The New Therapies Subgroup of the GMMMG considered the use of linaclotide for IBS.

The group does not recommend the use of linaclotide over other treatments for IBS – C. Linaclotide may be suitable for prescribing in patients with more severe disease who have not responded to other therapies and have had constipation for at least 12 months as per NICE CG 61.

The group does not recommend initiation of linaclotide in primary care unless there is a robust pathway in place which includes the appropriate tools to allow a primary care diagnosis.

Trials were of moderate to low quality and showed that about 50-60% of the patients did not sufficiently respond to linaclotide. If used it is recommended therefore that prescribers assess patients regularly and reconsider treatment if there is no improvement in symptoms after 4 weeks.

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

ACTION: BR to draft recommendation as above (changes highlighted in red)

3) Insulin Glargine and Biosimilar review

The group reviewed the data within the review document. It was agreed that two separate recommendations should be issued; one for high strength insulin glargine and one for the biosimilar.

Insulin Glargine Biosimilar (Abasaglar®)

The group noted that this was the first biosimiliar insulin approved in the European Union. This long acting insulin analogue has an identical amino acid sequence to that of the active ingredient in the reference product – Lantus®. It was also noted that Abasaglar® has the same licensed indications, dosing regimen, pharmaceutical form and strength as the reference product Lantus®. In order to gain approval in the EU a biosimilar medicine must demonstrate that they are as safe and as effective as the reference medicine, and have the same quality characteristics. The EU regulatory process demands an extensive comparability exercise is performed through a stepwise process that begins with structural, physicochemical and biological analysis, non-clinical, then pharmacokinetic (PK) and pharmacodynamic studies (PD), followed by clinical safety and efficacy trials. In the extensive comparability exercise it was shown that the PK and PD profiles, the relative bioavailability and the duration of action of Abasaglar® are comparable to those of Lantus®.

In addition to this, the clinical efficacy of Abasaglar® given once daily was compared to that of once-daily Lantus® (insulin glargine 100 units/ml) in two similarly designed randomised, active-control, parallel group studies. ELEMENT 1 was a 52 week study (24-week treatment period and 28-week extension) in patients with T1DM, and ELEMENT 2 was a 24-week study in patients with T2DM. Adult patients aged ≥18 years of age with a screening HbA1c of ≤11.0% for insulin pre-treated patients and ≥7.0% to ≤11.0% in insulin naïve patients were eligible for the studies. Exclusion criteria were largely unrestrictive and reflect the general population with diabetes mellitus. Both studies were designed to show non-inferiority of Abasaglar® versus Lantus® based on the primary endpoint of change in HbA1c from baseline to 24 weeks, with a non-inferiority margin of 0.4% HbA1c, and if met 0.3%. Results from both clinical trials demonstrated that Abasaglar® was non-inferior to Lantus® in reducing HBA1c in both T1DM and T2DM.

The safety profile of Abasaglar® has been well characterised in the context of the extensive comparability exercise. In clinical studies the overall safety profile of Abasaglar® was comparable to Lantus® and in line with the documented profile of the reference product. There were no major safety findings or signals identified. The list price of Abasaglar is currently approximately 15% lower than that of Lantus®.

The group therefore agreed that Abasaglar® should be considered for all new patients requiring insulin glargine in line with NICE guidelines. However, individual Trusts may wish to consider a managed therapeutic switch between products for existing patients who are not currently on a stable dose. Abasaglar® has been shown to be bioequivalent to Lantus® and the efficacy of the two

products are comparable. Nevertheless, as with other biosimilar medicines, some patients may still need an adjustment in dose.

The New Therapies Subgroup of the GMMMG considered the use of Insulin Glargine Biosimilars for type 1 (T1DM) and type 2 diabetes mellitus (T2DM).

The group recommends the use of insulin glargine biosimilars, as a first line option in all new patients requiring insulin glargine in line with NICE guidelines on the use of long acting insulin analogues for T1DM and T2DM.

A managed therapeutic switch programme could be considered for those patients who are not currently on a stable dose, however this would need to be carried out in conjunction with the initiating clinician and patient and monitored closely in case a dose adjustment is necessary; patients may also need to be shown how to use the pen device as these may differ.

Abasaglar® is currently the only insulin glargine biosimilar approved for use in the EU and it has been shown to be bioequivalent to Lantus® and the efficacy of the two products are comparable. Abasaglar is approximately 15% cheaper[1] than the reference product.

According to set criteria insulin glargine biosimilar was deemed to be a high priority for funding.

[1]prices correct at time of publication.

ACTION: BR to draft recommendation as above

Insulin Glargine – Toujeo®

The group discussed the data for the higher strength insulin glargine - Toujeo® and noted the following points:

- Toujeo® is a higher-strength formulation (300 units/mL), than the existing insulin glargine product on the market (Lantus®, 100 units/mL). Toujeo is intended to have a flatter and more prolonged pharmacodynamic profile than Lantus®.
- Toujeo® is licensed for the treatment of DM in adults.
- In clinical trials, Toujeo® was shown to be non-inferior to Lantus in reducing HBA1c in both T1DM and T2DM. The incidence of nocturnal severe and/or confirmed hypoglycaemia was a significantly lower with Toujeo in T2DM trials, but showed no difference in patients with T1DM.
- The overall safety profile of Toujeo® was comparable to the well-established safety profile of Lantus®. No new or unexpected safety signals were detected with respect to injection site reactions, insulin antibody response, hypersensitivity reactions and cardiovascular safety.
- In T1DM, NICE NG17 (2015) recommends multiple daily insulin injection basal-bolus regimens, rather than twice-daily mixed insulin regimens as the insulin injection regimen of choice for all adults with T1DM. Twice‑daily insulin detemir should be offered as basal insulin therapy. If a twice-daily insulin regimen is not acceptable, consider once-daily insulin glargine or detemir. Once-daily insulin glargine should also be considered if insulin detemir is not tolerated.
- In T2DM, NICE CG87 (2009) recommends that NPH insulin is the preferred choice when insulin therapy is needed to treat T2DM. Long-acting insulin analogues may have a role in treating specific patients.
- Toujeo® represents an additional treatment option for patients that require a long-acting insulin analogue who are not currently able to achieve optimal glycaemic control. Due to a flatter and more prolonged pharmacodynamic profile Toujeo® allows patients' greater flexibility in the timing of their once-daily injection compared with Lantus®. **However, switching from Lantus® to Toujeo® is not straightforward, as the drugs are not bioequivalent and are not directly interchangeable.** A switch can be done on a unit-to-unit basis, but higher doses of Toujeo® (approximately 10-18%) may be required to achieve similar levels of glucose control.
- The per unit acquisition cost of Toujeo® is lower than Lantus. However, Toujeo® and Lantus® are not bioequivalent and therefore are not interchangeable.

The group noted that several new insulin products have come to market recently, and healthcare professionals and patients need to understand the insulin strength of these products and how to use them correctly to minimise the risk of medication errors such as the wrong insulin dose being administered. The group was particularly concerned around the use of the Toujeo® around the interface on admission and discharge from hospital as it was felt that this was where the risk of medication errors was greatest. It was therefore agreed that a GM wide risk minimisation strategy on use of high strength insulin's is required before Toujeo® could be fully recommended. It was noted that whilst insulin passports were recommended by the MHRA when 200 units/ml of insulin degludec was launched, these are rarely used in practice therefore a more robust safety protocol needs to be drafted. It was noted that a protocol had been written for inpatient hospital use of high strength insulin's and was going to GMMMG for approval however a protocol that covered both primary and secondary care was required.

Post meeting note:

The group had been approached by various diabetes specialists regarding the use of the two insulin glargine Products. Specialists were keen to use Toujeo® in a defined patient population i.e. in those patients who would otherwise require high volumes of 100 units/ml insulin's. They also had some concerns around switching patients on Lantus® to the biosimilar. It was agreed that this agenda item would therefore be discussed again at the next meeting.

The New Therapies Subgroup of the GMMMG considered the use of Insulin Glargine Insulin Glargine – Toujeo® (300 units/mL), for type 1 (T1DM) and type 2 diabetes mellitus (T2DM).

The group recommends the use of 300 units/ml insulin glargine – Toujeo® as an option only in patients that require high volumes of 100 units/ml insulin and providing there are adequate measures in place for the safe prescribing of higher strength insulin across the health economy.

In clinical trials, Toujeo® was shown to be non-inferior to Lantus in reducing HBA1c in both T1DM and T2DM.

To note that switching from Lantus® to Toujeo® is not straightforward, as the drugs are not bioequivalent and are not directly interchangeable. Higher doses of Toujeo® (approximately 10-18%) may be required to achieve similar levels of glucose control.

According to set criteria insulin glargine Toujeo® was deemed to be a high priority for funding for the specific patient population defined above.

ACTION: BR to add to the agenda for November.

4) Ivermectin for the treatment of acne rosacea

The group discussed the data for ivermectin and noted the following points from the summary document:

- Ivermectin cream is licensed for the topical treatment of inflammatory lesions of papulopustular rosacea (PPR) in adults. Ivermectin is an avermectin antiparasitic which acts against demodex mites. It also appears to have anti-inflammatory properties.
- Rosacea is one of the most common skin conditions encountered by dermatologists. It typically presents in fair-skinned people between the ages of 30 and 50 and is three times more common in women but often presents as more severe in men.
- It follows a chronic relapsing pattern. Several subtypes exist with differing symptoms, but persistent erythema tends to be present in all types. Because it affects the face and can be thought to be disfiguring, it can significantly affect quality of life for those who suffer from it.

- The exact aetiology of rosacea is unknown, but it is likely multifactorial. Inflammation and dilation of facial blood vessels play a large part. A variety of trigger factors can exacerbate the condition, including alcohol, exercise, extremes of temperature, hot drinks, spicy food, stress and exposure to natural sunlight.
- The role of demodex folliculorum mites in rosacea remains controversial. Estimates suggest demodex mites may be present in as many as 80% of rosacea patients, though they are currently considered to be an aggravating factor rather than causative. The therapeutic benefit of most existing treatment is derived mostly from anti-inflammatory effects rather than bactericidal or other pharmacodynamic actions.
- The Primary Care Dermatology Society recommends a stepwise approach to treatment, depending on the predominant symptoms. General measures such as emollients and avoiding aggravating factors should be recommended. For patients with mild PPR, topical metronidazole or azelaic acid are considered first line. Systemic treatments such as a tetracycline antibiotic or erythromycin may be used in more severe symptoms or where topical measures fail. Flushing can be treated by propranolol or clonidine, with topical brimonidine and laser therapy being options for more persistent or recurrent symptoms.
- The efficacy of topical ivermectin versus vehicle has been assessed in two identical randomised double-blind vehicle controlled 12 week long trials. Both trials recruited adult patients (n=1371) with moderate or severe PPR and with 15-70 facial inflammatory lesions. Patients were randomised to either ivermectin 1% cream or vehicle cream once daily at bedtime.
- In both trials, topical ivermectin resulted in a higher success rate compared to vehicle alone at week 12.
- Ivermectin 1% cream was compared to metronidazole 0.75% cream in a randomized, investigator-blinded 16 week study in 962 patients. This trial was similar in design to the previous two trials. Significantly more patients achieved a clear or almost clear status in the ivermectin group compared to metronidazole.
- Ivermectin cream costs approximately £109.74 per patient per year, making it more expensive than other topical first line options such as metronidazole and azelaic acid.
- Ivermectin appears well tolerated. Safety data is limited to two 40-week trials. It may be a useful option in patients who cannot tolerate other topical products.

The New Therapies Subgroup of the GMMMG considered the use of ivermectin for the topical treatment of inflammatory lesions of papulopustular rosacea in adults.

The group recommends that ivermectin cream may be considered for use after more established therapies such as metronidazole gel and azelaic acid have failed.

The group recommends that if started then treatment should be reviewed regularly by the initiating clinician or high quality photos should be taken prior to starting treatment so an objective assessment of efficacy can be made. If there is no improvement after 3 months then it should be discontinued. Ivermectin is licensed for use for up to 4 months.

According to set criteria ivermectin was deemed to be a medium priority for funding.

ACTION: BR to draft recommendation as above and take to GMMMG.

5) Topical Gabapentin for the treatment of neuropathic pain.

The group had been asked to review the use of topical gabapentin which was being recommended for prescribing by a few pain clinics across GM. The group noted that there are no licensed topical preparations. The group reviewed the very limited evidence base for the use of topical gabapentin and noted the following points:

- Evidence for efficacy of topical gabapentin is extremely sparse, and mainly comprises case reports and case series; there are no robust randomised trials.
- Reports generally discuss treatment of neuropathic pain using extemporaneous preparations.
- Concentrations used vary from 2% to 10%, and the formulation may be either a cream or a gel.
- Reports are split between use of gabapentin as a single agent, and those which combine it with other drugs also intended to provide analgesia such as ketoprofen or amitriptyline.
- One paper reported two cases of women treated with gabapentin 5% gel for neuropathic pain which appeared to show some efficacy in these two cases.
- There is no licensed gabapentin gel available in the UK. A small trial of around 20 patients is currently ongoing in Wales, and is expected to finish in March 2016.
- There are no topical preparations currently in the pipeline for licensing. In the absence of a licensed product, topical gabapentin creams and gels must be obtained as specials, or extemporaneously dispensed. As such, price and quality will vary widely.

Due to the lack of any clinical data supporting efficacy of topical gabapentin in neuropathic pain, the group agreed that this should not be recommended and should also be proposed for the DNP list.

The New Therapies Subgroup of the GMMMG considered the unlicensed use of topical gabapentin for the treatment of neuropathic pain.

The group does not recommend the use of topical gabapentin for the treatment of neuropathic pain.

The group was concerned about:

- The paucity of data
- The low quality of data that is available (small patient numbers, case reports)
- Lack of a licensed preparation (quality, strength and price varies greatly)
- Lack of any safety data

According to set criteria topical gabapentin was deemed to be a very low priority for funding

ACTION: BR to draft recommendation as above and take to GMMMG.
BR to fill in DNP forms and send to Formulary Subgroup.

6) Review of Anal Irrigation Systems

The group had been asked to review the use of anal irrigation systems by CCGs. Data showed that Greater Manchester had spent approximately £500,000 on anal irrigation systems in 2014/15. The group reviewed the clinical data available and noted the following points from the review:

- Faecal incontinence is associated with a high level of physical and social disability and occurs in up to 10% of the population at some time (with approximately 2% of the population suffering severe incontinence). Available data suggest that the standard benchmark rate for a referral into a faecal continence service is 100 per 100,000 of the adult population (aged 15 years or older) per year.

- Peristeen®, Qufora® and Aquaflush® are different types of Transanal Irrigation Systems (TAIs) also known as Rectal Irrigation Systems (RIs). TAI is a method used to empty the bowel of faeces (up to the splenic flexure) using warm water which is introduced with a catheter via the anus into the rectum. The water and contents of the descending colon, sigmoid colon and rectum are then evacuated. Regular and controlled evacuation in this manner aims to prevent both constipation and faecal soiling.

- TAIs are designed for self-administration by patients, even if dexterity is poor. To ensure safe use, it is important that the patient is taught how to use the system by a competent

health care professional. It is important to carry out a full individualised assessment of patient suitability prior to commencing any kind of irrigation and obtain informed consent.

- For faecal incontinence in adults, NICE CG49 recommends transanal irrigation as one of a number of options following failure of initial management involving diet, bowel habit, toilet access, medication and coping strategies.

- NICE CG99 does not recommend transanal irrigation as an option for the management of idiopathic constipation in children, due to a lack of robust evidence for this indication.

- In addition transanal irrigation is considered to have a place in the care pathway for patients with faecal incontinence as supported by the Royal College of Surgeons (RCS) commissioning guide, however as an invasive method of bowel management its place in therapy should be after all other acceptable bowel management strategies have failed.

- There is however limited evidence base for use of this procedure at present and existing protocols for TAI are based largely on expert opinion and practical experience.

The group agreed that there was a place for TAI as per the RCS guide and NICE guidance but wanted more information on the products available and types of patients that may be suitable they therefore agreed to consult with a nurse specialist around use of TAI and proposed that this item be deferred till November when the specialist nurse from CMFT can attend.

ACTION: BR to defer item and invite nurse specialist to November meeting.

7) Current work plans & new submissions received since April & Horizon Scanning

The group discussed the current work plan and noted that they had agreed to look at the two PCSK9 inhibitors in November. BR asked the group if they could forward on details of any specialists that may be interested in attending the group.

The group agreed to add the following items to their work plan from the horizon scanning documents:

- Tafluprost/timolol
- Ferric citrate corordination complex
- Guanfacine for ADHD
- Sacubitril/Valsartan combination for heart failure

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ACTION: BR to update work plan as above.

8) Updates from other groups.

Formulary Subgroup
The group was updated on the last formulary subgroup meeting. The group discussed the COPD pathway and wondered if a more cost effective model would be to move from single agent to a LABA/LAMA combination inhaler and then add in a single steroid inhaler (for those patients that fulfil the criteria for steroid use) which involves fewer inhaler changes and is easier for the patient.

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 and noted that the issue around a maximum dose for melatonin may need to be referred back to NTS.

9) AOB

No other issues were raised under any other business.

10) *Date of Next Meeting: 17th November 2015, 12.30-2.30pm, CMFT*