Minutes of the GMMMG Clinical Reference Group Meeting
Tuesday June 13th, 2023, 12:00-14:00
via MS Teams

Name	Title	Organisation	Nov	Dec	Feb	Apr	May	Jun
Dr Peter Budden (PB) Chair	GP	St Andrews Medical Practice	✓	✓	✓	✓	✓	✓
Dr Helen Burgess (HB)	GP	NHS GM IC (Manchester)	✓	A	✓	✓	A	✓
Dr Jonathan Schofield (JS)	Consultant Physician Acute Medicine & Diabetes	Manchester FT	✓	✓	✓	A	✓	A
Suzanne Schneider (SS)	Medicines Information Pharmacist	Bolton FT	A	✓	✓	✓	✓	A
Gary Masterman (GM)	Associate Director of Pharmacy	Wrightington, Wigan and Leigh FT	A	A	✓	✓	✓	✓
Andrea Marrosu (AM)	High-cost Medicines and Home Care Pharmacist	Salford Royal FT	A	✓	A	✓	✓	✓
Peter Marks (PM)	LPC Board Member	GM LPC	A	A	A	A	A	
Mina Chowdhury (MC)	Medicines Optimisation Pharmacist	NHS GM IC (Heywood, Middleton & Rochdale)	✓	✓	✓	✓	✓	✓
Lucy Tetler (LT)	Medicines Optimisation Pharmacist	NHS GM IC (Bury)	✓	✓	✓	✓	✓	✓
Matthew Ling (MB)	Deputy Director of Pharmacy	GM Mental Health FT	SB	SB	✓	✓	✓	✓
Faduma Abukar (FA)	Head of Medicines Management	NHS GM IC (Stockport)	✓	✓	A	✓	✓	✓
Zoe Trumper (ZT)	Assistant Director of Medicines Management	NHS GM IC (Wigan)	✓	✓	A	✓	✓	✓
Faisal Bokhari (FB)	Deputy Head of Medicines Optimisation	NHS GM IC (Tameside)	A	✓	A	A	A	A
Jennifer Bartlett (JB)	Team Leader Neighbourhood Integrated Practice Pharmacists	Salford Royal FT	✓	✓	A	A	✓	✓
Claire Foster (CF)	Senior Medicines Optimisation Adviser	NHS GM IC (Manchester)	A (ZP)	✓	IH	✓	✓	IH
Jole Hannan (JH)	Interface Pharmacist	NHS GM IC (Bolton)	✓	✓	A	✓	✓	✓
Jacqueline Coleman (JC)	Medicines Optimisation, Interface Pharmacist	NHS GM IC (Stockport)	A	A	A	A	A	A
Leigh Lord	Head of Medicines Optimisation and Governance	Manchester FT	✓	✓	✓	✓	A	✓
Consultant Rheumatologist Audrey Low Ben Parker Charlie Filer Dipak Roy Louise Mercer		SRFT MFT Stockport TGH Stockport	✓ (AL)	✓ AP	A	A	A	A

Meghna Jani Sahena Haque Anindita Paul		SRFT UHSM Bolton						
Dan Newsome (DN)	Principal Pharmacist	RDTC	✓	✓	✓	✓	✓	✓
Nancy Kane (NK)	Senior Medical Information Scientist	RDTC	A	✓	✓	✓	✓	✓
Andrew Martin (AMart)	Strategic Medicines Optimisation Pharmacist	NHS GM IC	✓	✓	✓	✓	✓	✓
Karina Osowska (KO)	Medicines Optimisation Pharmacist	NHS GM IC	✓	✓	✓	A	✓	✓

1. General Business	
1.1	**Welcome and apologies** In attendance were Zoe Neilson, Lara Shah and Peter Elton for item 4.1 and Anna Pracz for items 3.2 & 4.4
1.2	**Declarations of interest** Previously declared where relevant. No further declarations of interest were made.
1.3	**Draft May 2023 CRG Minutes** The minutes were approved for publication to the GMMMG website
1.4	**Action log review** The owner of each action will be approached for updates if not already provided to CRG. Some items have full agenda items. Others have progress as follows: • Steroid eye drops: resource from MFT has been assigned and is undertaking this work. A draft leaflet is planned for submission to the trust MMC in July, after which it will come to CRG for consideration • Omalizumab for CIU: KO is liaising with both NCA and MFT clinicians to finalise this piece of work. • PB provided an update on Buvidal as an AOB item
2.0 Matters arising	
2.1	**CRG Consultation April 2023** The comments submitted through consultation were noted and discussed. All were supportive of the actions except for finerenone TA877. A response from the North West Kidney Network lead for CKD requested that the RAG status applied should be Green specialist advice to better facilitate the needs of the eligible cohort and avoid delays to treatment. It was argued that referral to a specialist would in many cases be unnecessary solely for the initiation of the medicine. CRG agreed with this request in principle but did discuss the practicalities of initiating the medicine in primary care. The main issue appears to be ensuring that normal potassium results are actioned appropriately, which, in the case of finerenone when taken 4 weeks after initiation, may result in a dose increase as per SPC. It was therefore requested by CRG that as part of the advice and guidance process which should be followed prior to initiation, the specialist should provide adequate information to safely manage the patient in primary care. PB agreed to contact the commenter for advice from the network on how this can be achieved. **The actions proposed were approved. Finerenone RAG will be submitted to GMMMG as Green specialist advice**

	Action: RDTC to submit all actions to GMMMG for approval.
3.0 Formulary and RAG	
3.1	**Formulary Amendments May 2023** CRG approved the formulary amendments to open for consultation and noted the following: • NG18: Diabetes in children and young people – the new recommendations on use of CGM for children and young adults with T2DM should be considered for approval as part of ongoing work to adopt NICE recommendations regarding CGM. • CG181: CVD risk assessment and reduction including lipid modification – The impact is likely to be small initially and will increase slowly, which is acknowledged by NICE in their costing report. Primary care does not have sufficient resource to be undertaking reviews of their patient lists and anecdotal evidence shows many patients at this CVD risk threshold are resistant to taking statins. **Action:** RDTC to open formulary amendments for GMMMG consultation
3.2	**Infliximab and vedolizumab subcutaneous injection presentations : formulary request** AP attended to present a retrospective request for the addition of subcutaneous infliximab and vedolizumab the GMMMG formulary for all their licensed indications. Both products are already in use in a number of GM trusts, predominantly (and entirely in the case of vedolizumab) in gastroenterology services. The anticipated use of sc infliximab in rheumatology services is low, however the updated pathways do now include this as an option. Vedolizumab was discussed first. It is licensed for use as in a 108mg pre-filled pen and syringe in Crohn's disease and ulcerative colitis and is approved by NICE as the IV formulation (TA342 and TA352). Based on the available evidence, the EMA concluded that overall, in both CD and UC, clinical efficacy of vedolizumab SC was in line with that of IV formulation. In terms of safety, the profile was acceptable and consistent with that of IV formulation with exception of injection-site reactions. It can be used in the sc form after IV initiation of at least 2 doses and is then given every 2 weeks instead of every 8 weeks as an IV infusion (or in some cases every 4 weeks as a dose escalation). Based on list prices, the annual treatment cost using the sc formulation is the same (using standard rather than dose escalated regime), but there are efficiency savings to be made on the reduced use of day case attendances and the associated nursing time. It was acknowledged that there is an associated homecare burden, however much of the clinical and logistical aspects are provided by the manufacturer-funded homecare service. Indeed most GM trusts are already using the product as it increases patient choice and contributes to better patient experience of treatment. Infliximab sc is available as Remsima SC 120mg/1mL and is licensed for use in CD, UC rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and psoriasis. The IV formulation has received a positive NICE TA and is therefore on formulary and included in the relevant HCD pathways for each of the indications above (TA187, TA199, TA329, TA375, TA383, TA715). This request relates to all the indications listed but the majority of use will be for CD and UC. The initial license in 2020 was for RA only and the EMA concluded that non-inferiority in efficacy of SC infliximab was demonstrated for use in this indication and based on provided data can be assumed for indications of CD and UC. In terms of safety, it was noted that long-term data on use of SC formulation is not extensive, however the safety profile of IV infliximab is well established, and in general that of SC formulation is comparable and the safety and efficacy profile was therefore

	extrapolated to other indications of ankylosing spondylitis, psoriasis, and psoriatic arthritis. Similar savings on day case and clinic time are seen with the use of sc infliximab as well as reducing aseptics unit activity, as a result many GM trusts are already using it for its licensed indications with switch programs either planned or being implemented in a number of organisations. Due to its dose being weight based when using the IV formulation, and existence of local contract prices, the cost comparison is complex and cannot be described here, however calculations provided by one of the GM trusts show saving in range of £1-2k per patient per year, depending on patient weight, assuming standard 8-weekly dosing, use of outsourced infusion bags and when factoring in the cost of day case attendances. CRG considered the information above and accepted that the use of these medicines is already happening, the widespread use of sc formulations at worst represent a cost-neutral option whilst improving patient choice for those who wish to receive more care at home. But may also release valuable day case resources to use on other services. CRG therefore approved the request pending a GM-wide consultation. **Decision**: Open for GM-wide consultation
3.3	**Hydrocortisone topical preparations - RAG change request** A piece of work undertaken by the Oldham locality MO team has shown that there is significant use across GM of very expensive hydrocortisone creams and ointments that are not supported by best practice guidance and clinical evidence. The request is to assign a DNP status to hydrocortisone 0.5% ointment, 2.5% cream and 2.5% ointment. These now cost £44, £52.97 and £44 respectively per pack of 15g, as a result GM ICB has spent in excess on £240k on these compared to the alternative 1% cream/ointment and 0.5% cream (all less than £3 per pack) in the last 12 months. There is no clinical rationale for the use of low strength (0.5% ointment) on which GM has spent over £180k so the recommended alternative would be 1% ointment or cream depending on patient preference, which would be licensed for use for all ages. A 100% switch in prescribing of this product could save GM £171k per year The higher strength of 2.5% represents a less significant spend in GM (~£60k per year of both cream and ointment) however the products are still very expensive, cheaper options are available and a complete switch to either the 1% products or a more potent steroid e.g. clobetasone 0.05% would save GM £58k per year. These recommendations have received the endorsement of Oldham's local dermatology service, and the primary care clinicians in the group agreed that they did not see a rationale for the 0.5% ointment or 2.5% products to be prescribed. AMarr agreed to ensure the consultation is reviewed by his dermatology colleagues at NCA. It was noted that 0.5% cream is likely to still have a place in therapy where application to the eyelids is required. CRG agreed that a number of DNP categories could apply here but selected criterion 2: Products which are clinically effective but where more cost-effective products are available, including products that have been subject to excessive price inflation. It was agreed any formulary/RAG amendments should recommend alternative products. **Decision** Open for GM-wide consultation as DNP
3.4	**Chloral hydrate/cloral betaine - RAG review**

	A review of the RAG status was undertaken by CRG in October 2022 following an audit in the Oldham locality which showed potentially inappropriate prescribing. The resulting RED RAG status was proposed based on the MHRA safety advice regarding a maximum duration of treatment of 2 weeks for all indications. The subsequent consultation attracted comments from primary care which agreed with a RED status and also from secondary care (all MFT) which disagreed, This disagreement was on the grounds of their service providing the regional service for the North West and included specialist indications which required long term treatment. It was argued that asking patients to travel long distances for prescriptions was unreasonable. The action was then paused to gather audit data from MO teams, but only a handful responded so the picture is not complete but there is likely to be over 100 patients in GM receiving long term (greater than 2 weeks) prescriptions for chloral products, some of which (e.g. in Bury) are all under the care of a specialist but others are not. CRG did not believe this long-term unlicensed use fit with a shared care agreement which was suggested as a consultation comment due to the lack of current best practice guidance and also no routine monitoring to be undertaken by primary care. CRG acknowledged the NPPG-Position-Statement-Chloral-Dystonia-V1.pdf and believed that this supports the hospital only prescribing status that has been proposed. A discussion was then had on the practicalities of prescribing for patients who live a long distance from their specialist service. CRG did not believe that the only way to prescribe for these patients was to request they attend to obtain a prescription from their specialist, and that other options should be explored. GMMMG RAG status should be based primarily on safety and there is strong advice and evidence to suggest that prescribing of chloral products should only be undertaken by a specialist. The inability to issue prescriptions to patients should therefore not override safety concerns. This position was supported by the secondary care representatives on CRG and LL agreed to discuss alternative methods of supply with the MFT service(s) involved. **Decision** Choral hydrate and cloral betaine to be assigned a RED RAG status
4.0 Pathways and Clinical Guidelines	
4.1	**Vitamin D proposal for antenatal care** Zoe Nielson, Lara Shah and Peter Elton were in attendance to present this agenda item. It is a proposal for the effective management of vitamin D provision to pregnant women at their first contact with maternity services in GM, which has been developed by a task and finish group derived from the GMMMG IMPO health inequalities and population health sub-group. It was explained that due to its geographical position, and high levels of deprivation, the population of GM are at high risk of vitamin D deficiency. When supplemented during pregnancy, vitamin D can reduce the risk of pre-eclampsia, gestational diabetes and low birth weight. There is no standardised offer of vitamin D supplementation in GM which results in significant variation in the availability and uptake of any vitamin D supplementation for GM's pregnant population. There are links to the GM equity and equality action plan which is scoping the feasibility of providing healthy start vitamins to all pregnant patients, and would align with this proposal. It is proposed that a 20,000 unit dose is provided to all pregnant women as a loading dose at their booking appointment or first contact with midwifery services, followed by 400 units daily. CRG were asked to consider the evidence and recommend if there is sufficient to further develop the proposal. The included papers summarise the available evidence and include commentary from the UK teratology information service (UKTIS) on the safety of the proposed regimen. CRG

	agreed that the available evidence strongly suggests that a loading dose of 20,000 units is safe in pregnancy, even for women who are vitamin D replete, but that it is not possible to be 100% certain on this. They also cautioned on the extrapolation of the evidence to fit the proposed regimen and if this request is consistent with the terms of reference and previous decisions made by the group. The efficacy of vitamin d supplementation was not in doubt, but there remain questions over the most beneficial dose. It was explained to CRG that there are many studies and none use the same dosing regimen that is proposed here but there is evidence of higher doses being used safely. It was suggested that the doses chosen represent a pragmatic balance between licensed products, ease of administration and supply, and the published evidence base. It was recognised that if the GM system waits for better evidence this inequality is likely to persist and may continue to cause harm. CRG noted that this proposal is yet to be fully costed and as yet has no implementation plan. It was recognised this should include a comms element to ensure rapid and widespread uptake. To ensure good governance, it would be prudent to put some monitoring of the project in place to look at uptake, safety and maternal outcomes. A discussion by RDTC with UKTIS suggests there may be interest in supporting the outcomes monitoring which it was recommended the working group should explore. CRG recognised the chosen dosing regime is not fully evidenced based, but there appears to be sufficient to demonstrate it is highly likely to be safe and effective. More work is required on the monitoring and practicalities of supplying the intervention, however CRG agreed with the principles of the project. **Decision** CRG supported the proposal for further development with GMMMG
4.2	**GMMMG DOAC statement** CRG undertook a review of the GMMMG edoxaban for NVAF position statement made in August 2022, which is now due for review. The group was informed that work is being undertaken by the GMMMG IPMO medicines value subgroup to develop a guidance document to switch patients from other DOACs to edoxaban for reasons of cost reduction. As the position statement document is currently written this practice remains an option for localities to undertake if it can be done safely and on an individual patient basis, however it was acknowledged that many of the system incentives to support this work have now been removed such as the IIF indicator, and that the value of the discount as part of the edoxaban rebate has decreased, as of January 2023. Members also raised the possibility of apixaban soon becoming the best value DOAC rather than edoxaban due to an ongoing patent dispute. It was explained that a further case is due to be heard in summer 2023 and the leave to appeal earlier decisions remains in place, but until this is resolved the drug tariff prices of apixaban are likely to remain the same as the originator product (Eliquis). GMMMG must continue to represent all parts of the system and it was thought that a further attempt to gain secondary care consensus for edoxaban use as first line was unlikely to be successful. Work done by the MFT pharmacy team has achieved a position of edoxaban being the preferred choice DOAC for AF which supports the GMMMG position. CRG agreed that the current statement is adequate for the needs of all stakeholders and agreed to review in a further 12 months. It was pointed out that any reference to the IIF should be removed. **Decision** The position statement will be updated as above and then be published to the GMMMG website as a technical update.

4.3	**Inclisiran prescriber information leaflet – technical update** AMart presented a minor technical update to the Inclisiran prescriber information leaflet. This item was previously approved by GMMMG but would make sense to be held by CRG in future. The update was primarily to amend the reimbursement arrangements which have recently changed, as well as provide some updated safety information. CRG were happy with the amended document. **Decision** Publish to website
4.4	**GMMMG HCDs pathways - technical updates** AP presented some important safety updates to the rheumatology HCD pathways to ensure the recent MHRA alert on the risks associated with JAK inhibitors was included, plus a recent addition to the formulary for TA861: upadacitinib for active non-radiographic AS. The addition of sc infliximab is pending the system approval of the formulary request discussed as an earlier agenda item. **Decision** Publish to web without sc infliximab until approved. PB agreed to take chairs action on the document once this decision is approved.
5.0 Shared care	
No agenda items	
6.0 Work plan and horizon scanning	
6.1	**Monthly horizon scanning May 2023** CRG considered the contents of the document and made the following comments. • The AposHealth device for knee osteoarthritis may be of interest to GMMMG although outcomes appear to be limited to delaying knee replacement and not for reduction in use of analgesia
7.0 AOB • PB provided a summary of his discussion on the use of Buvidal with the GM substance misuse lead. There is clearly a place in therapy for this product and the RAG would depend on the commissioning arrangements that are in place in each locality, but it would most likely be RED except where a service is agreed with primary care clinicians in which case there is a precedent of using “other” for this indication. A formulary submission has been requested.	
Date of next meeting: Tuesday 11th July 2023 12:00-14:00 via Teams	