http://www.devonformularyguidance.nhs.uk/

Meeting of the Devon Formulary Interface Group

Minutes

Wednesday 27th November 2024

Via Microsoft Teams

Present:

Name	Job Title	Organisation
Nick Keysell (Chair)	GP	NHS Devon ICB
Ailene Barclay	Pharmacist	UHP NHS Trust
Stuart Crowe	GP	NHS Devon ICB
Jess Danielson	GP	NHS Devon ICB
Matt Howard	Senior Clinical Effectiveness Pharmacist	NHS Devon ICB
Anne Jones	NHS Cornwall and the Isles of Scilly ICB	NHS Kernow ICB
Alisha Kaliciak	GP	NHS Devon ICB
Carole Knight	Medicines Information Pharmacist	RDUH NHS FT
James Leavy	Medicines Information Pharmacist	RDUH NHS FT
Rebecca Lowe	Joint Formulary Pharmacy Technician	NHS Devon ICB
Jess Parker	GP	NHS Devon ICB
Hilary Pearce	Clinical Effectiveness Pharmacist	NHS Devon ICB
Chris Sullivan	Deputy Chief Pharmacist	Devon Partnership NHS Trust
Charlie Thomas	Deputy Chief Pharmacist – Primary Care	NHS Devon ICB
Darren Wright	Joint Formulary Specialist Pharmacy Technician	NHS Devon ICB

Guests:

Name	Job Title	Organisation
Emma Gitsham	Specialised Medicines Service (SMS Guidelines Lead)	NHS Devon ICB
Mr Ben Peyton-Jones	Consultant Obstetrician and Gynaecologist	NHS Devon ICB
Nic Perrem	Healthcare Evidence Reviewer	NHS Devon ICB

Observers:

Name	Job Title	Organisation
Affreen Mohammed	Pharmacy Services Manager and Lead Clinical Pharmacist	NHS Devon ICB
Abbey Mole	Medicines Optimisation Pharmacist	NHS Devon ICB
Peter Collins	Chief Medical Officer	NHS Devon ICB

In attendance:

Fiona Dyroff	Clinical Effectiveness Governance Support Officer	NHS Devon ICB

1. Welcome and announcements

Meeting etiquette

Nick Keysell stated that he would be acting as Chair in the absence of Glen Allaway. Nick explained the meeting etiquette.

Chairman's welcome

Nick Keysell welcomed attendees to the meeting of the Devon Formulary Interface Group.

Nick reported that Beverley Baker had stepped down from the group after several year of involvement. The group thanked Beverley for her contribution to the group. It was noted that Beverley may attend as a guest for relevant items in the future.

Apologies

NAME	JOB TITLE	ORGANISATION
Dr Glen Allaway (Chair)	GP	NHS Devon ICB
Dr Andy Craig	GP	NHS Devon ICB
Dr Lucy Harris	GP	NHS Devon ICB
Dr Susie Harris	Consultant Physician/Geriatrician	RDUH NHS FT
Sarah Marner	Senior MO Pharmacist	NHS Devon ICB

Charlie Thomas attended the meeting as MO representative in the absence of Sarah Marner.

Dr Lucy Harris had provided written comments prior to the meeting.

Declarations of Interest

The Declarations made did not result in anyone being excluded from the meeting or from the discussion of any item.

DRUG TO BE CONSIDERED	PHARMACEUTICAL COMPANY/ MANUFACTURER
Opicapone for Parkinson's Disease **Alternative treatments:** • Entacapone • Levodopa with carbidopa and entacapone combination products • Tolcapone • Apomorphine • Co-careldopa intestinal gel • Deep brain stimulation	BIAL Pharma UK Ltd Various manufacturers Orion Pharma (UK) Ltd, Actavis UK Ltd, Teva UK Ltd Meda Pharmaceuticals Ltd Britannia Pharmaceuticals Ltd AbbVie Ltd
Chronic heart failure • Dapagliflozin (Forxiga) • Empagliflozin (Jardiance)	 Astra Zeneca UK Ltd Boehringer Ingelheim Ltd

DRUG TO BE CONSIDERED	PHARMACEUTICAL COMPANY/ MANUFACTURER
• Sacubitril valsartan (Entresto) • Various classes of drugs including diuretics, ACE inhibitors, angiotensin receptor blockers, beta-blockers, mineralocorticoid antagonists	Novartis Pharmaceuticals UK Ltd Various manufacturers
Continence products: • Continence appliance and accessories	Includes, but is not limited to: Bard, B.Braun Medical, Beambridge Medical, CliniMed, Clinisupplies, Coloplast, Flexicare Medical, Great Bear Healthcare, Hollister, LINC Medical Systems, MacGregor Healthcare, Optimum Medical, Renew Medical, Rochester Medical, Wellspect Healthcare
Nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG) (update): • Promethazine hydrochloride tablets • Cyclizine tablets • Xonvea (doxylamine / pyridoxine) 10mg/10mg gastro-resistant tablets • Metoclopramide tablets • Prochlorperazine maleate tablets • Ondansetron tablets • Prednisolone tablets	 Various manufacturers Various manufacturers Exeltis UK Ltd Various manufacturers Various manufacturers Various manufacturers Various manufacturers
Linzagolix for uterine fibroids (inc Ryeqo) • Linzagolix (Yselty) • Ryeqo	 Theramex UK Ltd Gideon Richter (UK) Ltd
Relugolix for prostate cancer • Relugolix (Orgovyx) **Alternative treatments** • Triptorelin • Goserelin • Leuprorelin • Degarelix	 Accord UK Ltd Ferring Pharmaceuticals Ltd, Ipsen Ltd Astra Zeneca Ltd Aspire Pharma Ltd, Takeda UK Ltd Ferring Pharmaceuticals Ltd
Buvidal (including updates to section 4.10.3 Opioid dependence) Buvidal Suboxone **Alternative treatments** • Buprenorphine tablets (including Espranor) • Methadone solution • Sixmo implant • Subsolv tablets	 Camerus AB Indivior UK Ltd Various manufacturers (including Martindale Pharmaceuticals Ltd) Various manufacturers Accord UK Ltd Accord UK Ltd

DRUG TO BE CONSIDERED	PHARMACEUTICAL COMPANY/ MANUFACTURER
Glycopyrronium bromide tablets • Various generic and branded **Alternative treatments for severe sialorrhoea** • Alternative presentations of glycopyrronium bromide including Sialanar oral solution • Alternative antimuscarinics, including hyoscine hydrobromide, trihexyphenidyl hydrochloride • Botulinum toxin type A (Xeomin, Botox, Dysport)	Various manufacturers including Morningside Healthcare Ltd, Dawa Limited, Strandhaven Limited t/a Somex Pharma Various manufacturers including Proveca Limited Various manufacturers Merz Pharma UK Ltd, AbbVie Ltd, Ipsen Ltd
Mycophenolate mofetil • 500mg tablets, 250mg capsules and 1g/5ml sugar free oral suspension **Mycophenolic acid** • 180mg and 360mg gastro-resistant tablets	Various manufacturers Various manufacturers
Topiramate containing medicines **Alternatives** • Various anti-epileptics, various medicines for migraine prophylaxis	Various manufacturers Various manufacturers
Valproate containing medicines **Alternatives:** • Various anti-epileptics, various antipsychotics	Various manufacturers Various manufacturers

Items discussed by e-FIG

e-FIG ITEM	PHARMACEUTICAL COMPANY/ MANUFACTURER
Cytisine 1.5mg tablets (Cytisinicline) • Cytisine 1.5mg tablets • Varenicline **Alternatives** • Long-acting nicotine replacement therapy (24-hour transdermal patches, 16-hour transdermal patches) • Short-acting nicotine replacement therapy (Medicated chewing gum, lozenges, sublingual tablets, inhalators, nasal sprays, oromucosal sprays) • Serotonin and noradrenaline re-uptake inhibitors (Bupropion hydrochloride modified-release tablets (Zyban)) • Nicotine-containing e-cigarettes / vapes (Various e-cigarettes / vapes)	Bonteque Consulting Ltd / Consilient Health Ltd Various manufacturers Various manufacturers Various manufacturers GlaxoSmithKline UK Various manufacturers
Direct-acting oral anticoagulants (DOACs): NHSE commissioning recommendations – September 2024 update • Edoxaban (Lixiana) • Rivaroxaban (Xarelto) • Rivaroxaban generic • Apixaban (Eliquis) • Apixaban generic • Dabigatran (Pradaxa)	Daiichi Sankyo UK Limited Bayer plc Various manufacturers Bristol-Myers Squibb-Pfizer Various manufacturers Boehringer Ingelheim Limited

Name	Job Title	Declaration
Rebecca Lowe	Joint Formulary Technician	I have secondary employment in Day Lewis Pharmacies.
Peter Collins	Chief Medical Officer	I'm married to the NHS Supply chain national clinical lead for these products *[continence appliances and accessories]*.

2. Minutes of the meeting held on 25th September 2024 and Actions

Minutes of the meeting held on Tuesday 25th September 2024

The minutes of the meeting held on Tuesday 25th September 2024 were approved.

Action log update

The action log was reviewed.

3. Matters Arising

Recent Drug Decisions

The FIG received a report of the recent drug decisions.

4. E-FIG

In October the FIG was asked to consider two items via the e-FIG process, these were:

1) Cytisine (Cytisinicline) & Varenicline

2) Direct-acting oral anticoagulants (DOACs): NHSE commissioning recommendations – September 2024 update.

Responses received indicated acceptance of the proposals.

ACTION 24/92: (eFIG): Cytisine (Cytisinicline) & Varenicline - update the formulary in line with the proposals.

ACTION 24/93: (eFIG): DOACs: NHS England commissioning recommendations - update the formulary in line with the proposals.

5. Opicapone for Parkinson's Disease

Following a recommendation by the Clinical Policy Recommendation Committee (CPRC) in 2018, opicapone was routinely commissioned as an alternative treatment option in individuals who are unable to tolerate entacapone. The decision to position opicapone as second line to entacapone was based on evidence available at that time demonstrating that opicapone was non-inferior to entacapone in reducing off times but was significantly more costly. The CPRC reviewed the policy following an application from a movement disorder specialist team for opicapone to be made a first-choice option alongside entacapone.

In light of new information on clinical benefit and a price reduction for opicapone, the CPRC voted in favour of recommending that the existing policy for opicapone be amended so that opicapone can be considered as a first-choice option alongside entacapone.

The Formulary Interface Group was asked to take a decision in principle on proposed updates to the formulary entry for Opicapone, pending organisational sign off by NHS Devon ICB of the updated clinical commissioning policy.

The FIG considered and accepted in principle the proposed update to the opicapone entry without amendment.

ACTION 24/94: Publish the amendments to the opicapone drug entry once the clinical commissioning policy has been ratified and published.

6. Chronic Heart Failure

At the July 2024 FIG meeting, a draft update to the Devon Formulary guidance for chronic heart failure (CHF) was presented for review following consultation with the heart failure specialist teams. For CHF with reduced ejection fraction (HFrEF), drug specific guidance was presented for initiation, monitoring, actions to take and formulary options. An introductory section for HFrEF was at an early stage in development to be informed by feedback from the FIG discussion.

The optimal method of initiation for the initial pharmacological options for HFrEF is a source of discussion in the literature. There are several published algorithms, and a large trial is underway to establish whether there is an optimal approach.

NICE has started work on an update to their guidance on CHF which will focus on pharmacological treatment. The final scope has been published. In HFrEF, NICE will review the clinical evidence and cost effectiveness of the first-line medicines. The new formulary guidance for CHF will be interim guidance until NICE publishes the update to NG106 in August 2025. The Formulary team will review the new NICE guidance when it is published and consult with local specialist teams.

The FIG was asked to consider a revised introductory section for the formulary guidance on HFrEF including whether the overall approach to this section was acceptable and whether there were any specific points to raise with the specialist teams. Proposed amendments will be included in the final draft of the formulary guidance for CHF to be sent to the specialist teams for consultation.

The FIG considered the draft update to the chronic heart failure guidance. There was discussion about:

- The importance of respecting patients' wishes on quality of life,
- the usefulness of having a recommendation on the lowest acceptable blood pressure measurement for frail patients.
- weight check to be added to the guidance, as a method of assessing fluid status.

ACTION 24/95: Update the chronic heart failure guidance in line with the discussion and circulate to specialists for consultation.

ACTION 24/96: Following specialist consultation, bring chronic heart failure guidance back to FIG for final decision.

7. Continence Products

Following some recent product discontinuations the formulary continence product recommendations have been reviewed with local specialists.

OpenPrescribing data for the last 12 months (up to Aug '24) show that in Devon approximately £7.35 million was spent on continence appliances and accessories in primary care. £4.59 million on catheters and £2.76 million on bags, systems and accessories.

A detailed assessment of the financial impact of the proposed recommendations has not been possible due to the range of products currently prescribed (including extensive use of non-formulary products) and the difficulty in assessing the proportion of current prescribing which may be replaced by one of the proposed alternatives. However, inclusion of all proposed products in the formulary is not expected to significantly increase primary care expenditure.

The FIG adopted the approach used recently when considering harmonisation of wound dressings and appliances listed in the formulary. Where a product is already recommended in either North & East or South & West Devon, the FIG accepted its inclusion Devon-wide, provided there is specialist support and there have been no significant changes to the product, or its comparators, which may prompt reconsideration.

The Formulary Team has worked with specialists with a breadth of experience to make recommendations on products for use in general practice, and to recognise when products are only suitable for use on the recommendation of a specialist team member.

The FIG reviewed and accepted the proposed harmonisation of continence products across the Devon Formulary. The discussion included that the:

- FIG supported the principle of developing a Devon Continence Product Group along the lines of the Devon Wound Group which had been set up with local providers to consider and provide local specialist advice to the FIG on wound products,
- FIG did not accept the inclusion of Conveen Prep Wipes at this time. Consideration was given to their usefulness and the environmental impact of disposable / single use wipes.
- it was agreed that silver coated catheters be removed due to lack of evidence

ACTION 24/97: Publish the updates to continence products in line with the discussion.

8. Nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG) (update)

The inclusion of Xonvea (doxylamine 10mg / pyridoxine 10mg) as a blue (second line) option for nausea and vomiting in pregnancy was considered and accepted at the FIG meeting in September 2024.

During the consultation for Xonvea, local specialists suggested changes to the current formulary guidance on NVP and HG, to include additional options as per guidance from Royal College of Obstetricians and Gynaecologists (RCOG).

The RCOG guideline on the management of NVP includes chlorpromazine as a first line option and oral domperidone as a second line option for mild-moderate NVP requiring treatment. These treatments were not included in the Devon Formulary NVP guidance. RCOG also recommends prochlorperazine as a first line option and ondansetron as second line; current formulary guidance recommends prochlorperazine as second line, and ondansetron as third line.

At the September FIG meeting, FIG members discussed the RCOG guidance and suggested that the existing formulary guidance provides GPs with enough options in primary care. It was agreed that cyclizine would be appropriate as a first line option alongside promethazine, with Xonvea, metoclopramide and prochlorperazine as second line. It was suggested that chlorpromazine would not be suitable for routine use in primary care for NVP, and the concerns over cardiac events with domperidone remained; FIG suggested that these not be included in the guidance. It was requested that ondansetron remain third line due to the increased risk of orofacial cleft. It was recognised that specialists may need to use or recommend alternative options or higher doses in more severe cases, and that the formulary guidance does not prevent this.

Following the September meeting, updated draft guidance on the management of NVP and HG was shared with local obstetrics and gynaecology specialists alongside the FIG feedback.

Feedback received from the specialists was understanding of the FIG recommendations and some additional information was incorporated into a revised draft which was recirculated for final comments. The final draft was presented to the FIG with key changes from the previous draft highlighted for consideration.

The FIG considered and accepted the proposed formulary guidance for nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG). This included the acceptance of oral prednisolone as a third line option, following initiation in secondary care.

ACTION 24/98: Publish updates to guidance on nausea and vomiting in pregnancy and hyperemesis gravidarum in line with the discussion.

9. NICE TA996 (Linzagolix for uterine fibroids) and reclassification of Ryeqo for uterine fibroids

A Consultant Obstetrician and Gynaecologist from RDUH was present for discussion of this item.

Linzagolix and the combination product, Ryeqo, are oral GnRH antagonists with positive NICE TA recommendations for treating moderate to severe symptoms of uterine fibroids in adults of reproductive age. The medicines are intended for long-term treatment. There is a potential risk of bone mineral density (BMD) loss with the use of GnRH antagonists.

Ryeqo contains the GnRH antagonist, relugolix, with estradiol and norethisterone. Estradiol is included to mitigate the risk of BMD loss and norethisterone is included to avoid the risk of endometrial hyperplasia with unopposed estradiol use. Linzagolix is licensed for use alone or with hormonal add-back therapy (ABT), specifically estradiol and norethisterone. The daily dose of estradiol and norethisterone included in Ryeqo and recommended for ABT with linzagolix is licensed for the prevention of osteoporosis.

A clinically significant and statistically significant reduction in bleeding from uterine fibroids was demonstrated for linzagolix and Ryeqo in the clinical trials supporting the licensing of the products, along with additional beneficial effects on pain. Linzagolix and Ryeqo were considered to be well tolerated with adverse events reflective of their mechanism of action.

NICE found Ryeqo to be a cost-effective option. Linzagolix is cost effective only if prescribed for long-term treatment, at the dosing regimen of 200mg once daily with add-back therapy or 200mg once daily for six months, followed by 100mg once daily without add-back therapy.

The SmPCs for Ryeqo and linzagolix include recommendations for a DXA scan at baseline for patients with risk factors for osteoporosis or BMD loss to determine whether treatment is appropriate, and a DXA scan after the first year of treatment for all patients to determine whether treatment should be continued. Thereafter, a DXA scan is recommended for Ryeqo and linzagolix with add-back therapy as considered appropriate, and annually for linzagolix without ABT. Treatment should be discontinued if the risk of BMD loss exceeds the potential benefit of treatment.

Ryeqo was discussed by the FIG in December 2022 when NICE TA832 was issued. At that time, GPs were unable to refer all pre-menopausal women for a DXA scan through the existing referral routes and it was agreed that Ryeqo would remain red (hospital only) until clarity was reached on the approach to the 12-month DXA scan. Since then, the Ryeqo SmPC has been updated to indicate that further DXA scans may be required during long-term treatment. Linzagolix has not been discussed previously by the FIG. NICE TA996 recommending linzagolix for the management of uterine fibroids was issued in August 2024.

The FIG had an initial discussion to identify an acceptable approach to support an amber classification for Ryeqo and Linzagolix. A consultation was ongoing with the gynaecology specialists at the time. The main points identified during the discussion were:

- That discussion with the specialist present highlighted when Linzagolix with ABT and without ABT would be used.
- There was concern about the robustness of systems in both primary and secondary care to identify patients receiving Ryeqo or linzagolix when a DXA scan is required.
- Arrangements for patients who fail to attend for a DXA scan would need to be addressed. Interpretation and communication of the results of a DXA scan also require consideration.
- It was agreed that advice from rheumatologists be sought on the Ryeqo and linzagolix SmPC statements on DXA scans before progressing this further.

The FIG considered it was acceptable for linzagolix to be added to the Formulary as a red (hospital-only) option for uterine fibroids in line with the approach taken for Ryeqo while further work was undertaken.

ACTION 24/99: Publish updates to Ryeqo and Linzagolix entries in line with the discussion.

ACTION 24/100: Consult with rheumatologists regarding DXA scan requirements for patients prescribed Ryeqo and Linzagolix.

10. TA995: Relugolix for treating hormone-sensitive prostate cancer

NICE TA995 recommends the use of relugolix in advanced hormone-sensitive prostate cancer and alongside radiotherapy or as neoadjuvant before radiotherapy for high-risk localised or locally advanced hormone-sensitive prostate cancer. The FIG reviewed the proposed formulary entry for relugolix and agreed a formulary traffic light classification.

Relugolix is the first oral gonadorelin receptor (GnRH) antagonist to be licensed for the management of hormone-sensitive prostate cancer. Sustained serum testosterone levels equivalent to medical castration was demonstrated for 96% of patients receiving relugolix over an eleven-month period in a phase 3 study, in which relugolix was also found to be non-inferior to leuprorelin. Treatment for testosterone flare was required for fewer than one percent of patients receiving relugolix compared with a quarter of patients receiving leuprorelin.

NICE found relugolix to be cost effective compared with GnRH agonists for its licensed indications and compared with degarelix for patients with spinal metastases. Existing options are given by injection administered by a healthcare professional. Prescribing of relugolix in place of the preferred formulary GnRH agonist, triptorelin, would incur an additional annual cost per patient of £114 and £183. Relugolix is cost saving compared with the most frequently prescribed dose of the second-line formulary GnRH agonist, goserelin, and the GnRH antagonist, degarelix, which has a positive NICE TA recommendation for patients with advanced hormone sensitive prostate cancer and spinal metastases.

It is proposed that relugolix is an amber (specialist-input) formulary option in line with the approach taken to GnRH agonists in the Devon Formulary. Feedback received from two consultants (UHP and RDUH) indicated a preference for GPs starting relugolix on the advice of a specialist, the specialist nurse (UHP) considered that first prescription to be started by secondary care would be the preferred option from a primary care perspective.

The FIG considered and accepted the proposed formulary entry for relugolix for treating hormone-sensitive prostate cancer including the 'amber' (specialist-input) classification with the addition of a note about dose due to drug interactions. The discussion noted that:

- Specialists to prescribe the first 28 days of treatment.
- A comment received suggested that there was unlikely to be a scenario in which the patient was not already under the care of a specialist, and this would ensure correct dosing, including the need for an initial loading dose.
- This is a useful addition as it is an oral option and has a low risk of tumour flare.

ACTION 24/101: Publish updates to Relugolix entry in line with the discussion.

11. Buvidal

A request for the inclusion of Buvidal (buprenorphine) prolonged release solution for injection in the Devon Formulary has been received from a Clinical lead and GP specialist in substance misuse, Together Drug & Alcohol Service. This prompted a review and harmonisation of formulary section 4.10.3 (Opioid dependence).

Products listed in formulary section 4.10.3 (Opioid dependence) should only be prescribed by the Drug & Alcohol service (DAS) and clinicians working under a locally commissioned enhanced service supported by the DAS teams. Updates to products are made at the request of a DAS team on confirmation the product will be funded via their commissioned service, which is commissioned by the Local Authority.

Buvidal products are licensed for opioid dependence in adults and adolescents aged 16 years or over. Buvidal is given by subcutaneous administration either weekly or monthly using prefilled syringes and should be administered by a healthcare professional. The Together service was the only service in Devon to have long-term funding for Buvidal confirmed by their local authority commissioner at the time of the FIG discussion.

A proposed harmonisation of the opioid dependence page was presented to the FIG for discussion. Clinicians are referred to local service guidance for further information on prescribing. For clarification, a note has been added under each entry stating that the product should only be prescribed by Drug and Alcohol services and clinicians working under a locally commissioned enhanced service.

Specific changes were the discontinuation of generic buprenorphine / naloxone and the proposed replacement with Suboxone which has the same tablet constituents. This was supported by the applicant for Buvidal and the Harbour DAS team.

The FIG reviewed and accepted the formulary entry for Buvidal with minor amendment and the proposed harmonisation to section 4.10.3 (Opioid dependence) with minor amendments.

A discussion took place. The main points were that:

- It was agreed that note 1 on every relevant formulary entry should state that opioid substitution therapy should only be prescribed by Drug and Alcohol services and clinicians working under a locally commissioned enhanced service.
- there was agreement that GPs must be notified when opioid substitution therapy is initiated to enable a GP to check for drug interactions if other medicines are prescribed for the patient. The Formulary team will update section 4.10.3 to make the DAS teams aware of this and consider adding links to the SmPC and the BNF for interactions.
- It was suggested the SmPC requirement for a test dose for Buvidal is included in the entry, although it was noted that DAS clinicians would be expected to refer to local service prescribing guidance and other relevant guidance for information on the use of Buvidal.
- Use of illicit opioids by patients receiving Buvidal was raised. The Formulary team will seek advice from the Together clinical lead.

ACTION 24/102: Add Buvidal to the formulary in line with the discussion.

ACTION 24/103: Publish updates to section 4.10.3 opioid dependence in line with the discussion.

12. Glycopyrronium bromide tablets for severe sialorrhoea (chronic pathological drooling)

A request for an update to the Devon formulary entry for glycopyrronium bromide has been received from the GP & Specialty Doctor in Healthcare for Older people; Primary Care Lead for Enhanced Health in Care Homes (EHCH) and Anticipatory Care, (RDUH), supported by the NHS Devon Medicines Optimisation team. The intention is to support primary care prescribing of glycopyrronium bromide tablets for excessive drooling in adults following recent queries from GPs who had been asked by specialists to undertake ongoing prescribing. The proposal includes an additional indication (severe sialorrhea in patients with chronic neurological disorders), additional supporting notes, and inclusion of the 2mg strength tablets.

Glycopyrronium bromide is an antimuscarinic medicine; it competitively blocks muscarinic receptors, inhibiting cholinergic transmission and (amongst other effects) reducing the rate of salivation. Additionally, it has limited ability to penetrate the blood brain barrier (although the extent of penetration is unknown). This may result in fewer central nervous system side effects and be preferable for patients with cognitive impairment.

Glycopyrronium bromide tablets are available in both 1mg and 2mg strengths from a range of manufacturers; 1mg tablets are currently classified as amber in the Devon formulary, 2mg tablets are currently non-formulary.

Licensed indications vary slightly but are generally similar to “symptomatic treatment of severe sialorrhoea (chronic pathological drooling) due to chronic neurological disorders of childhood onset in patients aged 3 years and older”. Some (but not all) products are also licensed for continuation into adulthood and initiation in “adults with chronic neurological disorders of childhood onset”.

NICE has published several guidelines of relevance. These are, NG42 (2016): Motor neurone disease: assessment and management, NG71 (2017): Parkinson’s disease in adults, NG62 (2017): Cerebral palsy in under 25s: assessment and management, and NG119 (2019): Cerebral palsy in adults.

Local specialists indicated support for the use of glycopyrronium for severe sialorrhoea (chronic pathological drooling) in adults; local specialists suggested dose ranges for use in adults starting between 0.2mg to 1mg two or three times daily, to be increased up to 2mg three times daily. It is noted that doses below 0.5mg cannot readily be administered using tablets.

All identified SmPCs for glycopyrronium bromide tablets state that “the elderly have a longer elimination half-life and reduced medicinal product clearance as well as limited data to support efficacy in short-term use. As such glycopyrronium bromide tablets should not

be used in patients over the age of 65 years." Local specialists also indicated that they routinely use glycopyrronium bromide in patients aged over 65 years and that in their experience it is well tolerated, and they do not often see delirium or cognitive side effects.

The FIG considered and accepted the proposed formulary entry. The discussion noted that:

- The FIG accepted the proposed indication of severe sialorrhoea in patients with chronic neurological disorders.
- Glycopyrronium for severe sialorrhoea should be started on the advice of a specialist. It was recognised that many patients have very complex needs and are not mobile to travel to a clinic.
- Specialist guidance would be needed on titrating the dose. Some GPs would want specialists to stabilise patients on a daily dose prior to taking over prescribing.
- There is a lack of long-term safety data and that this is an off-label treatment for adults, however it is supported by NICE guidelines.

ACTION 24/104: Publish updates to glycopyrronium bromide entry in line with the discussion.

13. Mycophenolate mofetil and mycophenolic acid for patients within adult dermatology, ophthalmology and neurology services (Devon wide)

There are currently four mycophenolate mofetil guidelines in Devon covering dermatology and rheumatology indications across north, east and west Devon. Mycophenolate is restricted to hospital only prescribing in South Devon. There are currently no shared care guidelines for mycophenolic acid in Devon.

Work has been undertaken to update and harmonise the dermatology content, extend the guideline scope to Devon-wide, and add ophthalmology indications and neurology indications following requests from local specialists.

Further work will be undertaken at a later date to harmonise the guidance with rheumatology specialists, with the intention of creating a single Devon wide "Shared Care" SMS guideline for mycophenolate mofetil (and mycophenolic acid).

The existing dermatology SMS guideline has been updated using national reference resources and professional guidelines, in consultation with local specialists. The format and general guideline content is consistent with other recently agreed SMS guidelines including addition of guidance for the management of adverse effects.

Devon wide dermatology, ophthalmology and neurology specialists are in support of the draft guideline.
Mycophenolate is a treatment option for a number of indications, several of which are unlicensed. National guidance published by the Regional Medicines Optimisation Committees and NHS England describe circumstances in which a shared care agreement may not be appropriate. This includes medicines, which are unlicensed and/or are being used outside of product license unless there is a recognised evidence base and/or it is standard treatment.

Local specialists were asked to provide specific indications for inclusion in the guideline, and an internet search was undertaken to identify any relevant guidelines, policies or service specifications which might support the off-label use of mycophenolate as having a recognised evidence base or being standard treatment for the proposed indications (and therefore suitable for "Shared Care". The findings were presented to the FIG.

The FIG accepted the following indications for which mycophenolate is a recognised (off label) treatment in national guidance, protocols or service specifications: uveitis, ocular pemphigoid, myasthenia gravis, autoimmune neuropathies including chronic inflammatory demyelinating polyneuropathy, inflammatory myopathies including immune mediated myositis, neuromyelitis optica spectrum disorder, autoimmune encephalitis and neurosarcoidosis. The FIG agreed to accept the treatments as approved indications in the SMS guideline.

The FIG considered but did not accept thyroid eye disease / Graves' Orbitopathy (TED / GO) as an approved indication in the SMS guideline. Guidance from EUGOGO includes mycophenolate as a treatment option, however a consensus statement published by the American and European Thyroid Associations (ATA and ETA) conflicts with this and as such gave room for doubt. On balance the FIG felt it did not represent a standard treatment and considered hospital only prescribing and monitoring should continue for these patients. It was noted that this applied to a very small number of patients in Devon.

The FIG considered but did not accept scleritis as an approved indication in the SMS guideline. No published nationally recognised management guidelines, policies or relevant service specifications were identified. No RCTs were identified. A protocol for a systematic review of the effectiveness of pharmacological agents for the treatment of non-infectious scleritis states that "although many pharmacological agents have shown promising results in the management of non-infectious scleritis, there are currently no widely accepted management guidelines". The FIG considered that there was not a sufficiently recognised evidence base, or evidence that mycophenolate is considered a standard treatment, to support inclusion of scleritis as an indication for "Shared Care". If mycophenolate is used for treatment of scleritis, prescribing and monitoring should remain with the specialist.

Discussion of the proposals noted:

- several amendments be made to the guideline to strengthen responsibilities in relation to contraception and exclusion of pregnancy prior to treatment initiation.
- that specialists' responsibilities will be updated to ensure that patients are on adequate contraception and to exclude pregnancy prior to initiation of treatment, rather than simply providing advice.
- 'every contact' to be amended to 'every opportunity'.
- That the tick boxes in the letter to GPs will be edited to require that two forms of contraception be used and if appropriate, date of insertion of device be noted.

ACTION 24/105: Update the SMS guideline for mycophenolate mofetil and mycophenolic acid for patients within adult dermatology, ophthalmology and neurology services (Devon wide) in line with the discussion and circulate to specialists for consultation.

ACTION 24/106: Following specialist consultation, bring SMS guideline for mycophenolate mofetil and mycophenolic acid back to FIG for final decision.

14. MHRA Drug Safety Updates

September 2024 update

Valproate use in men: as a precaution, men and their partners should use effective contraception.

Further recommendations have been made for males receiving valproate (oral and IV) in addition to the requirement published in the January 2024 Drug Safety Update.

Findings from a retrospective observational study indicate a possible increased risk of neurodevelopmental disorders in children born to men treated with valproate in the 3 months prior to conception, compared to those born to men treated with lamotrigine or levetiracetam. The MHRA recommend that male patients use effective contraception (condoms, plus contraception used by the female sexual partner) throughout the valproate treatment period and for 3 months after stopping valproate, to allow for one completed sperm cycle not exposed to valproate. The MHRA advice is precautionary as a causal link between these findings is possible but has not been confirmed. The Drug Safety Update includes a link to FSRH guidance with advice for women who have a male sexual partner using valproate and advice for men taking valproate. The MHRA has produced advice for male patients and there a risk communication aid for healthcare professionals to use in a conversation with patients.

The FIG indicated that there are male patients receiving valproate who are not under the care of the specialist team. In these cases, the GP will be responsible for communicating the new guidance to male patients receiving valproate under their care.

The Formulary team will include an interim update on the valproate safety measures page whilst there is a consultation with specialists. Formulary guidance and entries have been updated with details from the Drug Safety Update.

ACTION 24/107: Update formulary page on valproate safety measures with recommendations from the MHRA Drug Safety Update for September 2024 and consult with specialists.

October 2024

GLP-1 receptor agonists: reminder of the potential side effects and to be aware of the potential for misuse.

A reminder of the potential side effects and to be aware of potential for misuse of GLP-1 receptor agonists specifically with reference to their use for weight management (prescribed by specialist weight management teams).

Healthcare professionals are reminded to inform patients about the common and serious side effects associated with GLP-1 receptor agonists, the importance of staying hydrated and ensuring that private prescriptions are dispensed from authorised sources.

Existing notes on Drug Safety Updates for GLP-1 receptor agonists for weight management included in the formulary have been reviewed and will be replaced with the key points and a link to the October 2024 Drug Safety Update where appropriate.

Insulin pumps and continuous glucose monitoring (CGM) equipment: guidance for users on reporting suspected adverse incidents and safety concerns to the MHRA's Yellow Card scheme.

Healthcare professionals are asked to bring new guidance to support users of diabetes management equipment, to the attention of patients, families, care givers and representatives. The guidance explains how to report safety concerns to the MHRA using the Yellow Card scheme and describes the information required to support device investigations.

Formulary section 6.1.7 Continuous Glucose Monitors (CGM) will be updated with key points and a link to the Drug Safety Update.

Bromocriptine: monitor blood pressure when prescribing bromocriptine for prevention or inhibition of post-partum physiological lactation.

Advice for healthcare professionals includes when not to prescribe bromocriptine post-partum, blood pressure monitoring and reference to the Royal College of Obstetrics and Gynaecology guidance recommending cabergoline, rather than bromocriptine.

The Formulary team will review the formulary indications for bromocriptine and cabergoline and add key points and a link to the Drug Safety Update to the formulary entries.

Letters sent to healthcare professionals

Oxbryta (voxelotor): Withdrawal from UK market

The NICE TA and formulary entry have been removed.

BLENREP (Belantamab mafodotin): Revocation of the Great Britain conditional Marketing Authorisation for BLENREP (belantamab mafodotin)

This is not included in formulary. No further action is required.

NOXAFIL (posaconazole) new Gastro-Resistant Powder and Solvent for Oral Suspension not interchangeable with existing Oral Suspension including generics.

The existing oral posaconazole suspension is included in the South & West Devon Formulary as red (hospital-only). A note will be added to the formulary entry including a link to the communication to raise awareness.

ACTION 24/108: Update the relevant Devon Formulary sections with recommendations from the MHRA Drug Safety Updates for October 2024.

November 2024

Letters sent to healthcare professionals

Medroxyprogesterone acetate: Risk of meningioma and measures to minimise this risk

For contraception or non-oncological indications, medicines containing high doses of medroxyprogesterone acetate are contraindicated in patients with a meningioma or a history of meningioma. This applies to all injectable and ≥100 mg oral formulations.

Medroxyprogesterone tablets (100mg, 200mg, 400mg) are amber (specialist-input) options in the formulary for cancer indications. Depo-Provera is a green (first-line) option for contraception. Key points and a link to the Drug Safety Update will be added to formulary entries and relevant formulary guidance.

Glatiramer acetate: Anaphylactic reactions may occur months to years after treatment initiation

Glatiramer acetate is red (hospital-only) in the Devon Formulary for multiple sclerosis in line with NICE TAs. Key points and a link to the Drug Safety Update will be included in the formulary entry.

Topiramate (update)

NICE has not given an indication of when they will complete their review of the impact of the new topiramate safety measures on NICE guidance (CG150) for the prophylaxis of migraine.

The FIG discussed the potential place in therapy of Topiramate in the Devon Formulary guidance for the prophylaxis of migraine preceding further work in this area.

ACTION 24/109: MHRA Drug Safety Updates: Update the relevant Devon Formulary sections with recommendations from the MHRA Drug Safety Updates for November 2024.