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

Meeting of the Devon Formulary Interface Group

Minutes

Wednesday 22nd May 2024

Via Microsoft Teams

Present:

Name	Job Title	Organisation
Glen Allaway (Chair)	GP	NHS Devon ICB
Beverley Baker	Non-Medical Prescribing Lead	NHS Devon ICB
Ailene Barclay	Pharmacist	UHP NHS Trust
Heidi Campbell	Pharmacist	NHS Kernow ICB
Andy Craig	GP	NHS Devon ICB
Stuart Crowe	GP	NHS Devon ICB
Jess Danielson	GP	NHS Devon ICB
Susie Harris	Consultant Physician/Geriatrician	RDUH NHS FT
Matt Howard	Clinical Evidence Manager	NHS Devon ICB
Nick Keysell	GP	NHS Devon ICB
James Leavy	Medicines Information Pharmacist	RDUH NHS FT
Rebecca Lowe	Joint Formulary Technician	NHS Devon ICB
Sarah Marner	Senior MO Pharmacist	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
Darren Wright	Joint Formulary Specialist Pharmacy Technician	NHS Devon ICB

Guests:

Name	Job Title	Organisation
Emma Gitsham	Clinical Effectiveness Pharmacist – Specialist Medicines Service (SMS) Guidelines Lead	NHS Devon ICB
Nic Perrem	Healthcare Evidence Reviewer	NHS Devon ICB
Amy Rice	Clinical Effectiveness Pharmacist	NHS Devon ICB
Andrew Dickinson	Consultant Urologist	UHP NHS Trust
Jonathan Manley	Consultant Urologist	UHP NHS Trust
Sarah MacCourt	Clinical Nurse Specialist Bladder and Bowel Care	RDUH NHS FT

Observers:

Name	Job Title	Organisation
Alice Butler	GP Trainee	RDUH NHS FT

In attendance:

Name	Job Title	Organisation
Fiona Dyroff	Clinical Effectiveness Governance Support Officer	NHS Devon ICB

1. Welcome and announcements

Meeting etiquette

Glen Allaway explained the meeting etiquette.

Chairman's welcome

Glen Allaway welcomed attendees to the meeting of the Devon Formulary Interface Group.

Dr Allaway explained to the group that Dr Susie Harris had stepped down from the role of Chair of the group and that he was stepping into the role. On behalf of the group Dr Allaway thanked Dr Harris for her significant contribution to the group in the role of Chair and for her continued support as a group member.

Apologies

Name	Job Title	Organisation
Carole Knight	Formulary Pharmacist	RDUH NHS FT
Lucy Harris	GP	NHS Devon ICB
Larissa Sullivan	Pharmacist	SD&T NHS FT
Alisha Kaliciak	GP	NHS Devon ICB
Nicola Diffey	Pharmacist	Livewell Southwest

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
LUTS in men and urinary incontinence in women	
• Tamsulosin hydrochloride (generic and branded e.g., Contiflo XL)	Various manufacturers including Ranbaxy (UK)
• Alfuzosin hydrochloride (generic and branded e.g., Xatral XL)	Various manufacturers including Sanofi
• Solifenacin succinate (generic and branded e.g., Vesicare)	Various manufacturers including Astellas Pharma Ltd
• Tolterodine tartrate (generic and branded e.g., Detrusitol)	Various manufacturers including UpJohn UK Limited
• Oxybutynin hydrochloride (tablets, MR tablets and transdermal patches; generic and branded e.g., Ditropan)	Various manufacturers including Neon Healthcare Ltd
• Fesoterodine fumarate (generic and branded e.g., Toviaz)	Various manufacturers including Pfizer Limited
• Trospium (generic and branded e.g., Regurin)	Various manufacturers including Mylan
• Darifenacin hydrobromide (Emselex)	

Drug To Be Considered	Pharmaceutical Company/ Manufacturer
• Mirabegron (Betmiga) • Dutasteride with tamsulosin hydrochloride (generic and branded e.g., Combodart) • Solifenacin succinate with tamsulosin hydrochloride (generic and branded e.g., Vesomni) • Finasteride (generic and branded e.g., Proscar) • Desmopressin (tablets, oral lyophilisates, and oral solution; generic and branded e.g., DDAVP) • Duloxetine (generic and branded e.g., Yentreve) • Botulinum toxin type A (Botox, Dysport) **Demovo 360micrograms/ml oral solution** • Demovo 360micrograms/ml oral solution **Alternatives** • Desmopressin tablets (generic and branded e.g., DDAVP) • Desmopressin oral lyophilisates (DDAVP melt, DesmoMelt, Desmopressin Melt, Noqdirna)	Aspire Pharma Ltd Astellas Pharma Ltd Various manufacturers including GlaxoSmithKline UK Various manufacturers including Astellas Pharma Ltd Various manufacturers including Organon Pharma (UK) Limited Various manufacturers including Ferring Pharmaceuticals Ltd Various manufacturers including Eli Lilly and Company Limited AbbVie Ltd, Ipsen Ltd Alturix Limited Various manufacturers including Ferring Pharmaceuticals Ltd Ferring Pharmaceuticals Ltd, Aspire Pharma Ltd
Infected eczema: • Various emollients (creams/ointments/gels etc.) • Topical corticosteroids • Topical antibiotics (including generic fusidic acid and **Fucidin**) • Systemic antibiotics including flucloxacillin, clarithromycin, metronidazole, and erythromycin (various formulations)	Various manufacturers Various manufacturers Various manufacturers (including LEO Pharma) Various manufacturers

Management of Giardiasis:
• Metronidazole – Various formulations
• Antigiardial drugs (unlicensed treatments) – Various formulations:
  ○ Tinidazole
  ○ Albendazole
  ○ Mebendazole
  ○ Mepacrine hydrochloride
  ○ Paromomycin
	Various manufacturers
	
	Various manufacturers
	Various manufacturers
	Various manufacturers
	Various manufacturers
	Various manufacturers

Drug To Be Considered	Pharmaceutical Company/ Manufacturer
Update: Management of blood lipids • Statins, generic and branded, including atorvastatin (Lipitor), rosuvastatin (Crestor) and simvastatin (Zocor) • Ezetimibe (generic and Ezetrol) • Bempedoic acid (Nilemdo, Nustendi) • Inclisiran (Leqvio) • Alirocumab (Praluent) • Evolocumab (Repatha)	Various manufacturers (including Astra Zeneca UK Ltd, Organon Pharma (UK) Ltd, Viatris UK Healthcare Ltd) Various manufacturers including Organon Pharma (UK) Ltd Daiichi Sankyo UK Ltd Novartis Sanofi Amgen Limited
Rivastigmine: Zeyzelf twice weekly transdermal patches: • Zeyzelf (rivastigmine) twice weekly transdermal patches **Alternatives:** • Alzest (rivastigmine) daily transdermal patches • Rivastigmine daily transdermal patches • Acetylcholinesterase inhibitors (AChEIs), centrally acting – Various formulations: ○ Donepezil hydrochloride ○ Galantamine ○ Memantine	Luye Pharma Limited Dr. Reddy's Laboratories Various manufacturers Various manufacturers Various manufacturers Various manufacturers
Melatonin: Ceyesto 1mg/ml oral solution and Slenyto prolonged release tablets • Ceyesto 1mg/ml oral solution sugar free • Slenyto prolonged release tablets **Alternative treatments:** • Melatonin immediate release tablets (Generic and branded e.g Adaflex, Ceyesto) • Melatonin modified release tablets (generic and branded e.g. Circadin)	Alturix Limited Flynn Pharma Ltd Various manufacturer including AGB-Pharma AB and Alturix Limited Various manufacturers including Flynn Pharma Ltd
• **Hydroxychloroquine (generic and branded e.g., Quinoric)**	Various manufacturers including Bristol Laboratories Ltd
Drug Safety Update: Valproate Valproate-containing medicines (generic and branded e.g. Epilim and Episenta) **Alternative treatments** Various anti-epileptics, various antipsychotics	Various manufacturers, including Sanofi and Desitin Pharma Various manufacturers

Items discussed by e-FIG

E-FIG Item	Pharmaceutical Company/ Manufacturer
COVID meds • Nirmatrelvir and ritonavir tablets (**Paxlovid**) • Molnupiravir capsules (**Lagevrio**) • Remdesivir IV infusion (**Veklury**) • Sotrovimab IV infusion (**Xejudy**)	Pfizer Ltd Merck, Sharpe and Dohme UK Ltd Gilead Sciences Ltd GlaxoSmithKline UK
Deprescribing guidance for hypnotic drugs: • Benzodiazepines and Z-drugs (zopiclone, zolpidem) (various formulations) Melatonin (various formulations)	Various manufacturers Various manufacturers
Liothyronine • Generic capsules • Generic tablets	Roma Pharmaceuticals Ltd Various manufacturers

Name	Job Title	Declaration
Rebecca Lowe	Joint Formulary Pharmacy Technician	I work as a Relief Pharmacy Technician at Day Lewis pharmacies
Dr Jonathon Manley	Consultant Urologist	Have given a paid lecture to Plymouth GPs on overactive bladder and the pharmacological treatment on behalf of Astellas (manufacturer of Mirabegron).

2. Minutes of the meeting held on 27th March 2024 and Actions/Matters arising

Minutes of the meeting held on 27th March 2024

The minutes of the meeting held on 27th March 2024 were approved.

Actions/Matters arising.

The Action Log was reviewed and updated.

3. Recent drug decisions

The FIG received a report of the recent drug decisions.

4. Report of e-FIG decisions

April 2024

COVID-19 treatments: NICE TA878 update

In April, the FIG was asked to consider a proposed update to the formulary guidance for COVID-19 treatments in patients who do not require hospitalisation with NICE TA878 recommendations for additional patient groups for treatment with Paxlovid.

Responses received indicated acceptance of the proposals. The updates will be published on the website.

ACTION 24/28: Formulary team to publish the agreed updates to formulary guidance for COVID-19 treatments in patients who do not require hospitalisation.

May 2024

In May 2024 the Devon FIG was asked to consider two items via the e-FIG process.

Liothyronine capsules

The FIG was asked to consider:

- The inclusion of liothyronine 5 microgram and 10 microgram hard capsules in the Devon Formulary, and
- Whether the proposed update to the formulary entry for liothyronine is acceptable.

Responses received indicated acceptance of the proposals. The liothyronine 5 microgram and 10 microgram capsules will be added to the Devon Formulary.

ACTION 24/29: Formulary team to add liothyronine 5 microgram and 10 microgram hard capsules to the Formulary in line with the agreed entry.

Deprescribing hypnotic drugs

The FIG was asked to review a paper and consider whether a revision to the proposed formulary guidance for deprescribing hypnotic drugs is acceptable.

Responses received indicated acceptance of proposal. The proposed guidance for deprescribing hypnotic drugs will be included in the Devon Formulary.

ACTION 24/30: Formulary team to publish the agreed formulary guidance for deprescribing hypnotic drugs.

5. Lower Urinary Tract Symptoms (LUTS) in men and urinary incontinence in women: Including Demovo (desmopressin) 360micrograms/ml

A proposed update to formulary guidance on the management of lower urinary tract symptoms (LUTS) in men and urinary incontinence in women was presented to the FIG. The recommendations are based on the NICE guideline for LUTS in men (CG97), the NICE guideline for urinary incontinence and pelvic organ prolapse in women (NG123), and NICE Clinical Knowledge Summaries (CKS) for both conditions.

In addition, updates to the relevant drug entries to reflect the formulary guidance were proposed, together with a proposal for the addition of desmopressin oral solution, which has a lower acquisition cost than desmopressin oral lyophilisates.

Two Consultant Urologists from UHP and a Clinical Nurse Specialist for Bladder and Bowel Care from RDUH attended the meeting for the discussion.

The changes are not expected to increase expenditure in primary care; there is a potential for a reduction in the prescribing of higher cost anticholinergic drugs. The proposed update also includes strengthened advice to discourage use of the combination products solifenacin with tamsulosin and tamsulosin with dutasteride. This is not a change in local position; these products are considerably higher in cost with no additional clinical benefits compared to prescribing them as separate agents.

The FIG considered and accepted the proposed formulary entry for LUTS in men and urinary incontinence in women with some amendments.

The discussion noted:

- local expert opinion is that trospium is more suitable for patients at risk of cognitive impairment (e.g., dementia), because it does not cross the blood brain barrier and therefore may result in reduced cognitive side effects.

The amendments included:

- For anticholinergic drugs for storage LUTs in men and for urinary incontinence in women:
  - Reclassification of oxybutynin from blue to amber due to concerns about tolerability.
  - Limiting the use of fesoterodine to cases where other anticholinergics were effective but not tolerated due to concerns about the limited value of trialling a third anticholinergic drug if two previous options have been ineffective.
  - Addition of a reminder about the risk of acute angle closure glaucoma.
- Expansion of non-pharmacological advice for idiopathic nocturnal polyuria in LUTS in men and urinary incontinence in women guidance.
- Minor wording amendments to conservative management guidance to provide additional clarity on potential treatment options and requirements for review.
- Strengthened advice on topical oestrogen therapy for stress incontinence in post-menopausal women.
- Revision of advice regarding the risks of interoperative floppy iris syndrome with alpha blockers to better reflect the MHRA drug safety update advice.

Consideration of Demovo (desmopressin) 360 micrograms/ml oral solution

A paper was also presented to the FIG on the addition of desmopressin oral solution. The product was identified as part of the wider formulary review of LUTS and urinary incontinence, but inclusion in the formulary is supported by community continence teams and urology consultants. Demovo is licensed for diabetes insipidus and primary nocturnal enuresis; it is proposed that this product is added as an additional choice rather than a replacement of existing products. It is cheaper than oral lyophilisates with a potential average saving of £190 per person per annum for patients with primary nocturnal enuresis.

The specialist nurse present highlighted concerns regarding the potential for hyponatraemia (especially in older patients) and requested that its use be limited to patients under 65 years old, in line with the licensed status of oral tablets and lyophilisates.

The FIG considered and accepted the addition of desmopressin 360 micrograms/ml oral solution to the formulary and the proposed changes to the desmopressin formulary entry.

The discussion included:

- An amendment to note that local specialists do not recommend its use for primary nocturnal enuresis in patients aged over 65 years even though it is licensed for this age group.

The Formulary team will make the requested amendments and undertake a two-week consultation with specialists. If no significant changes are requested by specialists, the Formulary team will publish the formulary guidance for LUTS in men and urinary incontinence in women, and updated drug entries including the addition of desmopressin 360 micrograms/ml oral solution.

ACTION 24/31: Formulary team to update the draft formulary guidance for LUTS in men and urinary incontinence in women, and associated drug entries, in line with the discussion, and circulate to specialists for consultation.

ACTION 24/32: Subject to outcome of consultation with specialists, Formulary team to publish guidance for LUTS in men and urinary incontinence in women, and updated drug entries including desmopressin 360 micrograms/ml oral solution.

6. Management of infected eczema

Proposed guidance for the management of infected eczema was previously brought to the FIG meeting in December 2023, which was not quorate. At the FIG meeting in December those present requested additional consultation with specialists regarding the efficacy of topical fusidic acid and whether they would like to retain doxycycline as a treatment option. Doxycycline is currently recommended in N&E Devon, but not S&W Devon; it is not included in the NICE guideline (NG190).

Topical fusidic acid is recommended in NICE guideline NG190 (secondary bacterial infection of eczema and other common skin conditions: antimicrobial prescribing). The NICE committee discussion indicates that fusidic acid was considered an appropriate choice if the infection is localised, and repeated or extended use should be avoided. Local specialist feedback received after the FIG meeting suggested that if infection has not improved in response to topical fusidic acid, resistance should be considered and the use of a skin swab to determine antibiotic

sensitivities should be recommended. The proposed guidance was updated to reflect this advice. There were no other comments regarding fusidic acid.

The consensus of local specialist feedback regarding doxycycline was that it could be retained as an option. There were mixed specialist views regarding dosage (100mg once daily vs 100mg twice daily); the proposed guidance therefore included a dose range (200mg stat followed by 100mg once or twice a day to complete the 5-day course), to allow for GP discretion in selecting the most appropriate dose for their patient.

The FIG considered and accepted the proposed formulary guidance for the management of infected eczema without amendment.

ACTION 24/33: Formulary team to publish the accepted formulary guidance for the management of infected eczema.

7. Management of giardiasis

This item was deferred to a future meeting due to time constraints.

ACTION 24/34: Formulary team to bring management of giardiasis to a future FIG meeting.

8. Update: Management of blood lipids

A proposed update to the formulary guidance on the management of blood lipids was presented to the FIG. The proposed guidance is based on NICE Guideline NG238 (cardiovascular disease: risk assessment and reduction, including lipid modification) which incorporates updates to primary and secondary prevention of cardiovascular disease (CVD), and clarification of the previous NICE guideline (CG181).

The Formulary Team proposed that a consultation with the lipid specialists takes place following the FIG meeting so any questions from the FIG are included.

Visual summaries are being developed to accompany the proposed update to the formulary guidance. The key changes to the formulary guidance were outlined and a summary of the NG238 committee discussion and rationale for the changes was included in the meeting paper.

Primary prevention:

- QRISK3 is the current version of the QRISK calculator. NG238 indicates QRISK2 can be used if QRISK3 is not available. QRISK3 has been updated with indicators for certain patient groups to incorporate disease or medication specific risks of CVD. QRISK3 (on-line if necessary) is recommended for these patient groups.
- Consider using QRISK3-lifetime to inform discussions on cardiovascular risk and to motivate lifestyle changes particularly for people with a 10-year QRISK3 score less than 10%, and people under 40 who have CVD risk factors.

Secondary prevention:

- New target lipid level: LDL-C 2.0 mmol/L or less, or non-HDL-C 2.6 mmol/L or less
- Consider ezetimibe in addition to the maximum tolerated intensity and dose of statin to reduce cardiovascular risk further, even if the lipid target is met.

In addition, assessment and referral criteria for familial hypercholesterolaemia have been removed from the formulary section on familial hyperlipidaemia and replaced with a link to the clinical referral guideline.

The FIG considered in principle the proposed guidance pending consultation with specialists. The discussion included:

- QRISK3 is not embedded in practice computer systems.
- What is the additional reduction in cardiovascular risk of adding ezetimibe to a statin when the target lipid level has been achieved?

The FIG accepted in principle the proposed updates to the formulary guidance for the management of blood lipids.

ACTION 24/35: Formulary team to consult with specialists on the proposed update to the formulary guidance on the management of blood lipids.

ACTION 24/36: Following consultation with specialists the Formulary team will bring guidance on the management of blood lipids back to the FIG via an appropriate route if required.

9. Rivastigmine: Zeyzelf twice-weekly transdermal patches

Zeyzelf is a twice weekly rivastigmine transdermal patch indicated for the symptomatic treatment of mild to moderately severe Alzheimer's dementia; it is available in two strengths: 4.6mg/24 hours and 9.5mg/24 hours. Initiation and supervision should be by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. The licensed dose is for one patch to be applied twice weekly on fixed days (after four and three days, respectively)

Each application requires a rectangular, translucent transdermal patch containing the active ingredient and an oval, beige adhesive cover. The adhesive cover is exclusively used for fixation of the transdermal patch.

The dosing regime is 4.6mg/24 hours twice weekly for at least 4 weeks, increased if tolerated to 9.5mg/24 hours twice weekly. If further dose increases are necessary after 6 months of treatment with 9.5mg/24 hours twice weekly, the dose can be increased to 13.3mg/24 hours, however this dose cannot be achieved with Zeyzelf twice weekly. If the higher dose is required patients must switch to a daily patch.

Cholinesterase inhibitors are recommended by NICE for people with Parkinson's disease dementia (including severe Parkinson's disease dementia) and for mild to moderate Alzheimer's disease.

The Formulary currently recommends rivastigmine daily transdermal patches as amber (specialist input) for mild to moderate dementia in Alzheimer's disease and mild to moderate dementia in Parkinson's disease (*off-label*). Alzest brand are recommended by the NHS Devon Medicines

Optimisation team for prescribing in primary care to help ensure cost-efficient use of local NHS resources.

An application was received from a Clinical Pharmacist, Devon Partnership NHS Trust, supported by a Consultant Psychiatrist, for the addition of Zeyzelf twice weekly patches as an amber option. The applicants suggested Zeyzelf would be used where there is a clear advantage over a daily patch – e.g., where administration causes significant distress to the patient or where there is limited amount of carer/additional support.

Zeyzelf was licensed in the EU via the decentralised procedure; the marketing authorisation holder submitted pharmacokinetic and pharmacodynamic data to demonstrate equivalence between the test product (twice weekly rivastigmine patch) and the reference product, Exelon once daily patches. The regulatory authority concluded that Zeyzelf twice weekly patches are bioequivalent to Exelon once daily patches.

Zeyzelf twice weekly patches are more expensive than Alzest daily patches. The applicant estimated that 5-10% of patients will require a twice weekly patch. Based on recent prescribing data, a switch to Zeyzelf for this proportion of patients would result in increased costs of approx. £2,800 to £5,500 per year. If used in a higher proportion of patients, increased costs could become significant.

Local specialists were consulted in respect of the application; responses were in support of inclusion and confirmed that uptake is expected to be minimal.

An MHRA Drug Safety Update was issued in December 2014 highlighting the risk of medication errors with rivastigmine transdermal patches, most frequent issues were not removing the old patch or applying multiple patches. It is noted that there may be an additional risk of medication errors and confusion between use of daily / twice weekly patches, as well as risk of confusion from the need for a secondary adhesive cover patch with Zeyzelf; careful patient selection and carer counselling would be required.

As a result, if Zeyzelf is accepted for inclusion, it was proposed that the transdermal rivastigmine patches, Alzest and Zeyzelf, would be recommended for brand name prescribing to reduce the risk of confusion and error in dispensing and administration.

The FIG considered and accepted the addition of Zeyzelf twice weekly transdermal patches into the Devon Formulary together with proposed revised formulary entries for rivastigmine (oral) and rivastigmine transdermal patches (Alzest and Zeyzelf to support brand prescribing).

The discussion included that:

- the application suggested a potential benefit for patients who had limited carer support; the FIG noted that Social Care staff often do not administer medicines.
- there are potential benefits of not having to change the patches daily, but also risks (including the requirement for a second adhesive patch and the lack of a 13.3mg/24 hours patch). On balance it was felt that twice weekly patches would be useful for some patients, however patients need to be carefully selected by specialists, and carers must be given appropriate instruction on administration of the patches.
- because of the increased costs, Zeyzelf should only be used where there is a clear clinical benefit for the patient.

It was agreed that:

- a note should be added to reflect that Zeyzelf is reserved for specific patient groups where a twice weekly patch change has a clear clinical benefit to the patient
- there would be separate entries for Alzest and Zeyzelf to support brand prescribing
- the Medicines Optimisation team accepted the increased cost for appropriate use.

ACTION 24/37: Formulary team to publish the accepted formulary entries for rivastigmine (oral), Alzest and Zeyzelf transdermal patches.

10. Melatonin: Ceyesto 1mg/ml oral solution and Slenyto prolonged release tablets

Following a recent review of supportable indications for melatonin and the development of new formulary guidance for insomnia in adults and for deprescribing of hypnotics, all melatonin licensed products currently available in the UK were reviewed to consider whether any are either lower in cost, licensed for an indication where *off-label* use of alternatives is currently recommended, or provide a specific clinical benefit. Two additional products were presented for consideration by the FIG.

Ceyesto 1mg/ml oral solution

Ceyesto melatonin 1mg/ml oral solution is licenced for use for insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient and also for short-term sedation under medical supervision to facilitate EEG in children and adolescents from 1 to 18 years.

At present there are no melatonin oral liquids recommended by the formulary. However, work undertaken by the NHS Devon Medicines Optimisation team has identified that a significant number of such products are dispensed in Devon. As a proportion of immediate release melatonin preparations, melatonin 1mg/ml oral solution accounts for around 28% of the total items dispensed, suggesting that there is a clinical need for a liquid formulation. Oral solutions also equate to 64% of the total cost of immediate release melatonin products; Ceyesto brand is a less costly option compared with other melatonin oral solutions, meaning that the inclusion of this item in the formulary may result in financial savings.

The Formulary Team was unable to locate a public assessment report for Ceyesto. The MHRA and the marketing authorisation holder Alturix confirmed that it is currently not available. Alturix have also confirmed that the assessment was undertaken using published data for the effects of melatonin on the patient groups considered in the product licence and that clinical trials directly assessing the effect of Ceyesto brand oral solution were not submitted to the regulator.

When prescribed by brand Ceyesto is approx. £1,200 to £1,300 less costly per patient per year than generic prescribing. Using primary care prescribing data collected by the Medicines Optimisation team, it was estimated that if all patients received Ceyesto prescribed by brand in place of a generic prescription an annual saving of around £324,00 may be possible in Devon.

Local specialists were consulted on the proposed inclusion of Ceyesto; responses received were supportive.

Slenyto prolonged release tablets (1mg and 5mg)

Slenyto prolonged release tablets are licensed for insomnia in children and adolescents aged 2-18 with ASD and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient; this is a subgroup of patients for whom the formulary currently recommends *off-label* use of 2mg modified release melatonin tablets.

Slenyto was developed by Flynn Pharma who also hold the marketing authorisation for Circadin 2mg modified release tablets. Both products contain melatonin and the same excipients, however Slenyto tablets are physically smaller and were specifically developed for patient groups who may struggle with swallowing.

A European public assessment report for Slenyto was identified, which considered data from one clinical trial comparing Slenyto to placebo. At the end of the 13-week double blind period, patients receiving Slenyto demonstrated improved total sleep time compared with placebo. It was estimated that those receiving Slenyto slept for around 30 minutes more than those receiving the placebo, and this difference was deemed statistically significant. A review of longer term follow up data collected from an open label phase of the trial suggested that improvements in sleep continued for up to 39 weeks. The regulatory authority also considered a literature review of existing studies using melatonin for the treatment of insomnia in children with ASD and / or neurodegenerative conditions.

A cost comparison of Slenyto with 2mg modified release tablets indicates that at all doses, Slenyto is approximately 10 times more expensive than 2mg modified release tablets. Available prescribing data for 2mg modified release tablets do not allow for a breakdown by indication, as such, it was not possible to reliably estimate patient numbers and therefore overall budget impact.

An updated formulary entry which included both products was presented to the FIG.

Discussion points included:

- the FIG GPs experience of prescribing melatonin for children.
- Ceyesto offers an opportunity for significant savings but may not be suitable for all patients.
- there is a significant financial risk associated with routinely recommending Slenyto simply because this preparation has obtained a licence for a particular patient group.
- there may be exceptional circumstances where Slenyto is required and could be prescribed as a non-formulary item.

The FIG considered and accepted inclusion of Ceyesto 1mg/ml oral solution in the formulary.

The FIG did not accept the addition of Slenyto to the formulary. The FIG recognised guidance from the General Medical Council in respect of prescribing off label medicines. The FIG also considered that specialists and GPs have years of experience with off label use of the 2mg modified release tablets in these patients. Overall, the FIG considered that the increase in costs to the NHS did not justify a routine recommendation for Slenyto.

ACTION 24/38: Formulary Team to publish the accepted formulary entry for melatonin to include Ceyesto 1mg/ml oral solution.

11. Hydroxychloroquine (HCQ): enhanced entry/withdrawal of "Shared Care" guidelines

HCQ is an established disease modifying anti-rheumatic drug used in the treatment of a variety of autoimmune diseases in rheumatology and dermatology. HCQ should only be prescribed by clinicians who have a full understanding of the drug and risks of therapy. HCQ is considered a useful, efficacious drug with fewer systemic side-effects than many of the alternative drugs used for autoimmune conditions, however it is associated with a risk of retinal toxicity, which can be irreversible and can lead to significant visual impairment and sight loss. The risk is increased for patients taking more than 5mg/kg/day, those also taking tamoxifen, and those with renal impairment. The only intervention to prevent further damage is stopping the drug.

In December 2020, the Royal College of Ophthalmologists (RCOphth) published updated HCQ and chloroquine retinopathy monitoring guideline and recommendations.

There are currently five historic, unfunded shared care guidelines for HCQ in Devon: Three for rheumatology patients (N&E Devon, South Devon & Torbay, and west Devon) and two for dermatology patients (South Devon & Torbay and west Devon only). There is no dermatology shared care guideline for N&E Devon.

HCQ does not require routine laboratory blood monitoring or physical health monitoring by the GP and therefore no longer fits the local definition of formal "shared care". It is proposed that the existing shared care guidelines for HCQ in Devon are withdrawn and replaced by an enhanced Devon Formulary entry which will also link through to a Key Messages page on the Devon Referrals website. Between the two parts this will provide a GP with the practical mechanics of the system in Devon for monitoring for HCQ and chloroquine retinopathy.

The FIG considered and accepted the enhanced formulary entry for HCQ together with the withdrawal of the historic "Shared care" guidelines for HCQ.

The discussion included:

- The retinopathy monitoring service has been commissioned with In Health; it will be the specialist's responsibility (dermatologist or rheumatologist) to refer patients to the retinopathy service. The service will extract GP practice prescribing data to ensure that all patients prescribed HCQ and chloroquine are identified.
- Identification of patients currently receiving HCQ who may have been discharged from specialist services and how these patients access the monitoring services. The need to identify all patients has been identified and a system for this is included in the service specification.

ACTION 24/39: Formulary team to publish the enhanced formulary entry for HCQ

ACTION 24/40: Formulary team to withdraw the historic "Shared Care" guidelines for HCQ.

12. MHRA Drug Safety Updates

Two MHRA Drug Safety Updates were issued between March 2024 and April 2024. The contents have been reviewed by the Formulary Team.

March 2024

No articles were published in the March drug safety Update.

April 2024

Finasteride: reminder of the risk of psychiatric side effects and of sexual side effects (which may persist after discontinuation of treatment)

The product information for finasteride contains information on depression and suicidal ideation, and on the potential for sexual side effects to persist after discontinuation. The MHRA considered these side effects are not well known by prescribers and patients. A Drug Safety Update article and a patient card for inclusion in the pack was recommended to raise awareness. The patient card will be issued later in the year.

The formulary entry for finasteride has been updated with key points and a link to the Drug Safety Updates.

During the discussion on the formulary guidance on LUTS, the specialist present asked for additional information to be added to the finasteride formulary entry note on the drug safety article to provide some context to the frequency of reporting of these side effects and the extensive use of finasteride.

Montelukast: Reminder of the risk of neuropsychiatric reactions

Montelukast is included in the Devon Formulary as a green (first-line) option for asthma in children, adolescents and adults in line with national guidance. The formulary entry includes key points from a Drug Safety Update article 'Reminder of the risk of neuropsychiatric reactions' issued in 2019.

The MHRA has conducted a further review of neuropsychiatric reactions to evaluate new evidence. The review indicated a potential lack of awareness of the risk of neuropsychiatric reactions with montelukast amongst healthcare professionals, patients and their caregivers.

To increase awareness of the risks of neuropsychiatric effects with montelukast, new boxed warnings will be introduced to the SmPC and Patient Information Leaflet to make these risks more prominent to the reader.

Previous advice was to carefully evaluate the risks and benefits of continuing treatment with montelukast if neuropsychiatric reactions occur. The new advice based on the latest evidence review is to discontinue treatment if neuropsychiatric reactions occur as this may help prevent escalation to more serious events.

It was agreed that it would be helpful to add information from the article on the range and frequency of neuropsychiatric reactions reported to the formulary entry.

Oral valproate containing medicines – update

The FIG has reviewed a new page for the formulary on safety measures for oral valproate medicines. Following the meeting, the section on contraception was updated to include additional information based on FSRH guidance for contraception for patients receiving teratogenic medicines.

The draft page has been sent to ICS medicines safety officers and identified clinical leads from the relevant specialties within each provider trust. Consultation is ongoing and the Formulary Team will bring this back to FIG via the appropriate route.

ACTION 24/41: Formulary team to bring back valproate safety measures page to FIG by most appropriate route.
