SHORTAGE:

Fesoterodine (Toviaz) 4mg and 8mg modified release Tablets

Anticipated re-supply date: 30th April 2022

Actions for prescribers:

Where patients have insufficient supplies to last until the re-supply date, prescribers should:

- review if treatment is still required, and if deemed necessary, consider prescribing an alternative oral antimuscarinic agent, the choice of which will be determined by treatments already tried, if fesoterodine was not being used as a first-line treatment; and
- prescribers and pharmacists should counsel patients on the switch and advise them to seek advice from prescribers if there is a worsening in symptom control or they experience unacceptable side-effects.

Alternatives:

Alternative oral anti-muscarinic agents

Solifenacin

Available in 5mg and 10mg immediate release tablets and a 1mg/ml oral suspension.

Dose

5mg to 10mg daily.

Supply position

In stock and can support a full uplift in demand for the immediate release tablets.

Tolterodine

Available in 1mg and 2mg standard release tablets, as well as 2mg and 4mg prolonged-release capsules.

Dose for standard release tablets

1mg to 2mg twice daily.

Dose for prolonged-release capsules

2mg to 4mg daily.

Supply position

Both formulations are in stock and can support full uplift in demand.

Darifenacin

Available in 7.5mg and 15mg prolonged release tablets.

Dose

7.5mg to 15mg daily.

Supply position

In stock but cannot support an uplift in demand.

Trospium

Available in 20mg standard release tablets and 60mg prolonged-release capsules.

Dose for standard release tablets

20mg twice daily

Dose for prolonged-release capsules

60mg daily

Supply position

Standard release tablets are in stock and can support a partial uplift in demand.

Prolonged release capsules are in stock and can support a full uplift in demand.

Oxybutynin*

Available in 2.5mg and 5mg standard release tablets, as well as a 2.5mg/5ml and 5mg/5ml oral solution.

Dose

5mg twice daily or up to three times daily (2.5mg twice daily for elderly patients)

Supply position

In stock and can support a full uplift in demand for the immediate release tablets.

*Lyrinel XL® 5mg and 10 mg tablets are being discontinued in July 2022.

Considerations and background

Summary

- There will be intermittent supply of fesoterodine (Toviaz®) 4mg and 8mg modified release tablets until the end of April 2022.
- Alternative antimuscarinic agents remain available and can support an uplift in demand.
- Generic fesoterodine 4mg and 8mg modified release tablets are being launched and will be available from the beginning of May 2022

Clinical Information

Fesoterodine is an antimuscarinic agent licensed for the treatment of symptoms (increased urinary frequency and/or urgency and/or urgency incontinence) that may occur with overactive bladder syndrome. Dose is 4mg to 8mg once daily.

If fesoterodine is not being used as a first line treatment, choice of alternative antimuscarinc agent will be determined by treatments previously tried. In addition, some of the standard formulations must be administered more than once a day, which may not be as suitable for patients accustomed to a once-daily regimen or where adherence may be an issue.

Dry mouth is the most common and troublesome adverse effect of antimuscarinic medications. Newer agents such as solifenacin, tolterodine and darifenacin, may cause dry mouth to a lesser extent than oxybutynin. Extended-release preparations are also expected to reduce the risk of dry mouth. Oxybutynin (standard release) should usually be avoided in elderly, frail patients who are at greater risk of adverse reactions.

Please see the following links for further information:

- SmPC oxybutynin oral preparations
- BNF oxybutynin
- SmPC tolterodine oral preparations
- BNF tolterodine
- SmPC solifenacin oral preparations
- BNF solifenacin
- SmPC darifenacin oral preparations
- BNF darifenacin
- SmPC trospium oral preparations
- BNF trospium

SHORTAGE:

Levomepromazine 25mg/1ml solution for injection ampoules

Anticipated re-supply date: Supply returning. Nozinan 25mg/1ml solution for injection ampoules (Sanofi) 8th April 2022. Levomepromazine 25mg/1ml solution for injection ampoules (Wockhardt UK Ltd) 22nd April 2022.

Actions for prescribers:

Primary care should be aware that:

- prescription validation has been temporarily implemented at Sanofi (please see Supporting Supply Information on how to request supplies);
- community pharmacists/district nurses should work with their local hospitals and request mutual aid if wholesaler supplies are exhausted, to ensure continuity of supply to patients and hospices; and

 if supplies are unavailable via mutual aid, work with specialist palliative care teams to use alternatives wherever possible (see Supporting Clinical Information).

Alternatives

All the medicines listed below remain available and can support an increase in demand:

- Haloperidol 5mg/1ml solution for injection ampoules
- Midazolam 10mg/2ml solution for injection ampoules
- Cyclizine 50mg/ml solution for injection ampoules
- Metoclopramide 10mg/2ml solution for injection ampoules

Please refer to the SmPC's for further information:

Levomepromazine (Nozinan®) 25mg/ml solution for injection

Cyclizine 50 mg/ml solution for injection

Haloperidol 5mg/ml solution for injection

Metoclopramide 10mg/2ml solution for injection

Midazolam 10mg/2ml solution for injection

Considerations and background

Supporting Information

Clinical Information

Levomepromazine is an essential medication in the inpatient and community setting for those patients who do not respond to other antiemetics and/or in whom a level of sedation alongside control of nausea and vomiting can be helpful. Patients on levomepromazine will likely have been treated with first line parenteral agents such as haloperidol or midazolam, alone or in combination, for terminal agitation; or cyclizine, haloperidol, and metoclopramide for nausea and vomiting, so the multi-receptor blockade of levomepromazine makes it a useful choice when symptoms are thought to be due to more than one cause. Should stock of levomepromazine be exhausted, management options will need to be determined on a case-bycase basis, in consultation with the specialist palliative care team.

Supply Information

To obtain supplies via prescription validation, an email request needs to be sent to Sanofi (uk-gfd-dtpsupply@sanofi.com) with the following information (as shared by Sanofi);

- Phoenix or AAH account number;
- Phoenix or AAH order number; and
- anonymised prescription (s).

Once the request has been recieved, validation of the order will take place by Sanofi. Sanofi will then contact Phoenix to release the order against the

	order number provided. Phoenix or AAH will process the order. Once	
	complete, Sanofi will respond to email from pharmacy team advising this has been processed.	
SHORTAGE:	•	
Isosorbide Mononitrate 60mg	Anticipated re-supply date: 20 th April 2022 Actions for prescribers:	
modified-release tablets (Imdur)	If the brand is switched, reassure patients that they are receiving the same	
mounieu-release tablets (middi)	treatment and to seek advice in the unlikely event of experiencing an increase in side effects, such as headache, or an increase in use of glyceryl trinitrate.	
	tillitate.	
	Alternatives:	
	Parallel imports remain available as well as other brands of isosorbide mononitrate 60mg modified release tablets.	
SHORTAGE:	Supply returning. Anticipated re-supply date: 1st June 2022.	
Ketorolac 30mg/1ml solution for	Baxter are out of stock of ketorolac 30mg/1ml solution for injection	
injection ampoules	ampoules until 1st June 2022.	
,	Pharmanovia, the only other licensed supplier, are back in stock as of	
	18th March 2022 and can meet demand.	
	Toth Watch 2022 and can meet demand.	
	Actions / alternatives: Place orders for Pharmanovia ketorolac 30mg/ml	
	ampoules in line with patient demand.	
SHORTAGE:	Anticipated re-supply date: May 15 th 2022	
Colestyramine Oral Products		
Questran 4g oral powder sachets	Alternatives:	
Questran Light 4g oral powder sachets	Oth on any dusts	
Sacriets	Other products Colestyramine light (sugar free) 4g sachets (Mylan) remain available.	
	Limited supplies of Questran Light (parallel imports) are available	
	directly from Lexon UK Ltd.	
	Unlicensed imports	
	Specialist importers can source unlicensed products. Lead times	
	may vary.	
	SPS advice	
	Other bile-acid sequestrants are also available and an SPS owned	
	page Clinical management of the bile acid sequestrant	
	shortages contains further advice on this issue.	
	Considerations and background	
	Using unlicensed medicines Guidance	
	Any decision to prescribe an unlicensed medicine must consider the	
	relevant guidance and/or local governance procedures. Further	
	information is available at:	
	General Medical Council: Prescribing Unlicensed Medicines	
	MHRA guidance on the supply of unlicensed medicinal products	
	("specials")	
	Royal Pharmaceutical Society: Professional Guidance for the	
	Procurement and Supply of Specials	
	When prescribing a product that is not licensed in the UK due to a	
	supply issue with the licensed alternative, prescribers must indicate	
	on the FP10 prescription that an unlicensed product is required. This	
	can be done in one of the following two ways:	
	Electronic prescriptions	

If the required unlicensed product is shown on electronic prescribing systems, GPs should select Colestyramine 4g sachets (imported)

Paper prescriptions

Where the unlicensed product is not shown on electronic prescribing systems, GPs should use a paper prescription and annotate with the following wording: special order

SHORTAGE:

Disopyramide 100mg and 150mg capsules

Anticipated re-supply date: Supply returning. Rythmodan 100mg capsules (Neon Healthcare Ltd)- 31 March 2022, Disopyramide 100mg capsules-31 March 2022, Disopyramide 150mg capsules - 15 April 2022.

Actions for prescribers:

Community pharmacies should note that where patients have insufficient supplies to last until the resupply date:

- emergency orders can be placed directly with Drugsrus for supply of a limited volume of disopyramide 100mg capsules to cover until the resupply date (see supporting clinical information);
- if this stock is no longer available, pharmacists should refer the patient back to their GP to seek specialist cardiology advice on alternative treatment options;
- for patients requiring disopyramide 150mg capsules pharmacists should refer the patient back to their GP to seek specialist cardiology advice on alternative treatment options (see supporting clinical information).

In all settings patients should be counselled on any new formulation and dose change, and advised to report any adverse effects or recurrence of symptoms.

Alternatives:

Disopyramide 250mg MR tablets remain available and can support an increase in demand (see clinical information).

Considerations and background

Supply Summary

- Supplies of disopyramide 100mg capsules were very limited until the end of March 2022, they are now back in stock.
- Disopyramide 150mg capsules are out of stock until mid-April 2022.
- Disopyramide 250mg MR tablets remain available and can support an increase in demand.

Clinical Information

SPS MI have provided the following advice:

Disopyramide is licensed for the treatment of cardiac arrhythmias, with dose adjusted according to response. In addition to immediate release capsule formulations, it is also formulated as a prolonged release tablet. As disopyramide tends to be a last line antiarrhythmic agent, alternative treatment options are limited, thus switching to another disopyramide formulation would be the preferred option, in consultation with cardiology specialists (see dosing information below).

*Dosing information

Disopyramide

Half-life: 5-8 hours

Immediate release capsules (100 and 150mg)

Licensed dose range: 300mg to 800mg daily in divided doses (usually every 6 to 8 hours)

Prolonged-release tablets (250mg)

One side has a break-line and the tablets are licensed to be halved. Licensed dose range: 250-375mg (one to one and a half tablets) twice daily.

The total daily dose of the immediate release capsules should be converted to the closest equivalent dose of the prolonged release tablets administered twice daily. A decision will have to be taken, in conjunction with cardiology specialist, on whether to go under or above current dose for those patients on doses that cannot be exactly delivered by the prolonged-release tablets. In practice, lower dose conversions are likely to be used and the dose titrated up as needed based on response.* Patients should be counselled on the new formulation and dose change, and advised to report any adverse effects or recurrence of symptoms.

Dosing guide

Immediate release capsules total daily dose	Prolonged-release tablet dose regimens	Prolonged-release tablet total daily dose after switch
300mg	125mg BD or 250mg am 125mg pm	250mg to 375mg
400mg	250mg am 125mg pm or 250mg BD	375mg to 500mg
500mg	250mg BD	500mg
600mg	375mg am 250mg pm	625mg
700mg	375mg BD	750mg
800mg	375mg BD	750mg

See SmPCs below for further information

Disopyramide preparations

Guidance on obtaining emergency supplies of disopyramide 100mg capsules:

• Orders can be placed directly with Drugsrus for urgent patient need to cover until the resupply date.

	Email nhs@drugsrus.co.uk for further information
SHORTAGE: Adrenaline (base) 1mg/1ml (1 in 1,000) solution for injection pre-	Anticipated re-supply date: 8 th July 2022 Actions for prescribers
filled syringes	Alternatives: Adrenaline 1:1000 solution for injection ampoules (1mL) are available and can support an uplift in demand.
SHORTAGE: Estradiol (FemSeven) 100micrograms / 24 hours transdermal patches	Anticipated re-supply date: June 1 st 2022. Alternatives: A range of potential alternative HRT products exist. Specialist importers can source unlicensed products. Lead time will vary.
	Considerations and background Using unlicensed medicines Any decision to prescribe an unlicensed medicine must consider the relevant guidance and/or local governance procedures. Further information is available at: • General Medical Council: Prescribing Unlicensed Medicines • MHRA guidance on the supply of unlicensed medicinal products ("specials") • Royal Pharmaceutical Society: Professional Guidance for the Procurement and Supply of Specials
	When prescribing a product that is not licensed in the UK prescribers must indicate on the FP10 prescription that an unlicensed product is required. This can be done by annotating the prescription with the following wording: special order
SHORTAGE: Flumetasone 0.02% / Clioquinol 1% ear drops (Locorten Vioform)	Anticipated re-supply date: 31st May 2022 Actions for prescribers: Clinicians prescribing treatment should:
	 not initiate any new patients on Locorten Vioform ear drops consider prescribing an alternative combination steroid and antibacterial ear drops consider whether there is also a clear clinical need to co-prescribe antifungal ear drops counsel patients on how to administer two separate ear drops if both a steroid-antibacterial combination product and an antifungal is prescribed
	Alternatives: There are no other combination products on market that contain a steroid and an antimicrobial agent with both antibacterial and antifungal properties. Alternative topical combination steroid and antibacterial preparations for the ear are available. Betnesol-N eye/ear/nose drops This product contains betamethasone sodium phosphate 0.1%, neomycin sulphate 0.5% and can support a full uplift in demand.
	Refer to SPC for Betnesol-N eye/ear/nose drops for details. Otomize ear spray This product contains dexamethasone 0.1%, neomycin sulphate 0.5%, glacial acetic acid 2% and can support a full uplift in demand. Refer to SPC for Otomize ear spray for details. Otosporin ear drops

This product contains hydrocortisone 1%, neomycin sulphate 3400 units/mL, polymyxin B sulphate 10,000 units/mL and can support a partial uplift in demand.

Refer to SPC for Otosporin ear drops for details.

Sofradex ear/eye drops

This product contains Dexamethasone 0.05%, framycetin sulphate 0.5%, gramicidin 0.005% and can support a full uplift in demand.

Refer to SPc for Sofradex ear/eye drops for details.

Canestan (clotrimazole) 1% solution

This only topical antifungal preparation on the market for use in the ear and stock is available to support a full uplift in demand.

Refer to SPC for Canestan (clotrimazole) 1% solution for details.

Considerations and background

Clinical Information

Locorten Vioform is licensed for the treatment of inflammatory conditions of the external ear where a secondary infection is suspected, and otorrhoea. It contains the steroid flumetasone and clioquinol, which has anti-fungal and anti-bacterial properties. There are no other steroid/antifungal combination ear drops on the market; and flumetasone and clioquinol are not available as separate components. Where there is a need for an antifungal in addition to a steroid and antibacterial, an antifungal will need to be prescribed as a separate ear preparations. The only licensed antifungal ear drops are Canestan (clotrimazole) 1% solution.

Counselling Points

Clinicians should be aware of the following when counselling patients:

- Explain to patients the mechanism of action of the components being prescribed
- Anecdotally, the administration of Canestan solution into ear can be painful; patients should be counselled appropriately
- If prescribing both a combination steroid-antibacterial and antifungal ear drops, advise patients to allow a gap of 2-5 minutes before administering the second preparation; there is no guidance on optimal sequence, but the steroid preparation could be administered first in case of pain following use of Canestan solution.

Further advice on the management of otitis externa can be found here:

- NICE CKS: Otitis Externa
- BNF treatment summary: Ear

SHORTAGE:

Quinapril 10mg / Hydrochlorothiazide 12.5mg (Accuretic) Tablets Anticipated re-supply date: Resupply date is to be confirmed.

Alternatives:

Hydrochlorothiazide is not available as single agent; quinapril 10mg tablets and an alternative thiazide, bendroflumethiazide 2.5mg tablets, remain available as do alternative medicines containing a combination of an antihypertensive with a diuretic.

Considerations and background

Pfizer Ltd have <u>recalled</u> all stock of Accuretic 10mg/12.5mg film-coated tablets as a precautionary measure due to the identification of a nitrosamine above the acceptable limit.

SHORTAGE:

Lidocaine (Xylocaine) 1% and 2% with Adrenaline 100micrograms/20ml (1 in 200,000) solution for injection vials

Supply returning. Anticipated re-supply date: Dec 31st 2022 **Actions for prescribers:**

General Practice and other sites that use Xylocaine® 1% and 2% with adrenaline 100micrograms/20ml should:

- note the available alternative products (see alternatives); and
- consult the Medicines Information department at their local NHS Trust for advice where required.

Alternatives:

Alternative local anaesthetic with adrenaline products

Due to the fixed dose of adrenaline in the alternative products, clinicians should be aware of the risk of administering a larger dose of adrenaline than intended.

Lidocaine 0.5% with adrenaline 1:200,000 10ml ampoule

Supplier – Torbay

Supply – In stock. Unlicensed product.

Lidocaine 1% with adrenaline 1:200,000 10ml ampoule

Supplier -Torbay.

Supply – Out of stock. Resupply date to be confirmed. Unlicensed product.

Lidocaine 2% with adrenaline 1:200,000 10ml ampoule

Supplier – Torbay.

Supply – Out of stock. Resupply date to be confirmed. Unlicensed product.

Bupivacaine 0.25% with adrenaline 1:200,000 10ml ampoule

Supplier – Advanz.

Supply – In stock. Cannot support an increase in demand.

Bupivacaine 0.5% with adrenaline 1:200,000 10ml ampoule

Supplier – Advanz.

Supply - In stock.

Lidocaine 1% with adrenaline 1:200,000 injection

Supplier – Specialist Importers.

Supply – Unlicensed product. See below.

Lidocaine 2% with adrenaline 1:200,000 injection

Supplier – Specialist Importers.

Supply – Unlicensed product. See below.

Unlicensed imports

The following specialist importers have confirmed they can source unlicensed lidocaine 1% or 2% with adrenaline 1:200,000 injection. Lead times may vary (please note, there may be other companies that can also source supplies):

- Durbin PLC 1% and 2%
- Mawdsley's Unlicensed 1% and 2%
- Smartway Pharma 1%
- UL Global Pharma 1% and 2%

Considerations and background

Supply Summary

Xylocaine® 1% with adrenaline is currently in limited supply with full resupply expected in late December 2022.

Xylocaine® 2% with adrenaline is currently in limited supply with full resupply expected in late December 2022.

Guidance on unlicensed imports

Any decision to prescribe an unlicensed medicine must consider the relevant guidance and NHS Trust or local governance procedures. Please see the links below for further information:

- The supply of unlicensed medicinal products, Medicines and Healthcare products Regulatory Agency (MHRA)
- <u>Professional Guidance for the Procurement and Supply of Specials</u>, Royal Pharmaceutical Society
- <u>Prescribing unlicensed medicines</u>, General Medical Council (GMC)

SHORTAGE:

Mesalazine 400mg and 800mg (Asacol) MR gastro-resistant tablets

Anticipated re-supply date: May 31st 2022

Actions for prescribers:

For patients with insufficient supplies, clinicians should consider the following options:

- prescribing Octasa® MR tablets and reassure patients that this is a similar preparation to Asacol® MR gastro-resistant tablets;
- if Octasa® MR tablets are not considered appropriate refer to the <u>SPS Q&A</u> document for further information on licensed indications and dosing of other brands of mesalazine tablets, taking into account different release characteristics and counselling patients on any new product prescribed;
- monitoring patients for disease control and tolerability of treatment after switching products and ensuring they are maintained on this brand if the switch is successful; and
- deferring initiating any new patients on Asacol® MR gastro-resistant tablets until the supply issue is resolved.

Alternatives:

Availability of alternative products

Interchangeable mesalazine tablet preparations

Octasa® MR 400mg and 800mg tablets – *In stock and can support full uplift in demand*

Other mesalazine tablet preparations

The following mesalazine tablet preparations with different release characteristics remain available, should Octasa® MR tablets not be considered appropriate.

Zintasa® EC 400mg tablets – *In stock*

Salofalk® 250mg tablets, 500mg gastro-resistant tablets and 1g gastro-resistant tablets – $In\ stock$

Pentasa® 500mg and 1g slow-release tablets – *In stock*

Considerations and background Supporting Information

Alternative mesalazine tablet preparations

The <u>BNF</u> states 'there is no evidence to show that any one oral preparation of mesalazine is more effective than another; however, the delivery characteristics of oral mesalazine preparations may vary'.

Octasa® MR tablets were launched after publication of the BNF statement; they are a branded generic version of Asacol® tablets and have virtually the same in vitro dissolution profile, pH for release, site of drug release and same formulation.

Please refer to the following links for further information on alternative preparations:

Asacol® SmPC

Octasa® SmPC

Zintasa® SmPC

Salofalk® SmPC

Pentasa® SmPC

Mesalazine BNF

<u>SPS Q&A document – What are the differences between different brands of mesalazine tablets?</u>

SHORTAGE:

Colestipol 5g Granules Sachets Sugar Free

Anticipated re-supply date: No anticipated re-supply date **Actions for prescribers:**

For patients with insufficient supplies, clinicians should consider:

- prescribing an alternative bile-acid sequestrant; or
- prescribing unlicensed colestipol sachets if alternative medicines are not appropriate. Prescribers should work with pharmacy teams to ensure orders are placed within appropriate time frames as lead times may vary.

Alternatives:

Other colestipol products

Colestid orange sachets are available.

Unlicensed imports

Supplies of unlicensed imports of colestipol sachets have been sourced.

SPS advice

Other bile-acid sequestrants are also available and an SPS owned page <u>Clinical management of the bile acid sequestrant shortages</u> contains further advice on this issue.

Considerations and background

Using unlicensed medicines

Guidance

Any decision to prescribe an unlicensed medicine must consider the relevant guidance and NHS Trust or local governance procedures. Please see the links below for further information:

- The supply of unlicensed medicinal products, Medicines and Healthcare products Regulatory Agency (MHRA);
- <u>Professional guidance for the procurement and supply of specials</u>, Royal Pharmaceutical Society (RPS); and
- Prescribing unlicensed medicines, General Medical Council (GMC).

When prescribing a product that is not licensed in the UK due to a supply issue with the licensed alternative, prescribers must indicate on the FP10 prescription that an unlicensed product is required. This can be done in one of the following two ways:

Electronic prescriptions

If the required unlicensed product is shown on electronic prescribing systems, GPs should select: Colestid 5g sachets (imported) Paper prescriptions

Where the unlicensed product is not shown on electronic prescribing systems, GPs should use a paper prescription and annotate with the following wording: Special Order

SHORTAGE:

Oxybutynin (Kentera) 3.9mg / 24 hours transdermal patches

Anticipated re-supply date: 31st May 2022 **Actions for prescribers:**

Clinicians prescribing treatment in primary and secondary care should:

- defer initiating new patients on oxybutynin (Kentera®)
 3.9mg/24hours transdermal patches until the supply issue resolves;
- review patients currently on treatment to determine if this is still
 the most suitable therapy and where appropriate, consider
 switching to oxybutynin tablets or oral solution in those not
 previously on these treatments; or assess risk of a re-trial of these
 formulations in patients previously treated with them, titrating dose
 as needed, based on symptoms and tolerability (see clinical advice);
- consider use of another anticholinergic agent, which may be better tolerated;
- assess suitability of patients who are unable to tolerate the sideeffects of oral oxybutynin or other anticholinergic preparations for mirabegron prolonged-release tablets (see supporting information); and
- if above options not suitable, obtain specialist advice.

Alternatives:

Alternative Treatment Options

Alternative medicines for urinary disorders remain available and can support an uplift in demand.

Oxybutynin (Lyrinel XL®) 5mg and 10mg modified-release tablets are available but cannot support an increase in demand during this time.

Anticholinergic agents

- Oxybutynin 2.5mg and 5mg standard release tablets
 - Dose: 5mg BD to TDS (2.5mg BD elderly)
- Oxybutynin 2.5mg/5ml and 5mg/5ml oral solution
 - o Dose: 5mg BD to TDS (2.5mg BD elderly)
- Solifenacin 5mg and 10mg standard release tablets
 - o Dose: 5mg to 10mg OD
- Solifenacin 1mg/1ml oral suspension
 - o Dose: 5mg to 10mg OD
- Tolterodine1mg and 2mg standard release tablets
 - o Dose: 1mg to 2mg BD
- Tolterodine 2mg Modified release and 4mg Modified release capsules
 - o Dose: 2mg to 4mg OD

Non-anticholinergic agent

- Mirabegron (Betmiga®) 25mg and 50mg prolonged release tablets
 - o Dose: 25mg to 50mg OD

Considerations and background Clinical advice

Dry mouth is the most common and troublesome adverse effect of anticholinergic medicines and is the main reason for discontinuing oxybutynin. As many of the adverse effects of anticholinergic medicines are dose-related, it is recommended to start at a low dose and titrate according to efficacy and side-effects; older people require lower doses.

For patients experiencing side-effects or with inadequate response at maximum dose, changing to a different anticholinergic may be beneficial as side-effect profiles differ. Solifenacin and tolterodine are considered to cause dry mouth to a lesser extent than oxybutynin. Extended-release preparations are also expected to reduce the risk of dry mouth. Oxybutynin (Kentera®) transdermal patches are licensed for the symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in adult patients with unstable bladder. They are prescribed to patients who experience intolerable anticholinergic side-effects from oral oxybutynin.

Mirabegron (Betmiga®) is a non-anticholinergic agent, which is NICE approved for treating the symptoms of overactive bladder, only for people in whom anticholinergic drugs are contraindicated or clinically ineffective or have unacceptable side-effects. Appropriateness of this treatment will need to take into account co-morbidities such as hypertension, liver, and renal impairment, as well as interacting medicines. As mirabegron is a prolonged-release tablet, it cannot be crushed. Please refer to the SmPC's for further information:

- Oxybutynin (Kentera®) 3.9mg/24hours transdermal patches
- Oxybutynin tablets and oral solution
- Tolterodine preparations
- Solifenacin preparations
- Mirabegron (Betmiga®) 25mg and 50mg prolonged-release tablets

SHORTAGE:

Benperidol (Anquil) 250 microgram tablets

Anticipated re-supply date: No anticipated re-supply date **Actions for prescribers:**

Healthcare professionals in primary, secondary or specialist healthcare services should:

 defer initiating new patients on benperidol until the supply issue is resolved; and work together to identify and refer patients to the relevant specialist mental health services for an individualised review of management options (see clinical information).

Alternatives:

See clinical information

Considerations and background

Summary

- Benperidol (Anquil®) 250 microgram tablets will be out of stock from the end of March 2022 with a resupply date to be confirmed.
- Management options during this shortage should be determined on a case-by-case basis, in consultation with the appropriate mental health specialist.

Clinical Information

Benperidol is an antipsychotic in the butyrophenone class licensed for the control of deviant anti-social sexual behaviour. The usual dose range is 250 micrograms to 1.5 mg per day in divided doses.

Patients on this treatment should be reviewed by a relevant mental health specialist with a view to understanding why treatment was first initiated and if benperidol remains the most appropriate treatment. The review should consider the risks of stopping treatment, and whether other management options should be considered. If discontinuation of treatment is not suitable, management options should be determined on a case-by-case basis, based on history, response, tolerability, and any associated symptoms co-morbidities.

Withdrawal of antipsychotic drugs after long-term therapy should normally/usually be gradual and closely monitored to avoid the risk of acute withdrawal syndromes or rapid relapse.

Links to further information

Benperidol (Anquil®) 250microgram tablets SmPC

SHORTAGE:

Diamorphine 100mg and 500mg powder for solution for injection ampoules

Anticipated re-supply date: 31st May 2022 **Actions for prescribers:**

All healthcare professionals in primary and secondary care including hospices, (excluding specialist substance misuse treatment), who prescribe, dispense, or administer diamorphine, should continue to work with their local Medication Safety Officer (MSO), pharmacy procurement teams or local lead within their organisation to:

- review patients to determine if they can be switched to morphine sulfate solution for injection or another opioid;
- ensure that existing stock is reserved for patients unable to switch to an alternative opioid;
- monitor patients for symptom control or signs of overdose after switching agents; and
- review worksheets for those units producing prefilled syringes of diamorphine (for intrathecal administration) from high strength ampoules.

Those in specialist substance misuse treatment who prescribe, dispense, or administer diamorphine for the treatment of opioid dependence should work with their pharmacy or clinical leads to:

 ensure that patients are treated with an alternative opioid substitute, such as long-acting oral morphine, and monitor patients for sign of overdose and symptom control, adjusting the dose where necessary.

Alternatives:

All morphine preparations remain available and can support an increase in demand during this time.

Diamorphine 5mg, 10mg and 30mg ampoules remain available but are unable to support an uplift in demand.

Considerations and background Supporting Clinical Information

The UK is the only country that uses diamorphine for medicinal analgesic purposes. Diamorphine is metabolised to morphine and in terms of analgesic efficacy and effect on mood, it has no clinical advantages over morphine by oral or subcutaneous/intramuscular routes. In addition, morphine injection is less costly than diamorphine and does not have to be reconstituted. Information has previously been provided in a Supply Disruption Alert advising that morphine should be considered a first line treatment option.

Should stock of these high strength diamorphine ampoules run out, clinicians will need to review patients to determine whether morphine or another opioid is an appropriate agent to switch to.

Point to consider when switching to alternatives

- Diamorphine is much more water soluble than morphine and may be preferred to morphine in the very few patients where high dose injections are needed, as smaller volumes can be used. As the maximum concentration of morphine available is 30mg/mL, this may be an issue for patients requiring high doses of subcutaneous morphine, particularly bolus doses for breakthrough pain where the volume given should not exceed 2mL. If volume is an issue, advice should be sought from the palliative care team.
- Care is needed when switching from one opioid analgesic to another to ensure equipotent dosage. Diamorphine 100mg injection is approximately equivalent to morphine 150mg (SC/IV/IM) injection.
- As mentioned in the actions, patients should be carefully monitored after any drug switch and dose titration may be required.
- When converting from diamorphine to other subcutaneous opioids, consideration will also need to be given to drug compatibility in the syringe driver and the total volume of infused drugs.
- When converting to alternatives in regional anaesthesia, consideration will need to be given to use of preservative-free opioids.
- Opioid dependent patients in drug treatment programmes who are receiving high dose injectable diamorphine treatment may experience difficulties switching to alternatives; the local drug treatment service should be contacted for advice on managing this group.

Please refer to local guidance, the BNF or the Palliative Care Formulary for information on dose conversion to other opioids; and contact relevant specialist teams for advice on management of individual cases.

Please also refer to SmPC's, specialist guidance and previous Supply Disruption Alert issued in 2020 for further information.

- Diamorphine hydrochloride injection SmPC
- Morphine sulfate SmPC
- BNF (prescribing in palliative care)
- Obstetric Anaesthetists' Association: alternatives to intrathecal and epidural diamorphine for caesarean section analgesia
- Supply Disruption Alert Diamorphine 5mg and 10mg injection March 2020

All Serious Shortage Protocols (SPP's) can be found:

https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/serious-shortage-protocols-ssps

Shortage update taken from SPS Medicines Supply Toolkit 14th April 2022