# Shortage of Bumetanide 1mg and 5mg tablets

Anticipated re-supply date: 5 January 2024

#### Actions:

Healthcare professionals in primary and secondary care should not initiate any new patients on bumetanide 1mg and 5mg tablets until the supply issue has resolved.

Where existing patients have insufficient supplies of bumetanide tablets to last until the re-supply date, clinicians should:

review patients to determine if this is still the most suitable therapy;

reserve any remaining stock of bumetanide 1mg tablets for patients using this strength who are unsuitable for a switch to furosemide;

consider prescribing furosemide tablets which are able to support the market during this time, ensuring that the patient is not intolerant to any of the excipients and is counselled on the appropriate dose to take (see Supporting information);

only consider prescribing unlicensed products where licensed alternatives are not appropriate. Prescribers should work with local pharmacy teams to ensure orders are placed within appropriate time frames as lead times may vary (see Supporting information ); and

if the above options are not considered appropriate or symptoms are not controlled on furosemide, advice should be sought from specialists on management options.

A switch should be made before patients run out of tablets to avoid a break in therapy that could increase the risk of decompensation and unintentional fluid retention.

#### Alternatives:

Furosemide 20mg and 40mg tablets remain available and can support increased demand. Where these are not suitable, unlicensed supplies of bumetanide 1mg and 5mg tablets may be sourced, lead times vary.

Bumetanide 1mg/5ml SF oral solution remains available but is unable to support increased demand.

# **Clinical Information:**

Bumetanide is a loop diuretic licensed for the treatment of oedema associated with e.g., congestive heart failure, renal dysfunction including nephrotic syndrome and cirrhosis of the liver in adults. In oedema of renal or cardiac origin where high doses of a potent short-acting diuretic are required, a 5mg dose of bumetanide may be used in adults.

Furosemide is a loop diuretic licensed for use in all indications where a prompt and effective diuresis is required. It is similar in activity to bumetanide; both act within 1 hour of oral administration and diuresis is complete within 6 hours. The diuresis associated with these drugs is dose related.

Loop diuretics produce the same response if given at equipotent doses. When kidney function is normal, a 40mg dose of furosemide is approximately equal to 1mg of bumetanide. Selecting an equivalent dose is determined on a case-by-case basis as effects will differ based on clinical status and stability of patient, fluid status, and renal function. Patients switched from a stable dose of bumetanide to

	furosemide may require follow up to assess response, with dose titration if required, to ensure fluid balance remains stable.
	Medicine Supply Notification Number: MSN/2023/094
Shortage of Hydrocortisone 0.5% cream	Anticipated re-supply date: 10 November 2023
	Alternatives: Hydrocortisone 0.5% ointment remains available and can support a full uplift in demand.
Shortage of Progesterone (Crinone) 8% vagina gel and Progesterone (Lutigest) 100mg vaginal tablets	Actions: Where patients have insufficient supplies to last until the re-supply date, prescribers should:  • consider prescribing alternative progesterone products for supplementation of luteal phase as part of Assisted Reproductive Technology (ART), ensuring that the patient is not intolerant to any of the excipients and is counselled on the appropriate dose required (see Supporting Information below);  • where the above option is inappropriate and for the indication of use as an adjunct to In Vitro Fertilisation (IVF) where infertility is mainly due to tubal, idiopathic or endometriosis linked sterility associated with normal ovulatory cycles, consider alternative management options (see Supporting Information below).
	Alternatives: Alternative progesterone products and recommended doses for the supplementation of luteal phase as part of ART: Cyclogest 200mg and 400mg pessaries:  • 400mg twice daily vaginally, starting at oocyte retrieval and continuing for 38 days once pregnancy is confirmed
	Utrogestan 200mg vaginal capsules:  200mg three times daily from day of embryo transfer until at least week 7 of pregnancy up to week 12 of pregnancy
	Lubion 25mg/1.112ml solution for injection vials (in women for whom vaginal preparations are inappropriate):  • 25mg injected subcutaneously or intramuscularly from day of oocyte retrieval up to week 12 of pregnancy
	Clinical information: Progesterone (Lutigest) 100mg vaginal tablets are used for the supplementation of luteal phase as part of Assisted Reproductive Technology (ART). The recommended dose is 100mg administered vaginally three times daily starting at oocyte retrieval and continued for 30 days if pregnancy has been confirmed. Progesterone (Crinone) 8% vaginal gel is used for treatment of infertility due to inadequate luteal phase and for use as an adjunct to in-vitro fertilisation (IVF) where infertility is mainly due to tubal, idiopathic or endometriosis linked sterility associated with normal ovulatory cycles. For the treatment of infertility due to inadequate luteal phase, the recommended dose is one applicatorful applied once daily after ovulation or on the 18th to 21st day of the cycle. When used in IVF, it is applied daily starting on the day of embryo transfer

	and it should be continued for 30 days if there is laboratory evidence		
	of pregnancy.		
	MSN Number: MSN/2023/093		
Shortage of Exenatide (Byetta) 10microgram/0.04ml solution for injection	Actions:  A National Patient Safety Alert was issued on the 18 July 2023 for the shortage of GLP1 RA medicines.  Please refer to the National Patient Safety Alert for information and advice on alternatives		
Shortage of Lisdexamfetamine (Elvanse) capsules	Anticipated re-supply date: Elvanse 50mg capsules (Takeda UK Ltd) 31 October 2023 Elvanse 60mg capsules (Takeda UK Ltd) 20 October 2023 Elvanse 70mg capsules (Takeda UK Ltd) 6 November 2023 Elvanse Adult 30mg capsules (Takeda UK Ltd) 3 November 2023 Elvanse Adult 50mg capsules (Takeda UK Ltd) 20 October 2023		
	Actions: A National Patient Safety Alert was issued on the 27 September 2023 for the shortage of methylphenidate prolonged-release capsules and tablets, lisdexamfetamine capsules, and guanfacine prolonged-release tablets. Please refer to the National Patient Safety Alert for information and advice.		
	Alternatives: The following specialist importers have confirmed they can source unlicensed imports of lisdexamfetamine (Vyvanse) capsules (please note there may be other companies that can also source supplies and lead times vary):  • Alium • Target		
	Supply overview: Elvanse 20mg capsules will be out of stock on 06 Nov 23 with an anticipated resupply date of 01 Dec 2023		
Shortage of Atomoxetine capsules and oral solution	Anticipated re-supply date: Atomoxetine 60mg capsules 31 October 2023 Atomoxetine 25mg capsules 31 October 2023 Strattera 4mg/1ml oral solution (Eli Lilly and Company Ltd) 27 October 2023		
	Actions:  Primary and secondary care: Clinicians/prescribers in primary and secondary care should:  • proactively identify any patients on atomoxetine presentations;  • contact patients to establish how much supply they have left; and  • liaise with the patient's specialist team for advice on management options.		
	Specialist teams: Specialist teams should:  • ensure no new patients are initiated on atomoxetine presentations until the shortage is resolved		

- support primary care clinicians seeking advice for patients currently taking atomoxetine presentations, including provision of individualised management plans, where required; and
- offer alternatives in line with <u>NICE ADHD guidance</u> <u>NG87</u> where required.

Where the above options are not considered appropriate, supplies of unlicensed atomoxetine capsules may be sourced. Contact should be made with local pharmacy teams to ensure orders are placed within appropriate time frames as lead times may vary (see clinical information below).

#### Alternatives:

Other strengths of atomoxetine capsules remain available but in insufficient quantities to meet increased demand.

Refer to the following <u>link</u> for further information on the availability of methylphenidate prolonged release tablets,

# **Unlicensed imports:**

The following specialist importers have confirmed they can source unlicensed atomoxetine capsules (please note there may be other companies that can also source supplies and lead times vary):

- Alium
- BAP Pharma
- Qmed Pharma
- Target

# **Supply summary:**

Atomoxetine 10, 18, 40, 80 and 100mg capsules are currently in stock.

Atomoxetine 25mg and 60mg remain unavailable.

#### **Clinical information:**

Stimulants such as lisdexamfetamine or methylphenidate are recommended first-line treatments for attention deficit hyperactivity disorder (ADHD). Treatment with non-stimulants (e.g. atomoxetine or guanfacine) are an option in patients who are intolerant to both methylphenidate and lisdexamfetamine, or who have not responded to separate 6-week trials of both drugs (NICE ADHD guidance NG87). These treatments must be initiated by a specialist in the treatment of ADHD.

Atomoxetine selectively inhibits pre-synaptic noradrenaline reuptake and is licensed for the treatment of ADHD in children aged 6 years and older, in adolescents, and in adults. In the paediatric population up to 70 kg body weight, atomoxetine should be initiated at a total daily dose of approximately 0.5 mg/kg and dose titrated upwards after a minimum of 7 days. according to clinical response and tolerability. The recommended maintenance dose is approximately 1.2 mg/kg/day. For paediatric population over 70 kg, the initial dose is 40mg for minimum of 7 days followed by upwards dose titration. The recommended maintenance dose is 80mg. In adults, atomoxetine is initiated at 40 mg for a minimum of 7 days prior to upward dose titration and the recommended maintenance daily dose is 80 mg to 100 mg.

Guanfacine, a selective alpha2A-adrenergic receptor agonist, is licensed for the treatment of ADHD in children and adolescents aged 6-17 years for whom stimulants are not suitable, not tolerated or have been shown to be ineffective.

Use of atomoxetine and guanfacine in children aged 5 years as

per NICE guidance is off label, as is the use of guanfacine in adults, which should not be initiated without advice from a tertiary ADHD service. Patients on atomoxetine should be periodically reviewed in line with NICE guidance. Shortage of Methylphenidate Anticipated re-supply date: prolonged-release tablets Xenidate XL 27mg tablets (Viatris UK Healthcare Ltd) 31 October 2023 Xaggitin XL 18mg tablets (Ethypharm UK Ltd) 1 February 2024 Xaggitin XL 36mg tablets (Ethypharm UK Ltd) 1 February 2024 Actions: Where patients have insufficient supplies to last until the re-supply date, clinicians should: consider prescribing alternative bioequivalent brands (see clinical information) that are available, ensuring that the patient is not intolerant to any of the excipients; counsel patients to reassure them that Delmosart, Xaggitin XL and Xenidate XL tablets have a similar release profile to Concerta XL (see clinical information); and reassure patients that any changes to their prescription will be short-term and for the duration of the supply issue only, and they have the option to switch back to their original brand once the supply issue is resolved or continue the brand they have been switched to. Supply overview: Xaggitin XL 18mg tablets are out of stock. Xaggitin XL 36mg tablets are due to go out of stock on 17 November 2023. **Clinical Information:** Methylphenidate is a central nervous stimulant available in the UK in various licensed immediate, modified-release, oral, and solid dosage forms. It is a schedule 2 controlled drug, licensed for the treatment of attention deficit hyperactivity disorder (ADHD) in children aged over 6 years and adolescents and is the usual first line treatment for this condition for both children and adults. All the modified-release methylphenidate preparations include an immediate-release component as well as an extended-release component. This allows for rapid onset of action while avoiding the need to take further doses during the day to maintain effect. The biphasic release profiles of these products, however, are not all equivalent and contain different proportions of the immediate-release and modified-release component. The BNF states that different versions of modified-release preparations may not have the same clinical effect. To avoid confusion between these different formulations of methylphenidate, prescribers should specify the brand to be dispensed. Of the modified-release preparations, Delmosart, Xaggitin XL and Xenidate XL tablets have been approved based on bioequivalence data compared to Concerta XL tablets. Thus, these generic brands have been granted replicate marketing authorisation to Concerta XL on the basis that they have satisfied the criteria for equivalent release

Shortage of Levomepromazine 25mg and 50mg tablets

Anticipated re-supply date: 3 November 2023

profile for the reference Concerta XL product.

Actions:

Where supply of generic levomepromazine 25mg tablets are unavailable, clinicians should:

• consider prescribing the branded levomepromazine (Nozinan) 25mg tablets.

Where supply of generic levomepromazine 50mg tablets are unavailable, clinicians should:

- consider prescribing the branded levomepromazine (Nozinan) 25mg tablets;
- counsel patients on the requirement to take two tablets to make a 50mg dose for those patients who are usually prescribed levomepromazine 50mg tablets;
- if the above is not appropriate, consider prescribing Levomepromazine (Levorol) 5mg/ml oral solution, taking into consideration any cautions and contraindications (see Supporting Information).

#### Alternatives:

- Levomepromazine (Nozinan) 25mg tablets remain available from Neuraxpharm UK Limited and are able to fully support demand. Stock is available via Phoenix and Alliance Healthcare.
- Levomepromazine (Levorol) 5mg/ml oral solution remains available from Galvany Pharma Limited and are able to support with covering demand. Hospitals can order from either Alloga UK or Alliance Healthcare. Retail/community pharmacies can order from Alliance Healthcare.

#### Clinical Information:

Levomepromazine oral solution is contraindicated in children and adolescents under 16 years old.

The oral solution has cautions linked to its excipients and therefore prescribers would need to ensure patients do not have liver or renal impairment before prescribing this medicine:

- Benzyl alcohol this medicine contains 0.03 mg of benzyl alcohol in each 1 ml of oral solution. It may cause allergic reactions. High volumes should be used with caution and only if necessary, especially in patients with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).
- Propylene glycol this medicine contains 150.95 mg of propylene glycol in each 1 ml of oral solution. Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction. While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.

Shortage of Methylphenidate (Equasym XL) modified release capsules Anticipated re-supply date: 20 October 2023

# Actions:

A <u>National Patient Safety Alert</u> was issued on the 27 September 2023 for the shortage of methylphenidate prolonged-release capsules and tablets, lisdexamfetamine capsules, and guanfacine prolonged-release tablets.

Please refer to the National Patient Safety Alert for information and advice. Alternatives: Limited parallel imports of methylphenidate (Equasym XL) modified release capsules remain available but cannot support an uplift in demand. Shortage of Fixapost Anticipated re-supply date: 13 October 2023 preservative free eye drops Actions: Where supply of Fixapost (Latanoprost 50micrograms/ml / Timolol 5mg/ml) preservative free eye drops is not available, prescribers should: consider prescribing Monopost (Latanoprost) 50micrograms/ml eye drops 0.2ml unit dose and Tiopex (Timolol) 1mg/g eye gel 0.4g unit dose, ensuring patients are counselled on how to administer the products correctly. **Alternatives:** The following products remain available and can support an uplift in demand: Monopost (Latanoprost) 50micrograms/ml eye drops 0.2ml unit dose Tiopex (Timolol) 1mg/g eye gel 0.4g unit dose **Clinical Information** Fixapost (Latanoprost 50micrograms/ml / Timolol 5mg/ml) preservative free eye drops provide approximately 1.5 micrograms of latanoprost and 0.15mg timolol in a preservative-free formulation. The recommended dose is one drop in the affected eye(s) once daily. For patients that require a preservative-free alternative, it would be appropriate to prescribe the two components separately as Monopost (Latanoprost) 50micrograms/ml eye drops 0.2ml unit dose and Tiopex (Timolol) 1mg/g eye gel 0.4g unit dose. One drop of Monopost provides approximately 1.5micrograms of latanoprost and is given once daily. Tiopex is a gel-based formulation of timolol containing 1mg timolol per gram of gel and the recommended dose is 1 drop applied to the affected eye(s) once daily. Patients that are being switched from Fixapost to the individual components, must be counselled on the importance of administering the Monoprost (latanoprost) at least 15 minutes before administering the Tiopex (timolol) to allow time for the latanoprost to be absorbed. Shortage of Oxycodone Anticipated re-supply date: 30 October 2023 5mg/5ml oral solution Actions: Clinicians should: review patients to determine if oxycodone 5mg/5ml oral solution is still the most suitable therapy consider prescribing immediate release oxycodone capsules for patients who can swallow solid dosage forms and are on a regime comprising 5mg or 10mg doses, ensuring that the patient is not intolerant to any of the excipients and is counselled on the appropriate dose (see Supporting

information below)

consider prescribing morphine-based products as an

alternative agent, if clinically appropriate

- reserve stock of oxycodone 5mg/5ml oral solution for patients where doses such as 2.5mg or 7.5mg cannot be made up easily with capsules and alternatives are not considered suitable
- consider prescribing unlicensed oxycodone oral solution/suspension only where the immediate release capsules or other licensed opioid analgesics are not appropriate. Prescribers should work with local pharmacy teams to ensure orders are placed within appropriate time frames as lead times may vary (see supporting information below); and
- if the above options are not considered appropriate, advice should be sought on alternative pain management options from team who initiated oxycodone liquid.

#### Alternatives:

Oxycodone 5mg/5ml oral solution from other manufacturers remains available but will not be able to support increased demand.

# Solid dosage forms

Oxycodone 5mg and 10mg immediate release capsules remain available.

# **Liquid formulations**

Other liquid formulations of opioids, such as morphine, remain available.

# Unlicensed oxycodone liquid

A number of Specials manufacturers are able to produce unlicensed oxycodone 5mg/5ml oral suspension (including sugar free formulations).

Where the above options are not suitable, unlicensed imports of oxycodone 5mg/5ml oral solution may be sourced, lead times vary.

#### Clinical information:

Oxycodone is licensed for the treatment of moderate to severe pain in patients with cancer and post-operative pain, and for the treatment of severe pain requiring the use of a strong opioid. The usual starting dose for opioid naïve patients or patients presenting with severe pain uncontrolled by weaker opioids is 5mg, 4-6 hourly. The dose should then be carefully titrated, as frequently as once a day if necessary, to achieve pain relief. The capsules should be swallowed whole, and not chewed or crushed. There are no data on emptying out capsule contents (off label) to deliver a part dose or to administer to patients with swallowing difficulties.

#### **Unlicensed Imports/Specials:**

Guidance on ordering and prescribing unlicensed imports. The following specialist importers have confirmed they can source unlicensed oxycodone 5mg/5ml oral solution (please note there may be other companies that can also source supplies):

Mawdsleys

The following Specials manufacturers have currently confirmed they can manufacturer oxycodone 5mg/5ml oral suspension (please note, there may be other companies that can also manufacture):

- Eaststone
- Rokshaw

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)
- <u>Prescribing unlicensed medicines</u>, General Medical Council (GMC)

# **Medicine Shortage Notification Number** MSN/2023/042

# Shortage of Azelaic acid (Skinoren) 20% cream

Anticipated re-supply date: 3 November 2023

#### Actions:

Where patients have insufficient supplies of azelaic acid (Skinoren) 20% cream to last until the re-supply date, prescribers should:

- refer to treatment guidelines/local formularies and consider prescribing an alternative topical treatment, ensuring there are no contra-indications or intolerance of active drug/excipients, and if considering a topical retinoid, that patients of childbearing age, are not pregnant or planning a pregnancy; and
- counsel patients on use of the alternative product, including a discussion about whether there is a need to consider contraception for patients of child-bearing age, if prescribed a topical retinoid (see Supporting Information).

# **Clinical Information:**

Topical azelaic acid preparations are used for the treatment of acne and rosacea. Skinoren cream (20%) and Finacea gel (15%) differ in range of licensed indications:

- Skinoren (20% cream) is licensed for topical treatment of acne vulgaris in patients aged from 12 years.
- Finacea (15% gel) is licensed for use in patients aged from 12 years with mild to moderate papular-pustular acne of the facial area, and for use in adults with papulopustular rosacea.

# **Alternative topical treatments:**

The choice of alternative agent will be determined by indication, contra-indications, intolerance of active agent/excipients, licensed age groups, and treatments already tried.

Azelaic acid is a first-line topical treatment option for papulopustular rosacea, alternative topical treatments for rosacea include topical ivermectin and topical metronidazole.

Local/national guidance should be consulted for selection of an alternative preparation for acne. For those products containing known teratogenic drugs or drugs with teratogenic potential, such as topical retinoids (e.g., adapalene, tretinoin), pregnancy/plans to become pregnant, and acceptability of using contraception should be established in patients of child-bearing age.

The MHRA notes that systemic exposure is thought to be negligible following application of topical retinoids (adapalene, and tretinoin based products) during pregnancy, but since risk cannot be excluded, use is contraindicated during pregnancy as a precaution. It recommends that women and girls should be advised not to use topical retinoids if they are planning a pregnancy and to use effective contraception to minimise the risk of accidental exposure in pregnancy if they are of childbearing potential.

	Medicine Supply Notification Number: MSN/2023/090
Shortage of Guanfacine (Intuniv) modified-release tablets	Anticipated re-supply date: 20 November 2023  Actions: A National Patient Safety Alert was issued on the 27 September 2023
	for the shortage of methylphenidate prolonged-release capsules and tablets, lisdexamfetamine capsules, and guanfacine prolonged-release tablets.  Please refer to the National Patient Safety Alert for information and advice.
	Alternatives: The following specialist importers have confirmed they can source unlicensed guanfacine prolonged-release tablets, lead times may vary (please note there may be other companies that can also source supplies):  • Smartway  • Genetech  • Target  • Alium
Shortage of Disopyramide 100mg capsules and 250mg modified-release tablets	Anticipated re-supply date: 100mg capsules 3 November 2023, and 250mg MR tablets 15 December 2023
	Actions: Prescribers and pharmacy teams should:  • identify patients prescribed disopyramide 100mg capsules and establish if they have sufficient supply to last until the resupply date; and  • reserve remaining supply of 100mg disopyramide capsules for these patients with insufficient supply.
	<ul> <li>Where licensed disopyramide 100mg capsules are unavailable:         <ul> <li>consider prescribing unlicensed imports of disopyramide 100mg capsules, taking into account lead times;</li> <li>if the above option is not possible due to lag time in obtaining supply, convert patients to disopyramide 250mg prolonged release tablets at same total daily dose, if the formulation allows, or as close a dose as possible, and titrate dose as needed (see Supporting information);</li> <li>where licenced (parallel import) disopyramide 250mg prolonged release tablets are unavailable, consider prescribing unlicensed imports, taking into account lead times; and</li> <li>seek advice from cardiology specialists on management of unstable patients or patients newly started on treatment, or where there is uncertainly or concern about switching formulation and or/dose conversion.</li> </ul> </li> </ul>
	For patients commencing treatment with disopyramide, prescribers should:  • not prescribe 100mg capsules until the shortage has resolved and consider initiating patients on disopyramide 250mg prolonged release tablets; and • if the above option is unsuitable, consider prescribing unlicensed imports of disopyramide 100mg capsules, taking into account lead times

into account lead times.

Patients should be counselled on any change in formulation and/ or dose change and advised to report adverse effects and/or recurrence of symptoms after switching.

#### Alternatives:

# **Parallel imports:**

- Limited supply of disopyramide 100mg capsules are available and can partially cover the demand for the 100mg capsules.
- Disopyramide 250mg modified release tablets remain available and can fully cover the demand for the 250mg MR tablets for the duration of the shortage.

Orders can be placed directly with the following suppliers:

DrugsRUs Limited – via DrugsRUs Limited by contacting <u>Veer@drugsrus.co.uk</u>

# **Unlicensed imports:**

The following specialist importer companies have confirmed they can source unlicensed disopyramide 100mg capsules (please note there may be other companies that can also source supplies):

Alium

The following specialist importer companies have confirmed they can source unlicensed disopyramide 250mg tablets (please note there may be other companies that can also source supplies):

Mawdsley

# **Summary:**

- Disopyramide (Rythmodan)100mg capsules are out of stock until 3 November 2023.
- Disopyramide (Rythmodan) 250mg prolonged release tablets are out of stock until mid-December 2023 but parallel imports remain available and can fully cover demand.
- Limited stock of parallel imports of disopyramide 100mg are available and can partially cover demand for 100mg capsules.
- Unlicensed imports of disopyramide 100mg capsules and disopyramide 250mg prolonged release tablets have been sourced, lead times vary (see Supporting information).

# **Supporting information:**

# Clinical Information

Disopyramide is licensed for the treatment of cardiac arrhythmias, with dose adjusted according to response. In addition to the immediate release capsule formulation, it is also formulated as a prolonged release tablet. As disopyramide tends to be a last line antiarrhythmic agent, alternative treatment options are limited, and require specialist input.

# Dosing information

# Disopyramide

Half-life: 5 to 8 hours

# Immediate release capsules (100 mg)

Licensed dose range: 300 mg to 800 mg daily in divided doses

(usually every 6 to 8 hours)

# Prolonged-release tablets (250 mg)

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

#### **Switching**

The total daily dose of the 100mg 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 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 and tolerability.

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

Shortage of Acetazolamide (Diamox SR) 250mg modifiedrelease capsules Anticipated re-supply date: 31 October 2023

# **Actions:**

For patients with insufficient supplies, clinicians should consider:

- deferring initiating any new patients on acetazolamide (Diamox SR) 250mg modified-release capsules until the supply issue is resolved.
- prescribing acetazolamide immediate release 250mg tablets and monitoring patients after the switch (see clinical information):
- If acetazolamide immediate release 250mg tablets are not appropriate, consider prescribing one of the following unlicensed medicines:
  - acetazolamide SR 250mg capsules (imported)
  - acetazolamide oral suspension (various strengths available)

#### Alternatives:

Acetazolamide immediate release 250mg tablets remain available and can support an uplift in demand.

# **Unlicensed Imports:**

The following specialist importer(s) have currently confirmed availability of unlicensed acetazolamide SR 250mg capsules (please note, there may be other companies that can also source supplies):

Smartway

# Specials:

The following companies have indicated they can supply specials of acetazolamide oral suspension in various strengths (please note, there may be other companies that can manufacture supplies):

- Eaststone Specials
- IPS Pharma
- Nova Labs
- PCCA Ltd
- Quantum Pharmaceutical
- Rokshaw Ltd

#### **Clinical Information:**

Acetazolamide is a carbonic anhydrase inhibitor. In the eye, it decreases the secretion of aqueous humour and results in a drop of intraocular pressure. Acetazolamide (Diamox SR) modified-release capsules are a sustained release formulation designed to obtain a smooth and continuous clinical response. This formulation is licensed for the treatment of glaucoma and is administered at a dose of 250-500mg daily.

The licensed dose in glaucoma of acetazolamide immediate release tablets is 250-1000mg per 24 hours, usually in divided doses (plasma half-life of acetazolamide ~ 4 hours).

Advanz Pharma has advised that for glaucoma, patients on acetazolamide (Diamox SR) 250mg modified-release capsules twice daily could possibly be switched to acetazolamide 250mg tablets four times daily. This conversion is based simply on the maximum licensed dose of each formulation and would be at the discretion of the prescriber, as there are no bioequivalence studies comparing the two formulations.

The following data provided by the manufacturer from a single dose study of tablets and modified-release capsules may be helpful when making a dosing decision:

Formulation	Onset (hours)	Peak (hours)	Duration (hours)
Immediate release tablet	1	1-4	8-12
Modified release capsule	2	3-6	18-24

Modified-release capsules may be better tolerated than the equivalent dose of immediate release tablets, possibly due to the avoidance of high peak levels.

Alternatively, oral suspension specials are available in various strengths. If the liquid is used, dosing will be as for the immediate release tablets, with the aforementioned caveats.

# **Medicine Supply Notification Number:** MSN/2023/033

Shortage of Hyoscine hydrobromide (Scopoderm) 1.5mg patches Anticipated re-supply date: 5 January 2024

Actions:

Healthcare professionals in primary and secondary care should not initiate any new patients on hyoscine hydrobromide (Scopoderm) 1.5mg patches.

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

- review patients to determine if this is still the most suitable therapy
- prioritise any remaining stock of Scopoderm patches for patients who have no oral access
- consider switching patients who have oral access to an alternative formulation of hyoscine hydrobromide; or if not appropriate, a glycopyrronium bromide preparation (see below)
- consider prescribing unlicensed hyoscine hydrobromide (Scopoderm) 1.5mg patches if alternative options are not suitable, working with local pharmacy teams to ensure orders are placed within appropriate time frames, as lead times may vary (see below)
- if the above options are not considered appropriate, advice should be sought from specialists on management options

# **Alternatives:**

# Other hyoscine hydrobromide formulations:

These are other hyoscine hydrobromide formulations for the management of hypersalivation/ respiratory secretions. Hyoscine hydrobromide (Kwells) 150microgram and 300microgram tablets are used off label in this setting, with dosing titrated up based on response and tolerability. They are taken orally, sucked or chewed. In patients with swallowing difficulty, they can also be administered by sublingual or buccal route (off label route of administration).

# **Glycopyrronium bromide products:**

These are licensed for the symptomatic treatment of severe sialorrhoea (chronic pathological drooling/hypersalivation) in children and adolescents aged 3 years and older with chronic neurological disorders. Use in adults is off-label. They are an option if there is oral access/ patient can swallow. Preparations include:

- Glycopyrronium bromide 1mg and 2mg tablets
- Glycopyrronium bromide 1mg/5ml oral solution
- Glycopyrronium bromide (Sialanar) 2mg/5ml oral solution

As there are two separate glycopyrronium liquid products with different strengths, prescribing should clearly indicate the strength and dose to reduce the risk of selection and dosing error.

# Prevention of travel (motion) sickness:

NHSE guidance recommends that a prescription for treatment for motion sickness will not routinely be offered in primary care as the condition is appropriate for self-care. Alternative treatment options available OTC include:

- Hyoscine hydrobromide (Kwells) 150 and 300microgram tablets
- Promethazine teoclate 25mg tablets
- Promethazine hydrochloride 10mg and 25mg tablets
- Promethazine hydrochloride 5mg/5ml oral solution
- Cinnarizine 15mg tablets

# **Clinical Information:**

Hyoscine hydrobromide patches are licensed for the prevention of travel sickness symptoms e.g., nausea, vomiting and vertigo and used off-label for the management of hypersalivation and drying up respiratory secretions.

# **Specialist Importers:**

The following specialist importers have confirmed they can source unlicensed hyoscine hydrobromide 1.5mg patches (please note there may be other companies that can also source supplies):

- Alium
- Mawdsley
- Q MED

# Shortage of Clonazepam 500microgram and 2mg tablets

Anticipated re-supply date: 27 December 2024

#### Alternatives:

Clonazepam 500microgram and 2mg tablets from Neuraxpharm UK Limited remain available and are able to support with covering demand.

Parallel imports of clonazepam 500microgram and 2mg tablets are also available. Orders for parallel imports of clonazepam 500microgram and 2mg tablets can be placed directly with the following supplier:

 Drugsrus Limited (hospital pharmacies to email <a href="mailto:nhs@drugsrus.co.uk">nhs@drugsrus.co.uk</a> and retail pharmacies to email <a href="mailto:veer@drugsrus.co.uk">veer@drugsrus.co.uk</a> for further information)

<u>Discontinuation of lixisenatide</u> (<u>Lyxumia</u>) 20micrograms/0.2ml solution for injection 3ml prefilled disposable devices **Discontinuation:** 22 December 2023

# Actions:

Clinicians should:

- proactively identify and review patients established on lixisenatide (Lyxumia)
- review the need for a glucagon-like peptide receptor agonists (GLP-1 RA) and stop treatment if the patient has not achieved beneficial metabolic effect as set out in NICE NG28
- refer to the National Patient Safety Alert (<u>NatPSA</u>) to guide selection of alternative glucose lowering therapy

**Medicine Supply Notification Number:** MSN/2023/088

Shortage of Somatropin
(Genotropin MiniQuick) 1.4mg,
1.6mg and 1.8mg powder and
solvent for solution for injection
pre-filled disposable devices

Anticipated re-supply date: 5 January 2024

#### Actions

Secondary care pharmacy teams should work with clinical specialists and their local pharmacy homecare leads to:

- ensure that new patients are not initiated on Genotropin
   MiniQuick 1.4mg, 1.6mg and 1.8mg devices until resupply
- review all patients, including those under shared care arrangements, prescribed Genotropin MiniQuick 1.4mg, 1.6mg and 1.8mg devices, and determine:
  - which patients <u>need</u> to remain on these devices (e.g. visual impairment or have no refrigerator). Remaining stock of Genotropin MiniQuick 1.4mg, 1.6mg and 1.8mg devices is to be reserved for patients who cannot be switched. Please note, to obtain remaining stock contact Pfizer Customer Service Team: 0800 0327907

- issue a new prescription for:
  - Genotropin 12mg cartridges (0.2mg dose increments) to be used with a re-usable injection device (Genotropin Pen) to deliver doses of 1.4mg, 1.6mg or 1.8mg in patients able to manage the change in device or
  - Genotropin GoQuick 12mg reusable multi-dose pens (delivers dose increments of 0.15mg) for patients on 1.8mg dose who are able to use the pen
  - Genotropin Miniquick 1.2mg or 2mg device for those patients still being dose titrated and being considered for a change to these doses delivered by the Miniquick device
- ensure that patients switched from the single use MiniQuick injection devices to Genotropin 12mg cartridges and Genotropin GoQuick 12mg pens are aware these are multidose devices and need to be stored in a refrigerator
- ensure all new prescriptions are sent to their current homecare service provider or outpatient dispensary and
- communicate with home care providers if nurse led injection training is required on use of new device

# Homecare providers should:

- ensure that once a new prescription for Genotropin 12mg cartridges, Genotropin GoQuick 12mg pens or Genotropin MiniQuick 1.2mg or 2mg device is received, the patient's existing Genotropin MiniQuick 1.4mg, 1.6mg or 1.8mg device prescription is immediately cancelled
- call patients to inform them of the change to their prescription while arranging delivery and offer nursing support on how to use the new device and
- work with the prescriber and the Trust homecare lead to ensure nurse led training or, if available, administration support is offered where requested

# **Outpatient dispensaries should ensure that:**

- once a new prescription for Genotropin 12mg cartridges, Genotropin GoQuick 12mg pens or Genotropin MiniQuick 1.2mg or 2mg device is received, the patient's existing Genotropin MiniQuick 1.4mg, 1.6mg or 1.8mg device prescription is cancelled
- patients receive a patient education pack and are counselled about the change in prescription at the point of first dispensing and
- patients are directed back to their specialist team if they highlight a need for additional nurse-led training or ongoing nursing support

# GP surgeries who prescribe Genotropin MiniQuick 1.4mg, 1.6mg and 1.8mg devices should:

 proactively identify all patients on these products and refer them to their specialist for review and a switch to an appropriate alternative as above

# **Alternatives:**

- Somatropin (Genotropin GoQuick) 12mg powder and solvent for solution for injection pre-filled, multi-dose pens
- Somatropin (Genotropin) 12mg powder and solvent for solution for injection multi-dose cartridges

Somatropin (Genotropin MiniQuick) 1.2mg and 2mg powder and solvent for solution for injection pre-filled disposable (single dose) device **Summary:** Somatropin (Genotropin MiniQuick) 1.4mg, 1.6mg and 1.8mg powder and solvent for solution for injection pre-filled disposable (single dose) devices will be in limited supply until w/c 1st January 2024 The following somatropin preparations remain available and will be able to support increased demand: Somatropin (Genotropin GoQuick) 12mg powder and solvent for solution for injection pre-filled, multi-dose pens Somatropin (Genotropin) 12mg powder and solvent for solution for injection multi-dose cartridges Somatropin (Genotropin MiniQuick) 1.2mg and 2mg powder and solvent for solution for injection pre-filled disposable (single dose) device **Medicine Supply Notification Number:** MSN/2023/088 Anticipated re-supply date: 29 March 2024 Shortage of Strontium ranelate 2g granules sachets sugar free Actions: Where supply of strontium ranelate is not available, clinicians should: consider alternative treatments used in osteoporosis. where alternative treatments used in osteoporosis have been tried and have failed/not appropriate, refer patients back to specialists for review. Alternatives: Alternative treatments used in osteoporosis remain available. Shortage of Midazolam Anticipated re-supply date: 1 December 2023 (Epistatus) 2.5mg/0.25ml and 10mg/1ml oromucosal solution Actions: pre-filled oral syringes Until the shortage resolves, prescribers should: not initiate new patients on Epistatus 2.5mg/0.25ml or 10mg/1ml oromucosal solution pre-filled oral syringes and consider prescribing midazolam (Buccolam or the generic) 2.5mg/0.5ml or Buccolam 10mg/2ml oromucosal solution prefilled oral syringes where appropriate, ensuring that the parent/carer is advised on the change in volume being administered, counselled on how to administer the dose, and shown the patient information leaflet (see Supporting Information below) Alternatives: Buccolam 2.5mg/0.5ml oromucosal solution pre-filled oral syringes Buccolam 10mg/2ml oromucosal solution pre-filled oral

Clinical information:

filled oral syringes

Midazolam (generic) 2.5mg/0.5ml oromucosal solution pre-

syringes

Epistatus is indicated for the treatment of prolonged, acute, convulsive seizures. The 2.5mg/0.25ml strength is licensed for use in infants between 3-6 months of age in the hospital setting and the 10mg/1ml for use in children and adolescents from age 10 years to < 18 years. Buccolam/generic midazolam oromucosal solution pre-filled oral syringes 2.5mg/0.5ml and 10mg/2ml are licensed for the same indication and age groups as Epistatus but are formulated in twice the volume of Epistatus and also differ in administration technique. It is good practice to prescribe midazolam oromucosal solution by brand name and express strength in both milligrams and millilitres.

Please note an MHRA medicine recall was issued for Epistatus 2.5mg oromuscosal solution, pre-filled syringes on 30<sup>th</sup> August 2023.

# **Medicine Supply Notification Number:**

MSN/2023/086

Shortage of Estradiol valerate

1mg/ Medroxyprogesterone
acetate 5mg (Indivina) tablets

Anticipated re-supply date: 15 December 2023

# Actions:

Prescribers should:

- not initiate patients on Indivina 1mg/5mg tablets
- consider prescribing an alternative continuous combined hormone replacement therapy (HRT) product containing estradiol 1mg but a different progestogen component to Indivina, ensuring that the patient is not intolerant to any of the excipients and is counselled on the appropriate dose (see Supporting information below)
- consider prescribing unlicensed products only where licensed alternatives are not appropriate. Prescribers should work with local pharmacy teams to ensure orders are placed within appropriate time frames as lead times may vary (see Supporting information below)

# Alternative oral continuous combined HRT:

- Estradiol 1mg/ Dydrogesterone 5mg (Femoston Conti) tablets
- Estradiol 1mg/ Norethisterone 500mcg (Kliovance) tablets
- Estradiol 1mg / Progesterone 100 mg (Bijuve) capsules

#### **Clinical Information:**

The British Menopause Society (BMS) provides guidance from clinical experts on switching to alternative continuous combined HRT products. In this, BMS does acknowledge "The equivalence data included in this practical guide were based on a combination of pharmacokinetics, clinical trials and clinical experience. The dose equivalents included are subject to significant individual variations in absorption and metabolism." When switching patients to an alternative HRT product, prescribers will consider symptom control, side effect profiles, breakthrough bleeds etc. The BMS also provides <a href="mailto:advice-on-managing-side-effects">advice-on-managing-side-effects</a> of oestrogen and progestogens where the options for progestogen side effects are: change the type of progestogen, reduce the dose if available, change the route of administration, alter the duration.

The following specialist importers have confirmed they can source unlicensed Indivina 1mg/5mg tablets (please note there may be other companies that can also source supplies):

- Alium
- Target

	Medicine Supply Notification: MSN/2023/084
Shortage of Estradiol (FemSeven)	Anticipated re-supply date: 6 October 2023
75micrograms/24hours and	Actions:
100micrograms/24hours transdermal patches	For patients with insufficient supplies of estradiol (FemSeven) 75micrograms/24hours or 100micrograms/24hours transdermal patches prescribers should:  • consider prescribing Evorel or Estraderm transdermal patches (note differing frequency of administration) of the same strength ensuring that the patient is not intolerant to any of the excipients, is counselled on the appropriate dose and the change in brand at the point of supply.  • where the above is not appropriate, establish if ongoing treatment is required and switch to an alternative hormone replacement therapy (HRT), taking into consideration wider supply issues (see Supporting information below).
	Alternative estradiol transdermal patches: Please note the recommended administration frequency is different to FemSeven.
	<ul> <li>Evorel 75micrograms/24hours transdermal patches</li> <li>Evorel 100micrograms/24hours transdermal patches</li> <li>Estraderm 75micrograms/24hours transdermal patches</li> <li>Estraderm 100micrograms/24hours transdermal patches</li> </ul>
	Medicine Supply Notification: MSN/2023/085

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 on 13<sup>th</sup> October 2023. Information provided by DHSC and NHSEI Medicines Supply Teams and published on Specialist Pharmacy Services Medicines Supply Tool. Not formally reviewed by NHS Kent and Medway Medicines Optimisation. Practices are encouraged to register for access to the SPS website <a href="https://www.sps.nhs.uk/">https://www.sps.nhs.uk/</a> and access this tool directly in real time.