DISCONTINUATION: **Ikorel 10mg tablets**	**Date stock to be exhausted: Not known** **Alternatives:** Generic nicorandil 10mg tablets remain available. **Considerations and Background:** Ikorel has been discontinued by Sanofi.
DISCONTINUATION: **Normacol granules (Forum Health Products Ltd)** **Normacol Plus granules (Forum Health Products Ltd)**	**Date stock to be exhausted: Not Known** **Alternatives:** Isphagula Husk is an alternative to sterculia granules, provided patients do not have intolerances to the product or its excipients. Link: **BNF - Constipation**
DISCONTINUATION: **Insuman Basal 100units/ml suspension for injection 3ml cartridges (Sanofi)** **Insuman Basal 100units/ml suspension for injection 3ml pre-filled SoloStar pens (Sanofi)**	**Date stock to be exhausted: Cartridges: 28th Feb 2023** **Prefilled pens: 31st May 2023** **Action:** Prescribers should: • not initiate any new patients on Insuman products • review all patients prescribed Insuman Basal and consider prescribing alternative human isophane insulin preparations (See Clinical Information) • ensure that after switching, patients are counselled on how to use the new device, explain that the dose of insulin remains the same, but adjustments may be needed depending on blood glucose levels and signs of hypoglycaemia. **Alternatives**: Human Isophane Insulin *Brands include:* • Humulin I vials, cartridges and pre-filled pens • Insulatard vials, cartridges and pre-filled pens Only Humulin I can support a full uplift in demand. Insulatard can only support a partial uplift in demand. **Considerations and background** Supply Overview *Cartridges* Insuman Basal 100units/ml suspension for injection 3ml cartridges are discontinued and stocks are expected to exhaust at the end of February 2023. *Pre-filled pens* Insuman Basal prefilled pens are discontinued and stocks are expected to exhaust at the end of May 2023. **Clinical Information about Insulin** Choice of alternative will be determined by onset of action, peak activity and duration of action. Patients should be advised to be more vigilant with checking their blood glucose following a switch to an alternative. Patients should also be counselled on the symptoms of hypoglycaemia.

	There is unlikely to be any dose change when switching between insulins. However, after the switch, the dose should be guided by blood glucose control and signs of hypoglycaemia. As the injector device will also be different, patients should be counselled on how to use the new device. **Insuman Basal** Insuman basal is a human isophane insulin; these insulins are intermediate-acting: onset of action ~ 1–2 hours, peak activity between 3–12 hours, and duration of action of 11–24 hours. Other human isophane insulin products include Humulin I and Insulatard.
DISCONTINUATION: Insuman Rapid 100units/ml solution for injection 3ml cartridges (Sanofi)	**Date Stock to be exhausted: 31st May 2023** Actions Prescribers should: • not initiate any new patients on Insuman products • review all patients prescribed Insuman Rapid and consider prescribing alternative neutral (soluble) insulin • ensure that after switching, patients are counselled on how to use the new device, explain that the dose of insulin remains the same, but adjustments may be needed depending on blood glucose levels and signs of hypoglycaemia Alternatives: Neutral (soluble) Insulin *Brands include:* • Actrapid vials • Humulin S vials and cartridges All of the above alternative insulin preparations can support a full uplift in demand. **<u>Considerations and Background:</u>** **Supply Overview** Insuman Rapid 100units/ml suspension for injection 3ml cartridges will be discontinued with stocks being exhausted in May 2023. **Clinical Information about Insulin** Choice of alternative will be determined by onset of action, peak activity and duration of action. Patients should be advised to be more vigilant with checking their blood glucose following a switch to an alternative. Patients should also be counselled on the symptoms of hypoglycaemia. There is unlikely to be any dose change when switching between insulins. However, after the switch, the dose should be guided by blood glucose control and signs of hypoglycaemia. As the injector device will also be different, patients should be counselled on how to use the new device. **Insuman Rapid** Insuman Rapid is a neutral (soluble) insulin solution; these insulins are short acting insulins: onset of action ~ 30–60 minutes, peak activity between 1–5 hours, and duration of action of 5–9 hours. Other human neutral insulin products include Humulin S and Actrapid.

DISCONTINUATION: **Insuman Comb 25 cartridges and prefilled pens.**	**Date stock to be exhausted: Cartridges: 28th Feb 2023** **Prefilled pens: 30th June 2023** **Action:** Prescribers should: • not initiate any new patients on Insuman products • review all patients prescribed Insuman Comb 25 100units/ml suspension for injection 3ml cartridges; and consider prescribing Humolog Mix 25 in the first instance (see Clinical Information) • consider prescribing another biphasic insulin preparation if the above option is not deemed suitable (see Clinical Information) • ensure that after switching, patients are counselled on how to use the new device, explain that the dose of insulin remains the same, but adjustments may be needed depending on blood glucose levels and signs of hypoglycaemia Alternatives: Biphasic Isophane Insulin *Brands include:* • Novomix 30 cartridge and pre-filled pen • Humalog Mix 25 vials, cartridges and pre-filled pens • Humalog Mix 50 cartridges and pre-filled pens • Humulin M3 vials, cartridges and pre-filled pens All of the above alternative insulin preparations can support a full uplift in demand. **Considerations and Background:** Supply Overview *Cartridges* Insuman Comb 25 100units/ml suspension for injection 3ml cartridges are discontinued and stocks are expected to exhaust at the end of February 2023. *Pre-filled pens* Insuman Comb 25 prefilled pens are discontinued and stocks are expected to exhaust at the end of June 2023. **Clinical Information about Insulin** Choice of alternative will be determined by onset of action, peak activity and duration of action. Patients should be advised to be more vigilant with checking their blood glucose following a switch to an alternative. Patients should also be counselled on the symptoms of hypoglycaemia. There is unlikely to be any dose change when switching between insulins. However, after the switch, the dose should be guided by blood glucose control and signs of hypoglycaemia. As the injector device will also be different, patients should be counselled on how to use the new device. **Insuman Comb 25** Insuman Comb 25 is a biphasic isophane insulin consisting of 25% dissolved insulin and 75% crystalline protamine insulin. The only other biphasic formulation containing equal proportions of rapid and long-acting insulin is Humalog Mix 25 (25% insulin lispro solution and 75% insulin lispro protamine suspension). It is available in a KwikPen, a disposable pre-filled pen containing 3ml (300 units, 100 units/ml) of insulin and also in a 3ml

	cartridge for use in a Lilly 3ml pen. Insuman Comb 25 is injected subcutaneously 30 to 45 minutes before a meal whereas Humalog Mix 25 may be given shortly before meals or when necessary, soon after meals. Patients switched from Insuman Comb 25 to Humalog Mix 25 would need to be advised on difference in timing of administration of insulin. Other human biphasic insulin preparation containing different proportions of rapid and long-acting insulin include; Humalog Mix 50, Humulin M3 and NovoMix 30 (insulin aspart). Humulin M3 (30% soluble insulin and 70% isophane insulin) and Novomix 30 (30% soluble insulin aspart and 70% protamine-crystallised insulin aspart) are a closer match to Insuman Comb 25 than Humalog Mix 50 (50% insulin lispro solution and 50% insulin lispro protamine suspension).
DISCONTINUATION: **Diazepam (Diazemuls) 10mg/2ml emulsion for injection ampoules (Accord Healthcare Ltd)**	**Date Stock to be exhausted: Not Known** **Actions:** • Switch to an alternative agent as appropriate (see advice below) • Review local Patient Group Directions (PGDs) as the alternative agent(s) may not be covered. **Alternatives:** Refer to SPCs and local guidelines for further details of treatment options for status epilepticus and the other licensed indications of Diazemuls. **Parenteral options** *Lorazepam injection* Lorazepam injection 4mg/ml is licensed for control of status epilepticus in children and adults and is available to support a full uplift in demand. *Diazepam injection* Diazepam injection BP 10mg/2ml is a second line option; it is more irritant that Diazemuls. **Non-parenteral options** *Diazepam rectal solution* Diazepam rectal solution 5mg and 10mg can be used. Please note *Midazolam oromucosal solution* Midazolam oromucosal solution 2.5mg, 5mg, 7.5mg and 10mg can be used. **Specialist imports** The following specialist importers have confirmed they can source unlicensed diazepam 10mg/2ml emulsion for injection. • Durbin PLC • Target Healthcare Please note there may be other companies that can also source supplies and that lead times may vary. **Considerations and Background :** Supply position Diazemuls 10mg/2ml emulsion for injection has been discontinued.

	Clinical use The main use of Diazemuls is for the control of convulsions and status epilepticus. Other licensed indications include sedation prior to procedures, premedication prior to general anaesthesia, control of acute muscle spasm due to tetanus or poisoning, and management of severe acute anxiety or agitation including delirium tremens. **Ordering and Prescribing Unlicensed Imports** **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. • General Medical Council (GMC) advice on prescribing unlicensed medicines • Medicines and Healthcare products Regulatory Agency (MHRA): The supply of unlicensed medicinal products • Royal Pharmaceutical Society Professional guidance for the Procurement and Supply of Specials *Prescribing* 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. For **electronic prescriptions** where the unlicensed product is shown on electronic prescribing systems, GP's should select: • diazepam 10mg/2ml emulsion for injection (imported) For **paper prescriptions** where the unlicensed product is not shown on electronic prescribing systems, GP's should use a paper prescription and annotate with the words: • special order
SHORTAGE: **Fentanyl 400microgram buccal films sugar free**	**Anticipated re-supply date: 31st March 2023** **Actions:** For Effentora 200 microgram and 400 microgram buccal tablets, where patients do not have sufficient stock to last until the resupply date, clinicians should: • consider prescribing Effentora 100 microgram to patients using Effentora 200 microgram • if the above is not considered appropriate and for all patients on Effentora 400 microgram, consider prescribing alternative immediate-release fentanyl products, taking into consideration the patient's preferences (see clinical information); • ensure that the patient is not intolerant to any of the excipients in the alternative product and is counselled on any changes including changes to their dosing regimen and; • seek specialist advice, as necessary, to titrate the new formulation taking into consideration that immediate release fentanyl products are not interchangeable and patients should not be converted on a

	microgram per microgram basis from one product to another (see clinical Information). **Alternatives:** Effentora preparations The following Effentora preparations remain available: • Effentora 100 microgram buccal tablets – can support a partial uplift in demand • Effentora 600 microgram and 800 microgram buccal tablets • Effentora 200 micrograms buccal tablets- back in stock **Immediate release fentanyl formulations** The following alternative formulations of immediate release fentanyl remain available and will be able to support increased demand. *Actiq lozenges* Bioavailability 65% Time to response (minutes) 20 *Abstral sublingual tablets* Bioavailability 50% Time to response (minutes) 20 – 40 *Cynril lozenges* Bioavailability 50% Time to response (minutes) 2 – 40 *Fenhuma sublingual tablets* Bioavailability 54% Time to response (minutes) 22.5 – 240 *PecFent nasal spray* Bioavailability Not available Time to response (minutes) 15 – 20 **Considerations and Background**

	Supply overview Effentora 400 microgram buccal tablets are out of stock until late-March 2023. **Clinical Information** ***First line treatment of breakthrough pain in cancer related pain*** For cancer patients who require breakthrough pain relief, immediate-release oral morphine is the preferred treatment option. However, for those patients where immediate-release morphine is not considered appropriate, or in whom breakthrough pain management with immediate-release morphine has been unsuccessful, specialist advice should be sought to consider the most appropriate immediate release fentanyl dose and formulation. ***Patients on Effentora buccal tablets (200 microgram and 400 microgram)*** In considering an alternative immediate-release fentanyl product, the general recommendation is that patients need to be re-titrated according to manufacturer's instructions. For patients on relatively high doses of fentanyl for breakthrough pain specialist advice should always be sought to determine recommended starting doses. Transmucosal fentanyl including Effentora, is not licensed for the management of breakthrough pain in non-cancer related pain and therefore should not be considered as a first-line option for breakthrough pain relief in this setting. For existing patients currently on Effentora 200 microgram, Effentora 100 microgram can partially support an uplift in demand. Where this is not appropriate and for patients currently on Effentora 400 microgram, an alternative immediate-release fentanyl product may be substituted. For patients where immediate-release fentanyl is considered necessary, sublingual/lozenge formulations (see alternatives) may be preferred in those who have frequent nose bleeds, whilst the nasal formulation may be considered in those with dry mouth. It is important to note that, bioavailability across products is not equivalent. Patients should therefore **not** be converted on a microgram per microgram basis from one form to another, as this may result in variability in therapeutic efficacy, increase the risk of fentanyl related side effects and affect the patient's overall ability to tolerate the medicine. **Effentora bioavailability** ***Effentora lozenges*** Bioavailability 65% Time to response (minutes) 20
SHORTAGE: **Capimune 25mg capsules (Viatris UK Healthcare Ltd)** **Capimune 50mg capsules (Viatris UK Healthcare Ltd)** **Capimune 100mg capsules (Viatris UK Healthcare Ltd)**	**Anticipated re-supply date: 30th April 2023** **Actions:** Primary Care Where patients have insufficient supplies of Capimune brand of ciclosporin 25mg, 50mg and 100mg capsules to last until the re-supply date, GP prescribers should: • seek advice from the appropriate specialist team on switching to an available brand of ciclosporin (Deximune), ensuring appropriate monitoring requirements are followed (see supporting information)

	• ensure patients are counselled regarding any changes to their medicines and where to seek advice if needed. **Alternatives:** Alternatives supporting full uplift The following presentations can provide a full uplift in demand • Deximune 25mg, 50mg and 100mg capsules Alternatives supporting partial uplift The following presentations can support a partial uplift in demand • Neoral 25mg, 50mg and 100mg Soft gelatin capsules Alternatives unable to provide any uplift • Vanquoral 25mg, 50mg and 100mg capsules • Capsorin 25mg, 50mg and 100mg capsules • Sandimmun 25mg, 50mg and 100mg capsules. **Considerations and Background:** **Supporting Information** **Brand Prescribing** Patients should be stabilised on a particular brand of oral ciclosporin because switching between formulations without close monitoring may lead to clinically important changes in ciclosporin level. Switching between a branded and a generic formulation, or between generic formulations, should be carried out in consultation with the specialist team. If switching is necessary, the patient should be monitored closely for changes in ciclosporin level where clinically appropriate (specialist decision), serum creatinine, blood pressure, and disease control/ transplant function and adverse effects.

SHORTAGE:
Zopiclone 3.75mg tablets
	Anticipated re-supply date: 31st March 2023
	
	Actions:
	Where patients have insufficient supplies to last until the re-supply date, clinicians should:
	
	• review patients to determine if this treatment should be continued
	• if deemed necessary, consider whether zopiclone 7.5mg tablet preparations approved for splitting would be appropriate
	  ○ ensuring the patient is not intolerant to any of the excipients,
	  ○ can split the tablets (prescribe a pill splitter if needed), and
	  ○ is reassured there is no change in dose from use of half a 7.5mg tablet (see clinical information)
	• for patients who require ongoing treatment and have issues halving the tablets, consider switching to an alternative Z drug, zolpidem 5mg tablets, ensuring the patient is not intolerant to any of the excipients and is counselled on the change in medication (see clinical information) and
	• on ongoing basis, review need for continued treatment as hypnotics are not licensed for long-term use due to risk of dependence.
	
	Alternatives:
	Zopiclone 7.5mg tabletsThe following brands of zopiclone 7.5mg tablets are licensed to be halved along a break line into two equal doses.

	Zopiclone 7.5 mg film-coated tablets – Crescent Pharma Ltd. SPC description: *"White, round, biconvex film-coated tablets. The film-coated tablets are scored on one side and are divisible. The tablet can be divided into equal doses."* *Zopiclone 7.5mg tablets – Aurobindo Pharma – Milpharm Ltd.* SmPC description: *"White, round, (diameter: 7.6mm), biconvex film coated tablets debossed with 'Z & 2' separated with break line on one side and break line on the other side. The tablet can be divided into equal doses."* *Zimovane 7.5mg film-coated tablets – Sanofi* SmPC description: *"White, elliptical, biconvex film-coated tablets with a score-line on one side. The tablet can be divided into equal halves."* Zolpidem Zolpidem 5mg tablets are available (see clinical information). **Considerations and Background** **Clinical Information** Zopiclone is licensed for the short-term treatment of insomnia in adults. Ideally treatment should not be for longer than 4 weeks. The lower dose of 3.75 mg is used in the elderly, and in patients with liver or renal impairment, or chronic respiratory insufficiency. Zolpidem is licensed for the short-term treatment of insomnia in adults. It is available as 5mg and 10mg tablets and is taken as a single dose at night. The 5mg dose is used in the elderly and in patients with hepatic impairment. **Prescription quantity** Patients switched to one of the above zopiclone 7.5mg tablet preparations should be prescribed half the quantity of the usual prescription to avoid a surplus as this may present a patient safety risk i.e., patients usually prescribed zopiclone 3.75mg tablets x 28 tablets should only be prescribed zopiclone 7.5mg x 14 tablets.
SHORTAGE: **Sulfasalazine 250mg/5ml oral suspension sugar free**	**Anticipated re-supply date: 4th August 2023** **Actions:** Where patients have insufficient supplies to last until the re-supply date, prescribers should: • consider prescribing <u>non-enteric coated</u> sulfasalazine 500mg tablets, which are scored, and so can be split to facilitate administration of whole dose, noting that halving the tablet to deliver 250mg dose or crushing the tablets and dispersing in water to deliver a part dose, would be an unlicensed manipulation (see Supporting Information below); • review patients taking doses that are not in increments of 250mg to consider a dose adjustment to increments of 250mg, where possible; • counsel patients on the benefits of using a pill splitter (which can be purchased from a pharmacy or other retail outlets) to ensure a dose as close to 250mg as possible could be obtained, if the decision is taken to halve the tablet;

	• if above options are not appropriate, consider prescribing unlicensed sulfasalazine 250mg/5ml oral suspension available from Specials manufacturers (see Supporting Information below). **Alternatives:** **Licensed alternatives:** Sulfasalazine 500mg non-enteric coated tablets remain available. **Unlicensed alternatives:** The following Specials manufacturers have currently confirmed they can manufacturer sulfasalazine 250mg/5ml oral suspension (please note, there may be other companies that can also manufacture): • IPS Pharma • Nova Labs • Rokshaw **Considerations and Background:** **Supporting Information** Non-enteric coated sulfasalazine 500mg tablets are scored to facilitate administration of the tablet as two halves in patients who may find it difficult to swallow the tablet whole. Halving the tablet to deliver a 250 mg dose would be an unlicensed manipulation. If the patient cannot swallow the half tablet, it could be crushed and mixed in 15 to 30 mL water or soft foodstuff and swallowed. This is also an unlicensed manipulation. Information about halving tablets A recently published systematic review of the concerns regarding tablet splitting concluded that with the exception of sustained-release tablets, which should not be split, and excepting those older people who may struggle to split tablets based on physical limitations, there is little evidence to support tablet-splitting concerns. The halving of tablets to ease administration, to deliver a 250mg dose or the crushing tablets and dispersing in water to deliver a part dose, falls outside of the product licence and therefore, prescribers must consider relevant guidance and NHS Trust or local governance procedures as well as consulting with the patient or their carer. Guidance on ordering and prescribing unlicensed medicines 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) • Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS) • Prescribing unlicensed medicines, General Medical Council (GMC)
SHORTAGE: **Meptid 200mg tablets (Almirall Ltd)**	**Anticipated re-supply date:30th June 2023** **Actions:** Clinicians should: • not start any new patients on meptazinol tablets

- review existing patients on meptazinol, given its indication for the short-term management of moderate pain, to determine if analgesia is still required; and whether use has been on an acute or chronic basis.
- assess risk of drug withdrawal syndrome upon abrupt cessation or dose reduction of meptazinol in patients who have been taking it on chronic basis.
- determine if patients who have been on chronic therapy and deriving no benefit or no longer requiring treatment, have enough stock left to enable dose tapering and cessation of treatment (see link to Faculty of Pain Medicine guidance)
- consider prescribing an alternative analgesic if treatment is still needed (see Supporting Information), ensuring that the patient is counselled on the new medication and dose; and
- seek advice from specialist pain teams if above options are not considered appropriate.

Alternatives:
Alternative analgesic products including non-opioids remain available (see clinical information).

Considerations and Background:

Clinical Information
Meptazinol is a centrally acting analgesic, which has demonstrated mixed agonist and antagonist activity at opioid receptors. It is licensed for the short-term treatment of moderate pain. The usual dose is 200mg every 3-6 hours. The BNF notes it is claimed to have a low incidence of respiratory depression, though the SmPC advises that caution should be exercised in patients whose respiratory system is already compromised. As with other opioids, it warns that withdrawal syndrome may occur upon abrupt cessation or dose reduction of meptazinol.
Meptazinol tablets do not feature in pain management guidelines as a treatment option. NICE CKS guidance on analgesia for mild-to-moderate pain recommends weak opioids such as codeine, dihydrocodeine, or tramadol for patients who have an inadequate response to paracetamol and/or a nonsteroidal anti-inflammatory drug (such as ibuprofen or naproxen).
Guidance from the Faculty of Pain Medicine of the Royal College of Anaesthetists highlights that an individualised approach is necessary when switching opioids as conversion factors are an approximate guide only due to the lack of comprehensive data and significant inter-individual variation.

Opioid dose equivalence of weak oral opioids to oral morphine
The guidance suggests that in most cases, when switching between different opioids, the calculated dose-equivalent must be reduced to ensure safety. The starting point for dose reduction from the calculated equi-analgesic dose is around 25-50%.
Dose equivalence of meptazinol is not covered in this guidance or other standard sources. Hospital
guidelines that include meptazinol suggest that *200mg is approximately equivalent to oral morphine 4mg to 8mg.*
Codeine, dihydrocodeine and tramadol at a dose of 50mg is equivalent to a 5mg dose of oral morphine.
Thus 200mg of meptazinol would equate to a dose range of 40 to 80mg of above mentioned weak opioids. As it is recommended to start on 50-75% dose equivalence of the original opioid, the usual licensed dose for the weak

	opioids could be prescribed and titrated according to individual response and side effects.
SHORTAGE: **Sabril 500mg tablets (Sanofi)**	**Anticipated re-supply date: Not Known** **Actions:** Where patients have insufficient supplies to last until the re-supply date, prescribers should: • consider prescribing vigabatrin (Sabril®) 500mg granules for oral solution in the interim, ensuring that the patient is not intolerant to any of the excipients, is counselled that the dose remains unchanged, and is provided with advice on how to reconstitute the granules (see Clinical Information below); • advise patients to report any loss in seizure control and side effects after the switch; and • if the above option is not considered appropriate, seek advice from specialists on management options. **Alternatives:** **Summary** • Vigabatrin (Sabril®) 500mg tablets are out of stock without a confirmed resupply date. • An alternative formulation of the Sabril® brand of vigabatrin is the 500mg granules for oral solution, which remain available. • Restrictions are in place for the supply of vigabatrin 500mg granules for oral solution, limiting stock to 1 pack per community pharmacy/trust with further supplies requiring a valid prescription (see prescription validation process). **Clinical Information** Vigabatrin (Sabril®) tablets and granules are licensed in combination with other antiepileptic medicines for the treatment of patients with resistant partial epilepsy with or without secondary generalisation, where all other appropriate medicinal product combinations have proved inadequate or have not been tolerated. It is also licensed as monotherapy in the treatment of infantile spasms (West's syndrome). Both formulations have identical dosing. The granules are dissolved in half a glass of cold water or soft drink e.g. juice or milk. According to the SmPC, no direct correlation exists between plasma concentration and efficacy; duration of effect is dependent on the rate of GABA transaminase resynthesis rather than the concentration of vigabatrin in the plasma. The MHRA classifies vigabatrin as a category 3 antiepileptic agent, where there is essentially complete absorption after oral administration; dose-response curves for efficacy and safety are not steep; and therapeutic index is not narrow. It points out that differences between alternative products (e.g. packaging, appearance, and taste) may be perceived negatively by patients and/or carers, and may lead to dissatisfaction, anxiety, confusion, dosing errors, and reduced adherence. This should be taken into consideration when counselling patients switching to the granules

	Prescription validation process
	
	1. Pharmacies to email Sanofi (uk-gfd-dtpsupply@sanofi.com) with the following information
	    1. Phoenix or AAH account number,
	    2. Phoenix or AAH order number, and
	    3. anonymised prescription
	2. Sanofi will validate the order and contact Phoenix/AAH to place the order against the order number.
	3. PHD/AAH will process the order and aim to deliver on the next scheduled delivery date/time.
	4. Sanofi will send a confirmation email to the pharmacy team advising the order has been processed.
	5. If there are any issues with orders, Sanofi will get in touch with customers and advise accordingly.

SHORTAGE:
Pilocarpine 4% eye drops
	Anticipated re-supply date: 31st March 2023
	
	Actions:
	NHS Provider Trust pharmacy procurement teams, ophthalmology teams and primary care prescribers should:
	
	• review patients on pilocarpine 4% eye drops for open angle glaucoma or ocular hypertension and establish if they have sufficient supplies until the resupply date. If patients require further supplies:
	    ○ consider prescribing pilocarpine 1% or 2% eye drops and adjusting the frequency to control the intraocular pressure; or
	    ○ consider other therapies if appropriate (such as prostaglandins, betablockers, alpha agonists and carbonic anhydrase inhibitors) to control intraocular pressure;
	• refer to the Royal College of Ophthalmology guidelines on the management of acute angle closure glaucoma and treat all patients (irrespective of eye colour) with a stat dose of pilocarpine 2% eye drops (along with other treatments as laid out in the guideline);
	• consider prescribing unlicensed (specials) pilocarpine 4% preservative free eye drops if the options above are not suitable (see Supporting Information); and
	• review patients prescribed pilocarpine 4% eye drops off-label as treatment for dry mouth in palliative care settings and consider prescribing pilocarpine 5mg tablets, which are licensed for xerostomia (see Supporting Information).
	
	Alternatives:
	
	Licensed alternatives:
	Alternative strengths of pilocarpine 1% and 2% eye drops remain available and will be able to support increased demand.
	For off-label use of the 4% drops in the treatment of xerostomia (dry mouth) in palliative care, pilocarpine 5mg tablets are available and are licensed for this indication.
	
	Unlicensed alternatives:
	Specials of pilocarpine 4% preservative free eye drops are available if the licensed alternatives are not suitable.

Considerations and Background

Supporting information

Primary glaucoma is classified according to appearance of the iridocorneal angle. Aqueous humour drains mainly via the trabecular meshwork, in the iridocorneal angle. Depending on whether the iris is, or is not, occluding the angle, two variants are termed primary angle closure glaucoma (PACG) and primary open angle glaucoma (POAG) respectively.

Pilocarpine eye drops are licensed for the treatment of:

- chronic simple glaucoma
- acute (closed angle) glaucoma alone, or in conjunction with other agents to decrease intra-ocular pressure prior to surgical treatment
- miosis to counteract the effects of cycloplegic or mydriatic eye drops.

There is no other topical miotic licensed in the UK for the treatment of glaucoma.

In the treatment of open angle glaucoma, the dosage is usually one or two drops every six hours. The strength of the preparation and the frequency of use are determined by the severity of the condition and the response to treatment. When used prior to surgery for acute attacks of closed-angle glaucoma, the dosage is one drop every five minutes until miosis is obtained. To overcome weaker mydriatics, the normal dosage is one drop every five minutes until the effect is counteracted.

Acute angle closure glaucoma

Recent guidance from the Royal College of Ophthalmologists on the management of acute angle glaucoma recommends the use of a stat dose of 2% pilocarpine (along with other treatments) before performing laser treatment. It notes that although there are known differences in the behaviour of the iris between blue-eyed patients of Caucasian descent and brown-eyed patients of Asian and African descent, no race-specific management pathways have been developed or proven in objective research.

Primary open angle glaucoma and ocular hypertension

CKS guidance on the management of primary open angle glaucoma and ocular hypertension suggests that pilocarpine is one of a number of options that can be switched to or added in after first-line treatment is unsuccessful or not tolerated, but there are no recommendations on strength of product. It recommends that for acute angle closure crisis where immediate admission is not possible, one drop of 2% pilocarpine should be used for patients with blue eyes and one drop of 4% for those with brown eyes. This recommendation is based on guidance from the College of Optometrists, which acknowledges this is supported by low level of evidence.

In practice, some clinicians may start patient on pilocarpine 2% and if it does not control the intraocular pressure, move to the 4% drops, and some may determine strength based on eye colour. Other clinicians are of the opinion that 4% eye drops may not be as well tolerated, may cause headaches and are not necessarily more effective than 2% eye drops.

Use in palliative care

Pilocarpine 4% eye drops are included in the Palliative Care Formulary (PCF) as an off-label treatment for dry mouth, particularly after radiotherapy for

	head and neck cancer. It is used as an alternative to pilocarpine tablets 5mg (3 drops of 4% solution contain 6mg of pilocarpine) as it is less costly, but the PCF notes the eye drops appear to be less effective and are not always acceptable to patients.

SHORTAGE:
Bupropion (Zyban) 150mg modified-release tablets
	Anticipated re-supply date: Not Known
	
	Actions:
	All healthcare professionals in primary, secondary or specialist healthcare services including local stop smoking services, should work with clinicians and pharmacists to ensure the following actions are undertaken where relevant:
	
	• do not initiate patients on bupropion 150mg modified-release tablets
	for patients taking bupropion as a smoking cessation aid, consider (re)prescribing nicotine replacement therapy (see considerations and background)
	• identify patients currently prescribed bupropion 150mg modified-release tablets off-label (e.g. in the treatment of resistant depression); and
	  ○ make contact with patients/carers as soon as possible
	  ○ refer back to initiating specialists for individual review and consideration of alternative management options. This may include the possibility of de-prescribing, switching to another agent, and augmentation strategies
	• assess the need to taper off bupropion to reduce the risk of discontinuation effects, if patients have sufficient supply to do so.
	• consider prescribing unlicensed bupropion 150mg modified release tablets.
	
	Alternatives:
	Various nicotine replacement therapies are available and NICE guidance highlights a range of other types of interventions to aid smoking cessation.
	Specialist advice is required on alternative products where bupropion is used off-label.
	The following specialist importers have confirmed they can source unlicensed bupropion 150mg modified release tablets (please note there may be other companies that can also source supplies):
	
	• Chemys
	
	Considerations and Background
	
	Supply overview
	Bupropion (Zyban) 150mg modified-release tablets will be out of stock until further notice.
	
	Smoking Cessation
	Bupropion (Zyban) tablets are licensed as an aid to smoking cessation in combination with motivational support in nicotine-dependent patients. It is recommended that the patient sets a “target stop date” within the first two weeks of treatment. The initial dose is 150mg daily for six days, increasing on day seven to 150mg twice daily. Patients should be treated for 7-9 weeks. If at seven weeks no effect is seen, treatment should be

	discontinued. The SmPC notes that discontinuation reactions are not expected, but also mentions that a tapering-off period may be considered. Due to ongoing supply issues with varenicline (Champix) tablets, the only licensed pharmacological aid to smoking cessation currently available is nicotine replacement therapy. Patients should discuss their options with their prescriber or stop smoking advisor, including reconsideration of nicotine replacement therapies, where appropriate. Helping a patient to stop smoking should not be delayed if they are motivated to stop. Clinicians should consult NICE guidance on smoking cessation for consideration of other management options. Guidance on ordering and prescribing 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) • Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS) • Prescribing unlicensed medicines, General Medical Council (GMC)
SHORTAGE: **Triamcinolone hexacetonide 20mg/1ml suspension for injection ampoules (Esteve Pharmaceuticals Ltd) 10 ampoule**	**Anticipated re-supply date: 31st October 2023** **Actions:** Clinicians should consider: • prescribing an alternative steroid injection during this time **Alternatives:** Triamcinolone acetonide and other steroid injections remain available. **Considerations and Background:** Further Information Please see the following links for further information: • SmPC Triamcinolone hexacetonide 20 mg/ml suspension for injection • SmPC Adcortyl® Intra-Articular/Intradermal Injection 10mg/ml • SmPC Kenalog® Intra-articular / Intramuscular Injection
SHORTAGE: **Fluoxetine 20mg/5ml oral solution** **Olena 20mg dispersible tablets (Advanz Pharma)**	**Anticipated re-supply date: 24th March 2023** **Actions:** Where patients have insufficient supply of fluoxetine 20mg/5mL oral solution or fluoxetine 20mg dispersible tablets to last until the re-supply date, prescribers should: • not initiate any new patients on fluoxetine 20mg/5mL oral solution or fluoxetine 20mg dispersible tablets • review patients to determine if they are able to swallow solid dosage forms and consider prescribing an equivalent dose of fluoxetine using the capsules, where available strengths allow this • where patients are not able to swallow solid dosage forms, consider prescribing an equivalent dose of fluoxetine using the capsules,

where available strengths allow this, the contents of which can be emptied out and dispersed in water (off-label use) and ensure they are counselled on how to do this (see Supporting Information); or

- consider prescribing unlicensed fluoxetine 20mg/5mL oral suspension available from Specials manufacturers (see supporting information)
- where the above options are not considered appropriate, and a liquid formulation is required, consider an alternative selective serotonin reuptake inhibitor (SSRI) liquid preparation (see alternatives), taking into account the indication for use, previous treatments tried, current fluoxetine dose, and also the need to seek specialist advice on more complex patients being treated for depression or patients with bulimia nervosa.

Alternatives:
The following alternatives are available:

- Fluoxetine capsules, including the 10mg and 20mg strengths.
- Unlicensed fluoxetine 20mg/5mL oral suspension are available via a number of specials manufacturers
- Citalopram 40mg/mL oral drops and escitalopram (Cipralex) 20mg/mL oral drops.

Considerations and Background

Summary

- Fluoxetine 20mg/5mL oral solution is in limited supply until March 2023.
- Fluoxetine (Olena) 20mg dispersible tablets are out of stock until further notice.

Clinical Information

Fluoxetine indications
Fluoxetine is a SSRI licensed in adults for the treatment of major depressive episodes, obsessive- compulsive disorder, and bulimia nervosa as a complement of psychotherapy for the reduction of binge eating and purging activity. It is also licensed in children and adolescents aged 8 years and above for the treatment of a moderate to severe major depressive episode.

Off-label administration of fluoxetine capsules
NEWT guidelines suggest that the contents of the capsules can be dispersed in 120mL of water and will dissolve in approximately 5 minutes.

Alternative SSRIs for depression
As fluoxetine is not a usual first line agent, patients may have been on other SSRIs previously and advice may need to be sought from specialists on alternative treatment options. Unlike other SSRIs, fluoxetine has a very long half-life and a washout period is required when switching to another SSRI. If the decision is made to switch, it is recommended that the alternative SSRI is started at a low dose 4 to 7 days after stopping fluoxetine. Please see the SPS article How do you switch between tricyclic, SSRI and related antidepressants? for further information.

	Bulimia nervosa Fluoxetine is the only SSRI licensed for bulimia nervosa. It has been the most studied of the SSRIs for this condition. Specialists will need to be consulted on alternative treatment options. **Guidance on ordering and prescribing unlicensed imports** The following Specials manufacturers have confirmed they can manufacture unlicensed fluoxetine 20mg/5mL oral suspension (please note there may be other companies that can also source supplies): • Eaststone • IPS Pharma • Nova Laboratories • Target 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) • Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS) • Prescribing unlicensed medicines, General Medical Council (GMC)
SHORTAGE: **Norditropin FlexPro 5mg/1.5ml solution for injection pre-filled pens (Novo Nordisk Ltd)** **Norditropin FlexPro 10mg/1.5ml solution for injection pre-filled pens (Novo Nordisk Ltd)** **Norditropin FlexPro 15mg/1.5ml solution for injection pre-filled pens (Novo Nordisk Ltd)** **Norditropin NordiFlex 5mg/1.5ml solution for injection pre-filled pens (Novo Nordisk Ltd) 1 pre-filled disposable injection** **Norditropin NordiFlex 10mg/1.5ml solution for injection pre-filled pens (Novo Nordisk Ltd)**	**Anticipated re-supply date: 5th January 2024** Actions for GP surgeries: GP surgeries who prescribe Norditropin should: • proactively identify all Norditropin Nordiflex patients and refer them to their specialist prescribing centre for review and switching to Omnitrope SurePal • proactively identify all Norditropin Flexpro patients that do not have sufficient stock to last until the re-supply date and refer them to their specialist prescribing centre for review and switching to Omnitrope SurePal **Alternatives** Omnitrope (somatropin) SurePal 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml solution for injection cartridges remain available and will be able to support a full increase in demand during this time. If Omnitrope SurePal is not an appropriate alternative, other products containing somatropin remain available. Ultimately the decision on switching to an alternative device is one that will be made by clinicians taking into account the most suitable therapy for their patient. **Considerations and background** Supply Overview • Norditropin (somatropin) Flexpro 5mg, 10mg and 15mg Pen's will be in limited supply for the duration of 2023. This may result in intermittent stock outs for the rest of the year. Stocks will need to be reserved only for patients already established on this therapy.

	• Norditropin (somatropin) NordiFlex 5mg, 10mg and 15mg pens will be out of stock from mid-February 2023 for the remainder of 2023 and cannot support an uplift in demand for the above shortage. • Sciensus and Alcura have the capacity to offer virtual device training for all switched patients. • All Omnitrope (somatropin) SurePal patients will receive 4 weekly deliveries until all patients have been switched. **Clinical Information** The three presentations referenced in this Medicine Supply Notification all contain the same active ingredient, somatropin. This therefore means the monitoring of clinical parameters following a change in device is not required however, clinicians and providers should ensure that patients and their carers are thoroughly counselled on the use of the new device.
SHORTAGE: **Monopost 50micrograms/ml eye drops 0.2ml unit dose (Thea Pharmaceuticals Ltd)**	**Anticipated re-supply date: 17th March 2023** **Actions:** Where patients have insufficient supplies to last until the re-supply date, clinicians/prescribers should: • reserve remaining supplies for patients who require a preservative free formulation • assess whether a patient can be switched to preservative-containing latanoprost 50microgram/ml eye drops for the duration of shortage, with a view to revert to latanoprost (Monopost) 50microgram/ml preservative free eye drops when available • provide reassurance to patients who do not have a genuine allergy or severely compromised ocular surface on the use of preserved drops • where the above options are not suitable, consider prescribing preservative free bimatoprost or tafluprost eye drops, or a non-benzalkonium chloride preservative containing preparation, travoprost, ensuring that the patient is not intolerant to any excipients in these products (see clinical information below) • if the above options are not considered appropriate, advice should be sought from specialist ophthalmology team on alternative treatment options. **Alternatives:** Latanoprost 50microgram/ml eye drops which contain a preservative, remain available and will be able to support an increase in demand, but may not be suitable for patients with an allergy or intolerance to the preservative, benzalkonium chloride. Alternative preservative free eye drops containing prostaglandin analogues remain available, but no one product can support an increase in demand. **Alternative prostaglandin analogues eye drops** The following available products are licensed for reducing intraocular pressure in patients with open angle glaucoma or ocular hypertension. The recommended dose for all these preparations is one drop in the affected eye(s) once daily, in the evening. *Bimatoprost* Bimatoprost is available as LUMIGAN 300micrograms/ml eye drops, solution, in single-dose container (preservative free)

	Tafluprost Tafluprost is available as Saflutan 15micrograms/ml eye drops, solution, in single-dose container (preservative free) *Travoprost* Travoprost is available in the following presentations: • Visutrax 40 micrograms/ml eye drops, solution in single dose container (preservative free) • Travatan 40micrograms/ml eye drops (preservative containing, but contains a non-benzalkonium chloride preservative) *Latanoprost* Latanoprost is available as Xalatan 50micrograms/ml eye drops (preservative containing). **Considerations and Background** **Clinical Information** Latanoprost (Monopost) 50microgram/ml preservative free eye drops 0.2ml unit dose are licensed for the reduction of elevated intraocular pressure in patients with open angle glaucoma and ocular hypertension. Dose is one eye drop in the affected eye(s) once daily in the evening. Benzalkonium chloride is a common preservative in most eye drops. There are reports of damage to the tear film and corneoconjunctival surface, and various forms of conjunctivitis have been reported in patients receiving regular long-term treatment for glaucoma with eye drops preserved with benzalkonium chloride. Patients with dry eye syndrome and ocular surface disease are at increased risk of epithelial breakdown and exacerbation of their ocular surface disease. It is also reported that preservatives can cause excess fibrosis and have potential negative effects on drainage surgery. NICE glaucoma guidance recommends that preservative-free eye drops should be offered to: • people with ocular hypertension who have an allergy to preservatives or people with clinically significant and symptomatic ocular surface disease, but only if they are at high risk of conversion to chronic open angle glaucoma (COAG) • people with COAG who cannot tolerate a pharmacological treatment, with evidence of allergy to the preservative or presence of clinically significant and symptomatic ocular surface disease In practice, preserved drops will usually be avoided in contact lens wearers and in young patients starting on glaucoma treatment. Certain patients on multiple drop therapy are on the preservative free eye drops to restrict the number of preservatives that come into contact with the ocular surface. Clinical guidance is also available on the Royal College of Ophthalmologists' website.
SHORTAGE: **Phenergan 5mg/5ml elixir (Sanofi)**	**Anticipated re-supply date:14th April 2023** **Actions:** Where patients have insufficient supplies to last until the re-supply date, clinicians should:

- review patients to determine if treatment is still required and if this is still the most suitable therapy
- if required, determine if patients are able to swallow solid dosage forms and consider prescribing promethazine 10mg or 25mg tablets if the dosage regimen allows use of whole tablets, or if rounding the dose to the nearest 10mg is within the licensed dose range for the age of patient
- if patients are unable to swallow a solid dosage form or the dose cannot be delivered from use of the tablets, consider prescribing an alternative sedating antihistamine available as a liquid formulation, taking into consideration the indications and licensed age group, and ensure patient is not intolerant to any of the excipients, and is counselled on the appropriate dose required (see Alternatives); and
- if above options are not suitable, consider prescribing unlicensed promethazine hydrochloride 5mg/5ml oral solution or suspension (sugar free), which are available from Specials manufacturers (see Alternatives).

Alternatives:

Promethazine tablets
Promethazine hydrochloride 10mg and 25mg tablets remain available and can support an uplift in demand.

Alternative Sedating Antihistamine Liquid

Chlorphenamine
Available as 2mg/5ml oral solution.
Licensed age group: ≥1 year
Licensed indication: Symptomatic control of all allergic conditions responsive to antihistamines, including hay fever, vasomotor rhinitis, urticaria, angioneurotic oedema, food allergy, drug, serum reactions, insect bites, and symptomatic relief of itch.

Alimemazine
Available as:

- 7.5mg/5ml oral solution
- 10mg/5ml oral solution
- 30mg/5ml oral solution

Licensed age group: ≥2 years
Licensed indication:

- Management of urticaria and pruritus.
- Pre-medication sedation before general anaesthesia in children aged 2-7 years.

Ketotifen (Zaditen)
Available as: 1mg/5ml elixir
Licensed age group: ≥3 years
Licensed indication: Symptomatic treatment of allergic conditions including rhinitis and conjunctivitis.

Specials

	The following Specials manufacturers have confirmed they can manufacture unlicensed promethazine 5mg/5ml oral solution or suspension (please note there may be other companies that can also source supplies): • Eaststone • IPS Pharma • Nova Laboratories **Considerations and background** **Clinical Information** Promethazine hydrochloride 5mg/5ml oral solution sugar free (Phenergan elixir) is licensed for use in patients aged 2 years and above as symptomatic treatment for allergic conditions of the upper respiratory tract and skin including allergic rhinitis, urticaria and anaphylactic reactions to drugs and foreign proteins. It is also licensed for use as an antiemetic treatment of insomnia in adults and as a sedative in children. **Guidance on ordering and prescribing 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) • Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society (RPS) • Prescribing unlicensed medicines, General Medical Council (GMC).
SHORTAGE: **Paracetamol 120mg suppositories**	**Anticipated re-supply date:12th May 2023** **Actions:** For patients with insufficient supplies of paracetamol 120mg suppositories, community pharmacists may supply paracetamol 125mg suppositories in accordance with the SSP for eligible patients. If the patient is deemed ineligible, or does not consent to receive an alternative product via the SSP, clinicians can consider prescribing: • paracetamol 125mg suppositories, counselling patients regarding the switch at the point of prescribing; or • a suitable alternative medicine **Alternatives:** Paracetamol 125mg suppositories remains available and can support a full uplift in demand. **Considerations and Background:** **Clinical Information** The dose difference between paracetamol 120mg and 125mg suppositories is negligible in context of the overall dosing schedule. Based on the BNFc dosing instructions for paracetamol a switch from paracetamol 120mg suppositories to 125mg suppositories, has no clinical or licensing concerns.
SHORTAGE: **Capsaicin 0.025% cream** **Capsaicin 0.075% cream**	**Anticipated re-supply date: 30th June 2023**

Action:
Where patients have insufficient supply to last until the resupply dates, prescribers should:

- refer to local and national treatment guidelines for choice of an alternative agent, taking into account treatments already tried, and reasons for being on a topical agent (see Supporting information below); and
- where topical capsaicin is still considered the most suitable therapy, prescribe unlicensed products. 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).

Alternatives:
The following specialist importers have confirmed they can source unlicensed capsaicin 0.025% cream (please note there may be other companies that can also source supplies):

- Target Healthcare

Considerations and Background:
Clinical Information:
Axsain (capsaicin 0.075% cream) is licensed for the symptomatic relief of neuralgia associated with and following Herpes Zoster infections (post-herpetic neuralgia) after open skin lesions have healed, and the symptomatic management of painful diabetic peripheral polyneuropathy. Zacin (capsaicin 0.025% cream) is licensed for the symptomatic relief of pain associated with osteoarthritis.
Neuropathic pain
NICE guidance recommends oral therapies such as amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain in the non-specialist settings; if the initial treatment is not effective or is not tolerated, one of the remaining three drugs should be offered, and switching again if the second and third drugs tried are also not effective or not tolerated. Use of capsaicin cream is supported as an option for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments.
Osteoarthritis
NICE guidance notes that there was some evidence showing that topical capsaicin reduces pain in knee osteoarthritis, but not hand osteoarthritis, and it has minimal adverse events. However, it is more expensive and topical NSAIDs were considered a better option. If topical medicines are ineffective or unsuitable, an oral NSAID is recommended, taking into account potential gastrointestinal, renal, liver and cardiovascular toxicity, and any risk factors the person may have, including age, pregnancy, current medication and comorbidities. Paracetamol or weak opioids are not recommended unless they are only used infrequently for short-term pain relief and all other pharmacological treatments are contraindicated, not tolerated or ineffective.

Guidance on ordering and prescribing 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) ○ Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society ○ Prescribing unlicensed medicines, General Medical Council (GMC).
SHORTAGE: **Balneum 84.75% bath oil (Almirall Ltd)** **Balneum Plus 84.75% bath oil (Almirall Ltd)**	**Anticipated re-supply date: 28th February 2023, 13th March 2023** **Actions:** Clinicians should be aware that: • Balneum Bath Oil and Balneum Plus Bath Oil are out of stock; • bath and shower products are no longer considered an essential component of total emollient therapy, as the amount of bath additives deposited on the skin is lower than with directly applied emollient creams or ointments. They provide no clinical benefit when added to standard eczema care in children (BATHE Study); • an alternative approach is to use a regular leave-on emollient as a soap substitute. Many standard emollients can be used in this way e.g. by applying it to the skin before showering then rinsing it off. Alternatively, 1-2 tablespoons of any ointment (except LP:WSP 50/50 Ointment) can be dissolved in some hot water and added into bath water, as a bath additive; • bath products will coat the bath and make it slippery, and patients should be warned to take extra care; and • dermatologists may in exceptional circumstances, recommend bath/shower emollient products in cases of severe atopic eczema and ichthyosis when the patient requires more intensive emollient therapy and standard emollients used as soap substitutes have already been trialled. This is on the basis that these patients have severe skin disease, which is not represented in the BATHE study. **Alternatives:** Alternative bath and shower products and creams continue to remain available. **Considerations and Background:** **Summary:** Balneum Bath Oil and Balneum Plus Bath Oil are out of stock with resupplies expected late February 2023 and mid-March 2023, respectively.
SHORTAGE: **Trifluoperazine 5mg tablets (Advanz Pharma)**	**Anticipated re-supply date: 31st March 2023** **Alternatives:** Parallel imports of trifluoperazine 5mg tablets are available and can cover the demand. Orders can be placed directly with the following suppliers: • Sigma Pharmaceutical Plc (email cs@sigmaplc.com or info@sigmaplc.com for further information).
SHORTAGE: **Fragmin 10,000units/4ml solution for injection ampoules (Pfizer Ltd)**	**Anticipated re-supply date: 31st March 2023** **Actions:** Primary Care Clinicians should:

- not prescribe dalteparin (Fragmin) 10,000units/4mL ampoules for new patients and consider alternative dalteparin presentations or other low molecular weight heparins
- identify all patients prescribed dalteparin (Fragmin) 10,000units/4mL ampoules and ensure they have enough supplies until the resupply date; and
- for patients with insufficient supplies, work in partnership with the initiating secondary care clinician to consider alternatives (do **not** use dalteparin (Fragmin) 100,000units/4mL) taking into account the confidence of the patient/carer to use an alternative presentation
    - ensure doses and volumes are recalculated correctly and patients/carers are counselled on changes in dose and administration technique
    - be mindful of the potential risk of dosing errors and patient harm if an alternative presentation is not prescribed, dispensed or administered correctly
    - annotate prescriptions to highlight changes to dispensing pharmacies to ensure calculations are rechecked and counselling is provided to patients/carers on dose and administration method. For example, a prescription can be annotated with *'please be aware of change in strength and presentation from the previous prescription and consider this when dispensing'.*

Alternatives:
Dalteparin
Alternative dalteparin (Fragmin) solution for injection products remain available, however, the risk of dosing errors is high without appropriate consideration and training being implemented (see Patient Safety Considerations).

Ampoules

- 10,000 units/1mL

Supplies of 10,000units/1mL ampoules are subject to discontinuation (see Discontinuation of Dalteparin sodium 10,000units/1ml solution for injection ampoules), however, it can support some additional uplift for use in neonate/paediatrics (off-label).

Graduated pre-filled syringe

- 10,000 units/1mL

Pre-filled syringes

- 2,500 units/0.2mL
- 5,000 units/0.2mL
- 7,500 units/0.3mL
- 10,000 units/0.4mL
- 12,500 units/0.5mL
- 15,000 units/0.6mL
- 18,000 units/0.72mL

Alternative Low Molecular Weight Heparins

Alternative low molecular weight heparins, including enoxaparin and tinzaparin, may be a suitable alternative for some patients.

For Trusts
If protocols are changed to use enoxaparin or tinzaparin instead of dalteparin; Trusts should reach out to suppliers of enoxaparin and/or tinzaparin to ensure they can support anticipated demand.

Considerations and background
Summary

- Dalteparin (Fragmin) 10,000units/4mL solution for injection ampoule is due to be out of stock from mid-February 2023 until late March 2023 whilst the ampoules are converted into a vial presentation.
- Alternative strengths and formulations of dalteparin and other low molecular weight heparins remain available and will be able to support increased demand.
- Patient safety precautions including the review of local protocols and appropriate education and training for healthcare professionals, need to be implemented for the duration of this shortage. This includes ensuring the higher concentration multidose vials of dalteparin (Fragmin) **100,000units/4mL (10 times the strength) are not used** as an alternative option to the product in shortage to reduce the risk of dosing errors.
- Regional Pharmacy Procurement Specialist (RPPS) may be able to facilitate mutual aid between hospitals.
- Please note there is also discontinuation of dalteparin (Fragmin) 10,000units/1mL solution for injection ampoule in May 2023, see Discontinuation of Dalteparin sodium 10,000units/1ml solution for injection ampoules

Off-label use
Dalteparin (Fragmin) is used off-label in neonates and paediatrics for the treatment and prevention of any thrombotic event. Dalteparin (Fragmin) 10,000unit/4mL solution for injection ampoule is a commonly used presentation in this patient cohort as it allows for doses with high concentrations in low volumes to be achieved. In this patient population, there is a high risk of dosing errors when changing between dalteparin preparations of differing strengths and forms.
Pfizer, the sole supplier of dalteparin (Fragmin), have a 10,000unit/1mL graduated syringe available as well as alternative strength ampoules, vials and pre-filled syringe preparations. Not all presentations will be deemed suitable for use in neonates and paediatrics.

Patient Safety Considerations
Local guidelines and protocols **should not** include the higher concentration multidose vials (dalteparin (Fragmin) 100,000units/4mL) as an alternative option to the discontinued product, particularly for paediatrics and neonates, to reduce the risk of dosing errors. There are also increased risks of errors if using 'part-doses' from pre-filled syringes.
In addition, where patients/parents/carers are supplied with take-home doses to administer, if an alternative presentation is prescribed, they should be appropriately counselled on the new dose and how to use the device (see links below). Higher concentration multidose vials **should not** be prescribed/dispensed to paediatric and neonate patients.

	Training should be provided to all healthcare professionals on new protocols which advise on prescribing an alternative product or presentation. This is to ensure changes in drug, concentrations, strengths and formulations are clearly understood. Specific training should also be provided for those administering alternative formulations, particularly in neonates. Particular care should be taken if using alternative dalteparin (Fragmin) presentations due to the differences in concentration, presentation and the different processes for administration.
RECALL: **Drug/Brand/Strength/Formulation**	Summary of recall Access this recall on the MHRA website via the link below: Any specific information i.e. Batch numbers

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 21st March 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 https://www.sps.nhs.uk/ and access this tool directly in real time.