

COMMERCIAL-SENSITIVE

Supply Issues Update for Primary and Secondary Care: August 2019

This report has been produced by the Department of Health and Social Care (DHSC) Medicine Supply Team. We aim to update this report monthly to provide an update on current primary and secondary care medicine supply issues that we are working on. This information is confidential to the NHS; please do not upload to websites in the public domain. Please do share with relevant colleagues and networks.

Where it has been stated ‘a clinical memo from UKMI will be published on the SPS website’, this will be found at the following URL: <https://www.sps.nhs.uk/category/shortages-discontinuations-and-expiries/>

Contents

New Issues.....	3	Indocid (indometacin) 100mg suppositories .7	
Injectables	3	Sanofi and Zentiva: distribution issues	7
Acetylcholine Chloride (Miochol-E) 20mg powder and solvent for irrigation.....	3	Ongoing Issues	8
Amikacin 500mg/2ml injection.....	3	Injectables.....	8
Bufyl (bupivacaine 1mg/ml and fentanyl 2 micrograms/ml) solution for infusion 250ml 3		Aciclovir 500mg/1g injection	8
Emerade 500 microgram and 300 microgram adrenaline auto-injector (AAI) devices.....	3	EpiPen and EpiPen Junior	8
Haloperidol 5mg/ml injection.....	4	Erwinase injection.....	8
Ketalar 200mg in 20ml (ketamine hydrochloride 10mg/ml) injection.....	4	Fludarabine 50mg/2ml injection	8
Labetalol 5mg/mL injection	4	Gadovist preparations	8
Tobramycin 240mg/6ml injection	4	Mivacron (mivacurium chloride) injection	9
Phenylephrine 1mg in 10ml (0.1mg /ml) injection	4	Neurobloc (Botulinum Toxin Type B).....	9
Orals.....	5	Oncaspar (pegaspargase) 750 U/ml solution for injection/infusion	9
Colestid (colestipol) 5g granules.....	5	Tetracosactide 1mg depot injection	9
Disopyramide 150mg tablets.....	5	Urokinase injection	10
Physeptone (methadone) 5mg tablets.....	5	Orals.....	10
Quinapril 5mg tablets	6	Actiq (fentanyl) lozenges	10
Sinemet 10/100mg tablets	6	Adalat (nifedipine) tablets/capsules.....	10
Tiagabine tablets	6	Bumetanide 5mg tablets.....	11
Tuberculosis medications	6	Carbagen (carbamazepine) various preparations.....	11
Others	7	Cardura (doxazosin) XL tablets	11
BOC Medical Carbon Dioxide.....	7	Cefuroxime 125mg/5ml suspension (Zinnat)	11
		Disopyramide 100mg tablets.....	11
		Epanutin (phenytoin) 30mg/5ml oral suspension	12

COMMERCIAL-SENSITIVE

Epanutin (phenytoin) 50mg Chewable	Buplast (buprenorphine) patches (Accord) 18
Infatabs.....12	Cilest (norgestimate 250mcg and ethinylestradiol 35mcg) (Janssen-Cilag) 18
Heminevrin (clomethiazole) 192mg capsules12	Copegus (ribavirin) 200mg & 400mg tablets (Roche)..... 18
Hormone Replacement Therapy products (HRT)12	Finasteride 1mg tablets x 84 (Accord) 19
Joyrides (Hyoscine Hydrobromide 150 microgram Tablets).....13	Modecate (fluphenazine decanoate) injection 19
Metoprolol 50mg and 100mg tablets.....13	Myocrisin (sodium aurothiomalate) injection (Sanofi)..... 19
Nitrous Oxide and Entonox.....14	Resolved (date resolved) 20
Olena (fluoxetine) 20mg dispersible tablets14	Ancotil (flucytosine) injection (16/07/19) .. 20
Oral Contraceptive Pill products (OCP)14	Bezalip (bezafibrate) 200mg tablets (5/8/19) 20
<i>Norimin (ethinylestradiol/norethisterone) 0.035mg/1mg tablets</i> 14	Elleste Solo MX 40microgram and 80microgram patches (31/7/19)..... 20
Questran Powder for Oral Suspension15	Diamorphine 5mg injection (5/8/19)..... 20
Stemetil (prochlorperazine) 5mg in 5ml oral syrup15	Hiprex (methenamine hippurate) 1g tablets (25/07/19)..... 20
Trifluoperazine tablets15	Hypovase (prazosin) 0.5mg tablets (4/7/19) 20
Others15	Idarubicin 5mg injection (5/8/19)..... 20
Dalacin (clindamycin) 2% vaginal cream15	Instanyl (fentanyl) 50mcg nasal spray (23/7/19)..... 20
Instanyl (fentanyl) nasal spray.....15	Magnevist (09/07/2019)..... 20
Prostin E2 (dinoprostone) 3mg Vaginal Tablet16	Marcain Heavy (bupivacaine hydrochloride anhydrous) 0.5% injection (18/7/19)..... 20
Skinoren (azelaic acid) 20% cream17	Midazolam injection (7/19) 20
Tilade (nedocromil sodium 2mg/dose) Inhaler17	Mivacron (mivacurium chloride) injection (2/8/19)..... 20
Eye drops/treatments17	Thorens (colecalfiferol) 10,000i.u./ml oral drops (8/7/19)..... 20
Lacri-Lube17	Salbutamol 2mg/5ml syrup (11/7/19) 20
Betnesol Eye Ointment 0.1%.....17	Pneumococcal Polysaccharide Vaccine (16/07/19)..... 20
Betnesol (betamethasone 0.1%) eye/ear/nose drops17	
Vaccines17	
Hepatitis B Vaccines18	
Menveo.....18	
Rabipur (Rabies vaccine)18	
Discontinuations18	

COMMERCIAL-SENSITIVE

Information provided w/c 5th August 2019

New Issues

Injectables

Acetylcholine Chloride (Miochol-E) 20mg powder and solvent for irrigation

- Bausch and Lomb anticipate being out of stock until mid-September due to manufacturing delays
- We have been working with alternative suppliers Farmigee, who are able to supply Miphtel 20mg Ampoules available from Alloga (PIP code 3957834).
- UKMI have issued the following regarding switching to ampoules:
<https://www.sps.nhs.uk/articles/shortage-of-miochol-e-acetylcholine-20mg-powder-and-solvent-for-solution-for-intraocular-irrigation/>
- DHSC can also confirm that unlicensed Miochol-E is available from specialist importers, lead times can vary.

Amikacin 500mg/2ml injection

- Pfizer will be out of stock of amikacin 500mg/2ml injection by mid-August 2019 with a resupply around mid-September.
- Unlicensed imports are available in sufficient quantities to support the market during this out of stock period; lead times vary.
- Please contact your regional lead for further details about unlicensed import availability.

Bufyl (bupivacaine 1mg/ml and fentanyl 2 micrograms/ml) solution for infusion 250ml

- Advanz, sole supplier of this product, are experiencing a delay in manufacture and do not expect resupply until, at the earliest, week ending 23rd August 2019.
- Fresenius Kabi and Mandeville Medicines make an **unlicensed** bupivacaine 1mg/ml and fentanyl 2 micrograms/ml **240ml bag** which they have confirmed is available to support this out of stock period.
- UKMI have confirmed that the 240ml bag is compatible with commercially available epidural cases which are used in the NHS across the UK.
- To place an order, contact the customer services of the respective company named above.

Emerade 500 microgram and 300 microgram adrenaline auto-injector (AAI) devices

- Bausch & Lomb UK, the sole suppliers of Emerade 500 microgram and 300 microgram AAI devices, are experiencing a short-term disruption in supply of these products:
 - Emerade 500 microgram AAIs are currently unavailable, resupply is expected on the 28th August 2019.
 - Emerade 300 microgram AAI, is expected to be unavailable from early/mid-August until end of September 2019.
- A supply disruption alert has been issued via MHRA's CAS, which includes information on the issue and actions to be taken. Please see link below:
- <https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102885>
- Emerade 150 microgram AAIs remain available.
- Both Epipen 300microgram and Jext 300microgram remain available.

COMMERCIAL-SENSITIVE

Haloperidol 5mg/ml injection

- Advanz Pharma are out of stock of haloperidol 5mg/ml injection until mid-September.
- DrugsRUs, have confirmed they have sufficient supplies available to meet additional demand during this period.

Ketalar 200mg in 20ml (ketamine hydrochloride 10mg/ml) injection

- Pfizer, sole supplier of ketamine 200mg in 20ml injection are experiencing a manufacturing delay.
- The next scheduled delivery is expected 16th September. Current stock available in the wholesalers is expected to be depleted by week ending 2nd August.
- The CMU and DHSC have worked with Pfizer and the MHRA to make available additional 200mg in 20ml product from an alternate market. This product, which will be UK licensed stock, will be available from 16th August via the usual wholesaler channels.
- In the interim, a small amount of unlicensed 200mg/20ml ketamine injection is available from Waymade PLC and can be accessed via Oxford Pharmacy Stores.

Labetalol 5mg/mL injection

- Recipharm are currently out of stock of labetalol 5mg/mL injection due to an API issue. Recipharm anticipate further supplies to become available at the end of September.
- Synchrony Pharma, who also manufacture labetalol 5mg/mL injection, have confirmed they have sufficient supplies to meet additional demand during this period.
- Synchrony stock can be ordered from Alloga.

Tobramycin 240mg/6ml injection

- Pfizer will be out of stock of tobramycin 240mg/6ml injection from the beginning of September until w/c 7th October.
- There is sufficient 80mg/2ml available from both Pfizer and Flynn (via Alloga) to cover full usage and Trusts are advised to switch to this strength during the out of stock period.
- Reserve any 240mg/6ml injection for patients who are unable to switch to the 80mg/2ml, for example, those who use via a nebuliser.

Phenylephrine 1mg in 10ml (0.1mg /ml) injection

- NHS England and DHSC were informed that Martindale are experiencing a short term out of stock of Phenylephrine 100mcg/ml 10ml injection, re-supply is expected **w/c 26th August 2019**.
- CMU have contacted all suppliers of phenylephrine 1mg in 10ml (0.1mg/ml) injection (licensed and unlicensed) and no supplier is able to support this out of stock period. The sole supplier of a phenylephrine 0.5mg in 10ml Prefilled syringe is also likely to go out of stock shortly and is unable to make any additional supply available.
- We are working with the importers to see if they can source the product but at present no stock is available to order. The MST will contact regional procurement leads with further information if this situation changes.
- Advanz have confirmed they have sufficient phenylephrine 10mg in 1ml (10mg/ml) injection to support all trusts over this period. This stock is available to order from Alliance.
- Working with the Royal College of Anaesthetists, we have spoken with suppliers of the alternative agent Metaraminol (Torbay Pharmaceuticals) and they can support this out of stock period with either 0.5mg/ml or 10mg/ml Metaraminol ampoules.

COMMERCIAL-SENSITIVE

- Pharmacy should assess local stock holding and develop a careful management plan at a local level by an identified lead anaesthetist, in conjunction with the organisation's Medication Safety Officer
- The management plan should be communicated within pharmacy and to all relevant clinical teams including but not limited to Accident and Emergency departments, Theatres, Intensive Care Units and Obstetrics departments.
- The local management plan will need to document a risk assessment of the following potential actions, the agreed plan and supporting documentation:
 - Possible prioritisation of remaining phenylephrine 1mg in 10ml (0.1mg /ml) injection.
 - Management plan for a possible switch from Phenylephrine to Metaraminol.
 - Management of two different strengths of phenylephrine injection within pharmacy and across trust.
 - The development of supporting information for clinical colleagues. Please refer to national IV monograph for phenylephrine on MEDUSA for information on dilution and suitable diluent, or local guidelines, where available.
 - Risk minimisation measures developed with guidance from local Medication Safety Officers (MSO) need to be put in place to reduce the risk of a dosing error, such as flagging up the higher strength of the injection and standardisation of the dilution of the 10mg/1mL injection.
 - Trusts with aseptic manufacturing capabilities may want to consider preparing ready diluted phenylephrine solution to mitigate risk associated with ward-based dilution

Orals

Colestid (colestipol) 5g granules

- Pfizer are out of stock of Colestid orange and plain granules until end of September and end of October, respectively.
- Clinicians should refer to the UKMI memo for advice on alternatives: <https://www.sps.nhs.uk/articles/shortage-of-bile-acid-sequestrants/>
- DHSC has worked with the specialist importers and can confirm that unlicensed Colestid is available; lead times vary.

Disopyramide 150mg tablets

- Mylan, sole supplier of disopyramide 150mg tablets, are out of stock until end of September 2019.
- A supply disruption alert has been issued via MHRA's CAS, which includes information on the issue and actions to be taken. Please see link below: <https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102869>

Physeptone (methadone) 5mg tablets

- DHSC have been made aware of a supply issue with methadone (Physeptone) 5mg tablets from the sole licensed UK supplier, Ethypharm.
- Ethypharm are currently out of stock due to a packing issue with their contract manufacturer. Further stock is expected by the end of August 2019.
- During this time unlicensed methadone 5mg capsules are being manufactured and can be ordered directly from Ethypharm. The product code is **P034663** - Methadone Capsules 5mg 50 [CD]. Please allow 1-2 days delivery for the unlicensed supply.
- Clinicians can prescribe unlicensed products for their patients if they think it appropriate, on an individual patient basis, but do so entirely on their own responsibility.

COMMERCIAL-SENSITIVE

- Other presentations of methadone, including suspension, remain available.

Quinapril 5mg tablets

- Both suppliers of quinapril 5mg tablets are out of stock of this strength until the end of September at the earliest.
- Supplies of the 10mg and 20mg remain available.
- UKMI have issued the following advice regarding halving the 10mg scored tablets:
“The 10mg quinapril tablets are scored, however manufacturers state this scored line is for facilitating breaking of tablets for ease of swallowing and may not divide in equal doses. It is unlikely that the distribution in the tablet will be significantly different in the two halves. Therefore, the majority of patients should not experience problems with splitting the 10mg tablets and taking half of a 10mg tablet to equate 5mg dose”.
- Alternatives to this, are to switch to an alternative ACE-Inhibitor (Captopril, Enalapril, Fosinopril, Imidapril, Lisinopril, Perindopril, Ramipril, Trandolapril). There are no guidelines on converting doses between ACE Inhibitors, considering the 5mg of Quinapril is the lowest dose, it is recommended starting patients on lowest strengths of available ACE-Inhibitors and titrate doses upwards according to patient response.

Sinemet 10/100mg tablets

- Merck Sharp and Dohme (MSD) are out of stock of Sinemet 10/100mg tablets from 1st August due to capacity constraints.
- MSD anticipate resupply of this product at the end of August 2019.
- DHSC has confirmed with alternative generic suppliers of co-careldopa 10/100mg tablets that they have sufficient quantities to cover this out of stock period.

Tiagabine tablets

- Teva, sole supplier of tiagabine tablets, are out of stock of all strengths until the end of September 2019.
- A limited amount of stock remains available through Alliance Healthcare. If pharmacies are unable to obtain from their usual depot, inform Teva customer services who will liaise with the wholesaler to redistribute stock to where it is required.
- Once supplies are exhausted, if patients do not have sufficient supplies to last until end of September, they should be encouraged to return to their clinician for specialist advice.

Tuberculosis medications

Ethambutol 100mg tablets

- Thornton & Ross, framework holders for LSNE, are out of stock of this product until w/c 19th August.
- Morningside are in stock but are unable to support the LSNE region during this time.
- Trusts affected should review local stock holding and consider dispensing ethambutol prescriptions in instalments to ensure continuity of supply to patients until expected replenishment date.
- Following this, if Trusts are unable to ensure continuity of supply, contact your regional procurement lead who will support stock sharing between Trusts.

Pyrazinamide 500mg tablets

- Both suppliers of pyrazinamide 500mg tablets are currently experiencing supply issues.

COMMERCIAL-SENSITIVE

- Thornton & Ross are out of stock and expect to resupply wholesaler's w/c 12th August 2019.
- Morningside are also out of stock; resupply expected in October 2019.
- If there is less than three weeks' worth of stock remaining at Trust level, consider dispensing pyrazinamide prescriptions in instalments to ensure continuity of supply to patients until w/c 12th August.
- If the Trust is still unlikely to be able to maintain continuity of supply, please contact your regional procurement lead who will support stock sharing between Trusts.

Rifadin (rifampicin) 150mg/300mg capsules

- Sanofi are out of stock of Rifadin capsules with resupply expected for the 300mg strength w/c 26th August and the 150mg strength w/c 2nd September.
- Mylan can support this out of stock period with their 150mg presentation only.
- Drugs R Us have limited stock of rifampicin 300mg capsules that they will make available via direct orders.
- Review local stock holding. If stock is required, place orders with DrugsRUs for 300mg capsules while this stock is available, and with Mylan for 150mg capsules.
- Order in line with historic demand to ensure stocks are not depleted rapidly.

Rifater tablets

- Sanofi, the sole supplier of this combination anti-tuberculosis product are experiencing a delay in its manufacture and do not expect wholesaler stocks to be replenished until at the earliest, week ending 30th September 2019.
- Supplies of a parallel imported product (considered licensed UK stock) will be available from 24th July from Alliance Healthcare. Trusts are asked to only order according to historical demand for the duration of the out of stock period.

Others

BOC Medical Carbon Dioxide

- BOC are experiencing temporary delays in product availability due to an outage at one of their filling facilities.
- BOC have confirmed they can continue to meet demand however there will be an increased lead time of 3 days in order to manage the supply of carbon dioxide medical gas.
- NHS Trusts are advised to contact their local BOC account manager if they have queries.
- BOC have produced a *Dear HCP letter* which is attached to this update.

Indocid (indometacin) 100mg suppositories

- Aspen, sole supplier of this product are out of stock until early September 2019.
- Supplies of parallel imported products (considered licensed UK stock) are available.

Sanofi and Zentiva: distribution issues

- Sanofi and Zentiva's UK logistics provider (Kuehne and Nagel) experienced a technical issue with one of their IT systems which impacted on their ability to get stock to their agent's depots.
- Normal stock levels are expected to be restored by w/c 19th August. Back orders will be cancelled. Please place new orders when stock becomes available at local depots.

COMMERCIAL-SENSITIVE

Ongoing Issues

Injectables

Aciclovir 500mg/1g injection

- Several suppliers are currently experiencing issues with availability of aciclovir injection.
- Sufficient stock is available at wholesalers; however, Trusts may need to switch from aciclovir solution to powder and from 500mg and 1g vials to 250mg vials.

EpiPen and EpiPen Junior

- The supply situation for EpiPen and EpiPen Junior continues to improve, and further stock due in the coming months.
- Stock of EpiPen Junior is no longer subject to prescription validation and is available to order from wholesalers. Please order in line with demand, Mylan and DHSC will review stock levels regularly to ensure sufficient supplies remain available.
- Stock of EpiPen 0.3mg device is available via a prescription validation process. Information about this process is available on the EpiPen website under the 'Instruction to Pharmacists' section: <http://www.epipen.co.uk/>
- Hospitals are advised to contact Alliance if they wish to obtain EpiPen 0.3mg .

Erwinase injection

- Porton Biopharma, the manufacturer of Erwinase, have had ongoing manufacturing issues affecting this product for the past 1-2 years.
- Jazz Pharmaceuticals distributes Erwinase and are now out of stock.
- Further batches are currently expected to be available mid-September.
- There are likely to be ongoing intermittent supply issues which will continue during 2019.
- Jazz works closely with the clinical networks and supplies are prioritised on a patient need basis and in conjunction with the treating clinicians.

Fludarabine 50mg/2ml injection

- Teva had a supply issue with fludarabine solution for injection and expect to have limited supplies until 14th August due to API issues.
- Latest updates from Accord:
 - The 50mg/2ml solution for injection - limited supplies available through AAH and Alliance
 - The 50mg powder - limited supplies available through AAH and Alliance
- Sanofi have limited stock of the 50mg powder presentation (Fludara) and are not able to support any increase in demand.
- Specialist importers can source unlicensed fludarabine injection with variable lead times. Please contact your regional procurement leads for further information.

Gadovist preparations

- Manufacturing issues at Bayers' Berlin site is affecting supplies of Gadovist. This issue is likely to go on for several months.
- We have engaged with Bracco and Guerbet regarding their supply position on other gadolinium containing products. Both companies have good supplies available and have enough stock to support this supply issue.
- Please see full summary/stock position in table below.

COMMERCIAL-SENSITIVE

Manufacturer	Presentation	Stock Availability
Bayer Plc	Gadovist 1mmol/ml solution for injection 10ml PFS	Currently in-stock , anticipated to last until mid-September. A further OOS period is then envisaged until the next delivery that is scheduled to arrive in early/mid-September*.
Bayer Plc	Gadovist 1mmol/ml solution for injection 15ml vials	Currently in-stock . It is anticipated that current stock levels will be sufficient until the first week of September, followed by a short OOS period until the next planned delivery at the end of September*.
Bayer Plc	Gadovist 1mmol/ml solution for injection 5ml PFS	Currently, in-stock , it is anticipated that stock will provide cover until mid-November ; however, it is possible that restricted/interrupted supply may continue thereafter until year-end.
Bayer Plc	Gadovist 1mmol/ml solution for injection 7.5ml PFS	Currently in-stock . The next delivery is scheduled for beginning of October*.
Guerbet UK	Dotarem 5ml vial; 10ml vial; 10ml PFS; 15ml vial; 15ml PFS; 20ml vial; 20ml PFS	All presentations in stock and Guerbet have enough stock to support the shortage
Bracco UK Ltd	ProHance 0.5mmol/ml 10ml PFS; 10ml vial; 15ml via; 17ml PFS; 20ml vial	All presentations in stock and Bracco have enough stock to support the shortage

Mivacron (mivacurium chloride) injection

- Aspen Pharma are out of stock of 20mg/10ml Mivacron until end of August 2019.
- Mivacron 10mg/5ml injection is available.
- There are alternative non-depolarising neuromuscular blocking drugs in the benzylisoquinolinium group available on the market. Please consult local anaesthetists for advice on switching between agents, if necessary.

Neurobloc (Botulinum Toxin Type B)

- Neurobloc (Botulinum Toxin Type B) will not be available until end of September due to the product being divested from Eisai to Sloan Pharma.
- DHSC has worked with the specialist importers and can confirm that unlicensed Botulinum Toxin Type B is available; lead times vary.

Oncaspar (pegaspargase) 750 U/ml solution for injection/infusion

- Servier will be supplying Oncaspar in Irish packaging from July until October 2019 due to supply issues with the UK packaging.
- There is no difference to the product. Differences in the packaging and the PIL are detailed on the Dear Healthcare Professional letter (attached).

Tetracosactide 1mg depot injection

- Mallinckrodt have informed DHSC that tetracosactide 1mg depot injection will be unavailable until the second half of 2019.
- Specialist importers have sourced an unlicensed product.
- NHS Trusts should continue to order unlicensed stock from the specialist importers. Further information has been circulated to regional procurement specialists.

COMMERCIAL-SENSITIVE

Urokinase injection

- Syner-med are currently out of stock of urokinase strengths, 10,000unit, and 100,000 unit, with limited supplies of 25,000IU. Further detail is provided below:
 - 10,000IU – further stock available late September;
 - 25,000IU – in stock; supply restrictions to remain in place until late September to ensure stock remains available.
 - 100,000IU – further stock available late September.
- We are aware that unlicensed imports are not readily available or in sufficient quantities to fully meet demand during this time and therefore Trusts are asked to review their current usage of urokinase and consider using an alternative product. Details of suggested alternative products can be found in a memo produced by UKMi (see below).
- <https://www.sps.nhs.uk/articles/shortage-of-urokinase-injection-syner-kinase-10000-iu-25000-iu-and-100000-iu-powder-for-solution-for-injection-or-infusion/>
- We have been in contact with all the suppliers of the suggested alternatives and can confirm that they have sufficient supplies available to support during this time.
- Additional information for the product Taurolock is also attached. If you would like to place orders for this product, please contact customerservice@kimal.co.uk and copy louise.kelly@kimal.co.uk

Orals

Actiq (fentanyl) lozenges

- Teva are experiencing supply issues with several strengths of Actiq lozenges with no supplies of the 200mcg, 400mcg or 600mcg strength available until end of August. All other strengths remain available.
- Immediate release fentanyl products are not interchangeable and when considering switching patients from one product to another, patients should not be converted on a microgram per microgram basis from one to another; it is necessary to titrate the new formulation with advice from a specialist.
- See the link below for advice from UKMI:
<https://www.sps.nhs.uk/articles/shortage-of-actiq-lozenges-and-instanyl-nasal-spray-immediate-release-fentanyl-citrate/>

Adalat (nifedipine) tablets/capsules

- As previously communicated, there are ongoing supply issues with the Adalat range. We have been in contact with generic suppliers and can confirm that supplies are available with additional deliveries expected in the coming weeks.
- Please see the attached letter from Bayer and the shortages memo from UKMI:
<https://www.sps.nhs.uk/articles/shortage-of-adalat-nifedipine/>

Ammonaps (sodium phenylbutyrate) 940mg/g granules

- SOBI, the sole supplier of Ammonaps (sodium phenylbutyrate) 940mg/g granules, has had an interruption in supply due to a change in the marketing authorisation holder.
- Currently, they are unable to advise on a resupply date.
- Ammonaps (sodium phenylbutyrate) 500mg tablets continue to remain available.
- As per UKMI advice, for those patients that are unable to take tablets, Ravicti 1.1g/ml (glycerol phenylbutyrate) liquid is available, **please note** a dose conversion is required.

COMMERCIAL-SENSITIVE

- Specialist input should be sought prior to switching a patient.
- If switching a patient to Ravicti 1.1g/ml liquid is deemed appropriate; prescribers should consult the dose conversion guidance closely as outlined in the Ravicti SPC and patients should be counselled about the administration of the new formulation.
- Please see the link below for the Ravicti 1.1g/ml (glycerol phenylbutyrate) liquid SPC:
<https://www.medicines.org.uk/emc/product/2494/smpc>

Bumetanide 5mg tablets

- Mylan, the sole supplier of bumetanide 5mg tablets, have informed DHSC they are out of stock of this strength with next deliveries planned for early September 2019.
- Supplies of the 1mg tablet remain available.
- There is a bumetanide 1mg/5ml liquid available from Chemidex however there is insufficient stock to cover an uplift in demand.

Carbagen (carbamazepine) various preparations

- As carbamazepine is considered a Category 1 anti-epileptic medication, patients should normally be maintained on the same brand, however Mylan (manufacturers of Carbagen) have informed DHSC that the following preparations of Carbagen will be unavailable until late 2019.
- The affected products are:
 - Carbagen 200mg and 400mg immediate release tablets – unavailable until late 2019
 - Carbagen 200mg and 400mg modified release tablets – unavailable until late 2019
- Patients currently prescribed Carbagen tablets by brand will therefore need to be switched to an alternative brand of carbamazepine tablets during this time.
- Novartis, the manufacturer of Tegretol tablets, which is the alternative brand of carbamazepine, have confirmed that all presentations are currently available that they are able to support additional demand during this time for all affected strengths and formulations.
- DHSC have worked with NHSE, NHSI and UK Medicines Information to develop a clinical memo, which has been produced to support clinicians in prioritising and switching patients. This is available on the SPS website via the following link: <https://www.sps.nhs.uk/articles/shortage-of-carbagen-carbamazepine-tablets/>

Cardura (doxazosin) XL tablets

- Pfizer have a supply issue with of Cardura XL 4mg and 8mg tablets. Further stock is expected mid-August 2019.
- Pfizer are the sole UK supplier of Cardura XL 8mg tablets but supplies of doxazosin XL 4mg tablets are available from alternative suppliers.

Cefuroxime 125mg/5ml suspension (Zinnat)

- GSK the sole supplier of cefuroxime 125mg/5ml suspension will be out of stock until end August 2019.
- Cefuroxime 125mg tablets are available from GSK.
- UKMI have advised that tablets can be crushed and dispersed for oral administration. However, please note that doing so is considered off-label use.

Disopyramide 100mg tablets

- All UK suppliers of disopyramide 100mg tablets are out of stock. Sanofi will have stock available in wholesalers by end of August; Mylan are currently unable to provide a date for resupply.

COMMERCIAL-SENSITIVE

- A supply disruption alert has been issued via MHRA's CAS, which includes information on the issue and actions to be taken. Please see link below:
<https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102869>

Epanutin (phenytoin) 30mg/5ml oral suspension

- DHSC are aware of a supply issue with Epanutin oral suspension by Pfizer.
- Please see below for a link to the CAS alert:
<https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102868>
- You can sign up to receive Supply Disruption Alerts directly from the Medicine and Healthcare Regulatory Agency's Central Alerting System (CAS) by sending an email to: safetyalerts@mhra.gov.uk and requesting this facility.

Epanutin (phenytoin) 50mg Chewable Infatabs

- Pfizer have a temporary supply issue with Epanutin Infatabs until November 2019 due to a delay in manufacturing.
- To help mitigate the shortage Pfizer has obtained approval from the MHRA to import stock of Dilantin (phenytoin) Infatabs from Canada.
- Canadian packs of Dilantin are considered as an unlicensed product in the UK. A copy of the product information and the DHCP letter can be found attached to this update.
- Epanutin 30 mg/5 ml Oral Suspension is currently experiencing a supply issue (see above) and as such patients should not be switched to Epanutin Oral Suspension.

Heminevrin (clomethiazole) 192mg capsules

- Cheplapharm, the sole supplier of Clomethiazole 192mg Capsules have a short-term supply issue due to packaging issues.
- Cheplapharm anticipate the resupply date to be the end of September.
- They manufacture Heminerin (Clomethiazole) 31.5mg/ml syrup, however, there is insufficient supplies to meet any additional demand.
- We have been working with the importers who have confirmed that limited supplies are available – hospitals requiring stock should place orders NOW for unlicensed imports as lead times will vary.
- UKMI have prepared the following shortages memo, which has been published on the SPS website:
<https://www.sps.nhs.uk/articles/shortage-of-heminevrin-clomethiazole-192-mg-capsules/>

Hormone Replacement Therapy products (HRT)

FemSeven Products

- Theramex, the supplier of FemSeven Conti and Sequi patches are experiencing long term supply issues affecting both products and expect to be out of stock until late 2019.
- This supply issue does not affect supplies of FemSeven Mono.
- Supplies of other HRT patches and products continue to remain available.

Evorel Products

- Janssen-Cilag, the supplier of the Evorel transdermal patches has confirmed that supplies of all presentations are currently available.
- However, where supplies for the Evorel 50 and Evorel Conti (24 pack size) are lower than normal, the supplier is applying restrictions on orders as a precaution to ensure stock is maintained.
- Supplies of other HRT patches and products also continue to remain available.

COMMERCIAL-SENSITIVE

Elleste Range

- Mylan, the sole manufacturer of the Elleste HRT product line has reported that some of the Elleste range (Elleste Solo 1mg and 2mg; Elleste Duet 1mg,) are currently unavailable due to manufacturing issues.
- The resupply date for the Elleste range is now expected to be from end of July to the middle of August.
- As per UKMi advice, please see the table below for equivalent oral alternatives currently available on the market, if required.

Table 1. Equivalent HRT alternatives for the Elleste HRT range

Brand	Ingredient(s)	Current Availability	Equivalent	Ingredient(s)	Current Availability
Elleste Solo 1mg	estradiol hemihydrate	OOS	Progynova 1mg	estradiol hemihydrate	In stock
			Zumenon 1mg		OOS
Elleste Solo 2mg	estradiol hemihydrate	Out of Stock	Progynova 2mg	estradiol hemihydrate	In stock
			Zumenon 2mg		OOS
Elleste Duet Conti	estradiol 2mg/ norethisterone 1mg	In stock at wholesalers	Kliofem	estradiol 2mg/ norethisterone 1mg	In Stock
Elleste Duet 1mg	estradiol 1mg/ norethisterone 1mg	OOS	NovoFem	estradiol 1mg/ norethisterone 1mg	In Stock

Indivina (Estradiol/ Medroxyprogesterone) 2mg/5mg tablets

- Orion, the sole manufacturer of Indivina 2mg/5mg HRT tablets have reported that they will be out of stock of this strength until end of August 2019.
- Orion have advised there is sufficient stock of Indivina 1mg/2.5mg tablets (lower strength) to cover an uplift in demand until the higher strength is back in stock.
- Please note: patients normally prescribed the higher strength of Indivina (2mg/5mg), would require two tablets of the lower strength (1mg/2.5mg) to ensure equivalence.

Joyrides (Hyoscine Hydrobromide 150 microgram Tablets)

- Teva have a manufacturing issue and are currently out of stock until mid-August 2019.
- Bayer also supply this product (Kwells Kids) and are in stock and aware of the issue.

Metoprolol 50mg and 100mg tablets

- There are ongoing supply issues affecting metoprolol 50mg and 100mg tablets.
- The issue has been caused by some manufacturers discontinuing the products and others having supply difficulties.
- Milpharm/Aurobindo, are currently the sole supplier of both presentations to the UK market.
- Supplies of both presentations are currently available but may be limited, supply is likely to be intermittent for several months.
- Please see the link below for a memo developed by UK Medicine Information with input from clinical experts at NHSE and NHSI, which advises on management options for patients affected by this supply issue, including the use of alternative beta blockers, dosing information for these alternative beta blockers and monitoring requirements. <https://www.sps.nhs.uk/articles/shortage-of-metoprolol-50mg-and-100mg-tablets/>

COMMERCIAL-SENSITIVE

- The manufacturer of carvedilol has indicated it would be unable to meet demand if patients were switched to this product. Manufacturers of bisoprolol, atenolol and propranolol have indicated they have capacity to support any additional demand on their products.

Nitrous Oxide and Entonox

- BOC have experienced recent manufacturing issues with Nitrous Oxide and Entonox.
- Stock of both products is currently being closely managed and lead times for delivery has been reduced to two days.
- BOC have provided an updated Dear HCP which is attached.
- If Trusts are having difficulty obtaining stock, they are advised to contact their local BOC account managers.

Olena (fluoxetine) 20mg dispersible tablets

- Advanz Pharma, the sole manufacturer of fluoxetine 20mg dispersible tablets, are currently out of stock; further supplies are expected in October 2019.
- An oral solution, fluoxetine 20mg/5ml, is available from alternative manufacturers.

Oral Contraceptive Pill products (OCP)

Loestrin 20 and Loestrin 30 tablets

- Galen Limited are currently out of stock Loestrin 20 tablets and anticipate they will go out of stock of Loestrin 30 tablets at the beginning of June and are currently unable to provide a resupply date.
- Galen Limited have produced the attached *Dear Health Care Professional* letter providing further details on the issue.

Noriday (norethisterone) 350 micrograms tablets

- Pfizer, the supplier of the oral contraceptive pill, Noriday, have advised that due to a delay at the manufacturing site, it will be out of stock until end of September.
- UKMI have advised that there are no exact equivalent preparations in the UK market and clinicians should refer to CKS guidance for advice on alternative POPs:
<https://cks.nice.org.uk/contraception-progestogen-only-methods#!scenario:>

Norimin (ethinylestradiol/norethisterone) 0.035mg/1mg tablets

- Pfizer, the supplier of the OCP Norimin, have advised due to delay at the manufacturing site, Norimin will be OOS until the end of September.
- UKMI have advised that there are no exact equivalent preparations to Norimin available in the UK market.
- Other ethinylestradiol and norethisterone OCP products should be available.
- Clinicians are advised to refer to CKS guidance for advice COCs:
<https://cks.nice.org.uk/contraception-combined-hormonal-methods>

Ovranette (ethinylestradiol 30 mcg/levonorgestrel 150mcg) tablets

- Due to capacity constraints, Pfizer will be out of stock of Ovranette tablets from early June until end of August 2019.
- Patients who do not have sufficient supply of Ovranette tablets to last throughout the affected period should be prescribed Rigevidon, Levest, E Levin or Microgynon 30 tablets, if clinically appropriate.
- Prescribers are advised not to switch to Microgynon 30 ED, Leandra or Maexeni during the affected period as they are unable to support.

COMMERCIAL-SENSITIVE

Questran Powder for Oral Suspension

- Bristol-Myers Squibb (BMS) divested the entire Questran range to Cheplapharm at the end of July 2019.
- Cheplapharm are out of stock of Questran Powder 4g sachets until mid-2020.
- Supplies of Questran Light are currently available through Alliance Healthcare.

Stemetil (prochlorperazine) 5mg in 5ml oral syrup

- Sanofi are out of stock of Stemetil oral syrup until end of November 2019.
- Other presentations of prochlorperazine remaining are:
 - Buccal (maleate) 3mg
 - Injection (mesylate) 12.5mg
 - Tablets (maleate) 5mg
- UKMI have prepared the following shortages memo, which provides potential advice on management options:
<https://www.sps.nhs.uk/articles/shortage-of-stemetil-prochlorperazine-5mg-5ml-syrup/>

Trifluoperazine tablets

- There have been ongoing manufacturing issues affecting trifluoperazine 1mg and 5mg tablets causing long term issues with supplies not expected before mid-2020.
- Concordia and Rosemont have trifluoperazine liquid and good supplies are available.
- We are aware that unlicensed supplies of the 1mg and 5mg tablet are available from both Ennogen and several other specialist importer companies.

Others

Dalacin (clindamycin) 2% vaginal cream

- Pfizer, sole supplier of clindamycin 2% vaginal cream, are out of stock until end of August due to delays in packaging.
- There are two other topical products licensed for the treatment of bacterial vaginosis:
 - Zidoval (metronidazole 0.75% w/w) vaginal gel (one application [5g] inserted into the vagina once daily, at bedtime, for 5 consecutive days)
 - Fluomizin (dequalinium chloride 10 mg) vaginal tablets (one vaginal tablet daily, at bedtime, for 6 days)
- Please refer to local formulary and guidelines for management of bacterial vaginosis which also cover systemic therapies. CKS guidance is also available: <https://cks.nice.org.uk/bacterial-vaginosis>

Instanyl (fentanyl) nasal spray

- Takeda are currently out of stock of some strengths of Instanyl nasal spray with resupply date as follows: 100mcg mid-September; 200mcg mid-September.
- Instanyl 50mcg nasal sprays are available.
- Immediate release fentanyl products are not interchangeable and when considering switching patients from one product to another, patients should not be converted on a microgram per microgram basis from one to another; it is necessary to titrate the new formulation with advice from a specialist.
- See the link below for advice from UKMI:

COMMERCIAL-SENSITIVE

<https://www.sps.nhs.uk/articles/shortage-of-actiq-lozenges-and-instanyl-nasal-spray-immediate-release-fentanyl-citrate/>

Prostin E2 (dinoprostone) 3mg Vaginal Tablet

- Pfizer are out of stock of Prostin E2 vaginal tablets until end-August.
- Below are the medicinal products and devices that may be considered alternatives to the dinoprostone 3mg vaginal tablet and a summary of their availability:

Product (brand)	MAH	Availability	Notes
Significant support available			
Dinoprostone (Prostin E2) 1mg vaginal gel	Pfizer	Able to support vaginal tablet shortage	Not bioequivalent to vaginal tablet, please refer to SPC for further detail and see Pfizer comparison summary (attached)
Dinoprostone (Prostin E2) 2mg vaginal gel	Pfizer	Able to support vaginal tablet shortage	Not bioequivalent to vaginal tablet, please refer to SPC for further detail and see Pfizer comparison summary (attached)
Imported Dinoprostone (Prostin E2) 3mg vaginal tablet	Unlicensed import	Good availability, currently approximately 40-60% of usage. Ordering imports may stimulate importers to source further stock from other markets.	Further information will be circulated from regional procurement leads. Please note lead times are approximately 2 weeks.
Limited support available			
COOK Cervical Ripening Balloon	Cook Medical	Can make additional stock available to cover 10-25% of usage.	Consider training requirement if Trust has no experience of using this product. Please contact Cook Medical (detail below) for further information and support with training as well as to inform them of your preference for their product and the likely quantities required. Leisl de Lafontaine, Senior Area Manager, COOK Medical +44 7766 426154 +44 207 365 4183 leisl.delafontaine@cookmedical.com
Not able to support market – do NOT order above forecasted demand			
Dinoprostone (Propess) 10mg vaginal delivery system	Ferring	Not able to support uplift in demand	Unable to uplift volumes due to long lead times and storage requirements. Any ordering in excess of forecasted demand could precipitate an out of stock on this line.
Misoprostol (Mysodelle) 200mcg vaginal delivery system	Ferring	Not able to support uplift in demand	Unable to uplift volumes due to long lead times and storage requirements. Any ordering in excess of forecasted demand could precipitate an out of stock on this line.

COMMERCIAL-SENSITIVE

Skinoren (azelaic acid) 20% cream

- Bayer, sole suppliers, are out of stock of Skinoren 20% cream with resupply expected in mid-October 2019. The license will be transferred to Leo Pharma from 1st July 2019.
- UKMI has provided the following advice on alternative options:
 - Azelaic acid has antimicrobial and anticomedonal properties and is considered less likely to cause local irritation than benzoyl peroxide; it is an alternative in facial acne if benzoyl peroxide or topical retinoid poorly tolerated.
 - There are other topical products available and choice will be determined by what patient has already tried/ tolerated. Systemic treatments are also an option
 - Please refer to local formulary or to following guidelines for alternative treatment options:
 - NICE Clinical Knowledge Summary (April 2018): <https://cks.nice.org.uk/acne-vulgaris#!scenarioRecommendation>
 - Primary Care Dermatology Society (April 2019): <http://www.pcds.org.uk/clinical-guidance/acne-vulgaris#management>

Tilade (nedocromil sodium 2mg/dose) Inhaler

- Sanofi are the sole supplier of Tilade inhaler and are currently out of stock until late November.
- UKMI have advised that Intal (Sodium Cromoglicate-5mg/dose) is interchangeable and we have confirmed with Sanofi that sufficient stock is available.
- Please note differences in maintenance doses for these inhalers: -
 - Sodium cromoglicate (Intal) - Initially TWO puffs (10 mg) four times a day, additional dose may also be taken before exercise, increased if necessary, to TWO puffs (10 mg) six to eight times a day. Maintenance dose is ONE puff (5 mg) four times a day.
 - Nedocromil sodium (Tilade)- Initially TWO puffs (4 mg) four times a day, when control achieved, may be possible to reduce to twice daily.
 - For further information visit: <https://cks.nice.org.uk/asthma#!prescribingInfoSub:21>

Eye drops/treatments

Allergan

Lacri-Lube - out of stock due to an ongoing manufacturing issue. Allergan are unable to provide a re-supply date at this stage.

The Royal College of Ophthalmology is aware of the Lacri-Lube shortage and is recommending Xailin Night Ointment. <https://www.rcophth.ac.uk/standards-publications-research/quality-and-safety/medicines-safety/drugs-shortages/>.

RPH Pharmaceuticals AB

Betnesol Eye Ointment 0.1% w/w x 3g - RPH Pharmaceuticals AB, who distribute this product through Focus Pharmaceuticals, have advised about the discontinuation of Betnesol Eye Ointment 0.1% w/w x 3g and plan to launch a generic Betamethasone Eye Ointment 0.1% w/w x 3g towards the end of 2019.

Betnesol (betamethasone 0.1%) eye/ear/nose drops - RPH Pharmaceuticals are currently out of stock of betamethasone 0.1% eye/ear/nose drops with a resupply date of late 2019. Martindale Pharma can support the full market during this time.

Vaccines

COMMERCIAL-SENSITIVE

For updates on other vaccine supply position, please refer to PHE's Vaccine Update Bulletin found at the following address:

<https://www.gov.uk/government/collections/vaccine-update#2019>

Hepatitis B Vaccines

Renal dose

- MSD's renal vaccine HBVAXPRO 40micrograms are still out of stock of until further notice. Please see statement: <http://www.msduk.com/products/vaccines.xhtml>.
- GSK's Hepatitis B renal vaccine, Fendrix, is currently available.

Adult dose

- MSD are out of stock HBVAXPRO 10mcg vaccine until further notice
- GSK are confident they can support the increased demand during this time.

Menveo (meningitis A, C, W, Y):

- GSK have confirmed there is limited supply of Menveo.
- Pfizer have confirmed they are in stock of Nimenrix and currently able to support increased demand.

Rabipur (Rabies vaccine)

- Limited supply of GSK's Rabipur is currently available. Supply issues resulting from manufacturing constraints have now resolved, however, GSK do not expect the situation to fully normalise until late 2019.
- Sanofi Pasteur have confirmed they are able to support the full market during this time with their unlicensed Rabies vaccine, Verorab
- NATHNAC have issued further information available at the following link: <https://travelhealthpro.org.uk/news/389/rabies-vaccine-availability>

Discontinuations

Buplast (buprenorphine) patches (Accord)

- Accord is discontinuing Buplast (buprenorphine) patches from the UK market but stock is currently available.
- Buprenorphine patches remain available from a number of other suppliers.

Cilest (norgestimate 250mcg and ethinylestradiol 35mcg) (Janssen-Cilag)

- Janssen Cilag is discontinuing Cilest (norgestimate 250 mcg and ethinylestradiol 35 mcg) and expects stocks to be exhausted by the end of July
- We have been in contact with other suppliers of norgestimate 250 mcg and ethinylestradiol 35 mcg and have confirmed that the alternatives Cilique (Consilient) and Lizianna (Morningside) are both fully available and able to meet any increase in demand.

Copegus (ribavirin) 200mg & 400mg tablets (Roche)

- Roche is discontinuing the Copegus (ribavirin) tablet range from the UK market from September 2019 due to low volume sales; generic ribavirin tablets remain available from other suppliers.

COMMERCIAL-SENSITIVE

Finasteride 1mg tablets x 84 (Accord)

- Accord is discontinuing finasteride 1mg tablets in the 84 pack with immediate effect, however, they will continue to market the 28-tablet pack.

Modecate (fluphenazine decanoate) injection

- Manufacture of Modecate (fluphenazine decanoate) injection has ceased
- Existing stock of Modecate Injection (25 mg/ml) will expire in August 2019 – supplies should be ordered now to treat any patients who have yet to be switched to an alternative treatment.
- Existing stock of Modecate Concentrate Injection (100 mg/ml) will expire in August 2020 – stock will not be released after 29 February 2020.
- Prescribers should complete arrangements to transfer patients on Modecate to therapeutic alternatives under medical supervision.
- Some unlicensed importer companies have confirmed that they can source supplies of unlicensed fluphenazine decanoate injection from abroad going forward.

Myocrisin (sodium aurothiomalate) injection (Sanofi)

- Sanofi is discontinuing Myocrisin 20mg/ml & 100mg/ml Injection in the UK, due to an API compliance issue which they are unable to overcome and manufacturing has now ceased
- Existing stock of Myocrisin Solution for injection (100 mg/ml) will last until the end of June 2019 – (based on current pattern of use)
- Existing stock of Myocrisin Solution for injection (20 mg/ml) are likely to last until end of July 2019 – (based on projected pattern of use)
- The company is recommending that no new patient should commence treatment with Myocrisin injection
- Sanofi advice that prescribers should complete arrangements to transfer patients on Myocrisin to suitable therapeutic alternatives under medical supervision

COMMERCIAL-SENSITIVE

Resolved (date resolved)

Ancotil (flucytosine) injection (16/07/19)
Bezalip (bezafibrate) 200mg tablets (5/8/19)
Elleste Solo MX 40microgram and 80microgram patches (31/7/19)
Diamorphine 5mg injection (5/8/19)
Hiprex (methenamine hippurate) 1g tablets (25/07/19)
Hypovase (prazosin) 0.5mg tablets (4/7/19)
Idarubicin 5mg injection (5/8/19)
Instanyl (fentanyl) 50mcg nasal spray (23/7/19)
Magnevist (09/07/2019)
Marcain Heavy (bupivacaine hydrochloride anhydrous) 0.5% injection (18/7/19)
Midazolam injection (7/19)
Mivacron (mivacurium chloride) injection (2/8/19)
Thorens (colecalfiferol) 10,000i.u./ml oral drops (8/7/19)
Salbutamol 2mg/5ml syrup (11/7/19)
Pneumococcal Polysaccharide Vaccine (16/07/19)