

COMMERCIAL-SENSITIVE

## **Supply Issues Update for Primary and Secondary Care: June 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 as it may be commercially sensitive; 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	Ongoing Issues .....	7
Injectables .....	3	Injectables .....	7
Diamorphine 5mg injection .....	3	Ancotil (flucytosine) injection .....	7
Voriconazole 200mg injection .....	4	Arsenic acid .....	7
Orals .....	4	Dimercaprol 50mg/ml injection .....	8
Actiq (fentanyl) lozenges .....	4	EpiPen and EpiPen Junior .....	8
Bezalip (bezafibrate) 200mg tablets .....	5	Erwinase injection .....	8
Cardura (doxazosin) XL tablets .....	5	Fentanyl 50mcg/ml 2ml injection .....	8
Epanutin (phenytoin) 30mg/5ml oral suspension .....	5	Fludarabine 50mg/2ml injection .....	8
Heminevrin (clomethiazole) 192mg capsules .....	5	Gadovist preparations .....	9
Hiprex (methenamine) 1g tablets .....	6	Idarubicin injection .....	9
Hypovase (prazosin) 0.5mg tablets .....	6	Midazolam injection .....	10
Megace (megestrol) 160mg tablets .....	6	Mivacron (mivacurium chloride) injection ..	10
Microgynon 30 (ethinylestradiol 30 mcg/levonorgestrel 150mcg) tablets .....	6	Neurobloc (Botulinum Toxin Type B) .....	11
Ovranette (ethinylestradiol 30 mcg/levonorgestrel 150mcg) tablets .....	6	Pentamidine 300mg in 5mL injection .....	11
Others .....	6	Tetracosactide 1mg depot injection .....	11
Dalacin (clindamycin) 2% vaginal cream .....	6	Urokinase injection .....	11
Instanyl (fentanyl) nasal spray .....	7	Orals .....	11
Sancuso (granisetron) transdermal patches 3.1mg/24hours .....	7	Adalat (nifedipine) tablets/capsules .....	11
		Bumetanide tablets .....	12
		Carbagen (carbamazepine) various preparations .....	12
		Cycloserine 250mg capsules .....	12

## COMMERCIAL-SENSITIVE

Epanutin (phenytoin) 50mg Chewable Infatabs .....	12	Discontinuations .....	18
Hormone Replacement Therapy products (HRT) .....	13	Diflucan (fluconazole) 200mg/100ml solution for infusion (Pfizer) .....	18
Labetalol tablets .....	13	Lartruvo (olaratumab) (Lilly) .....	18
Lofexidine tablets .....	14	Memantine initiation pack (Accord) .....	18
Metopirone 250mg capsules .....	14	Modecate (fluphenazine decanoate) injection .....	18
Metoprolol 50mg and 100mg tablets.....	14	Refolinate (calcium folinate) 30mg/10ml injection (Pfizer).....	18
Olena (fluoxetine) 20mg dispersible tablets	15	Zeridame SR (tramadol) prolonged release tablets (Accord).....	18
Questran Powder for Oral Suspension/Questran Light (colestyramine) 4g sachets .....	15	Resolved (date resolved) .....	18
Sandimmun (ciclosporin) capsules .....	15	• Fusidic Acid 1% Viscous Eye Drops 04/6/19).....	18
Sinemet (co-careldopa) tablets .....	15	• Gastrografin (5/19) .....	18
Stemetil (prochlorperazine) 5mg in 5ml oral syrup .....	16	• Iopidine (apraclonidine hydrochloride) 0.5% eye drops (22/5/19) .....	18
Thorens (colecalfiferol) 10,000i.u./ml oral drops.....	16	• Methadone 1mg/ml oral solution (sugar free) (3/6/19) .....	18
Tizanidine 4mg tablets.....	16	• Microgynon 30 tablets.....	18
Trifluoperazine tablets .....	16	• Qlaira tablets (21/5/19) .....	19
Eye drops/treatments .....	16	• Rifadin (rifampicin) 300mg capsules (16/5/19).....	19
• Lacri-Lube .....	16	• Sabril (vigabatrin) 500mg tablets (06/19) 19	
• Betnesol Eye Ointment 0.1% .....	16	• Sinemet (co-careldopa) 10/100mg tablets (17/5/19).....	19
• Betnesol (betamethasone 0.1%) eye/ear/nose drops .....	17	• Vibramycin D (doxycycline) dispersible tablets (20/5/19).....	19
Vaccines.....	17	• Zolmitriptan 2.5mg orodispersible tablets (1/5/19).....	19
Hepatitis B Vaccines .....	17		
Menveo.....	17		
Pneumococcal Polysaccharide Vaccine .....	17		
Rabipur (Rabies vaccine) .....	17		

COMMERCIAL-SENSITIVE

## **Information provided w/c 3<sup>rd</sup> June 2019**

### New Issues

#### Injectables

##### Diamorphine 5mg injection

- DHSC and NHSE have been notified by Accord and Wockhardt that they are experiencing issues with the manufacture and availability of diamorphine 5mg injection.
- We are likely to go out of stock of diamorphine 5mg injection by 27 May 2019 with a resupply date of w/c 5<sup>th</sup> August 2019. All other strengths of diamorphine injection are available.
- After consulting with all key stakeholders and the national Medicine Shortages Response Group (MSRG), we have developed the following management plan below, which differs for primary and secondary care.
- For any concerns around patient safety, please contact your local Medication Safety Officer who will escalate to Nicola Wake (Medication Safety Lead, Specialist Pharmacy Service).

##### **Primary care, private hospitals, hospices and substance misuse treatment centres**

- There is sufficient diamorphine 10mg injection to support forecasted use of diamorphine 5mg injection. Diamorphine will be available to order from usual wholesalers.

##### **Recommended Local Action for Primary Care:**

- Please share this information with relevant networks locally including GP practices, community pharmacies and substance misuse networks.
- Prescribers should be made aware that only diamorphine 10mg ampoules will be available during this period and ensure that prescriptions specify this preparation. Prescribers should take extra care when calculating the dose to be administered.
- Locally, health care professionals should follow local controlled drug policies for the safe management and disposal of excess waste of diamorphine during this time and should ensure that:
  - Any wastage should be rendered irretrievable and must be disposed of.
  - Clear records should be kept of what was administered, and what was discarded and should be witnessed wherever possible.
  - Please work with your Controlled Drug Accountable Officer where necessary.

##### **Secondary care NHS trusts in UK**

- There is insufficient diamorphine 10mg injection to support secondary care use of diamorphine 5mg injection. Any overordering of the 10mg injection will lead to this presentation going out of stock.
- Hameln's morphine 10mg injection (preservative free) should be considered first line alternative and is available to order direct from Hameln.
- Other opioids are available to support this supply issue but should only be used following approval by regional procurement lead.
- The following UKMI clinical memo has been developed to support with the use of alternatives: <https://www.sps.nhs.uk/articles/shortage-of-diamorphine-5mg/> provides more information about the alternatives to diamorphine, the first line agent being Morphine injection.

COMMERCIAL-SENSITIVE

**Recommended Local Action for secondary care:**

- Discuss this supply issue with clinical colleagues and review and share UKMI guidance.
- Do not consider using other presentations of diamorphine to cover shortfall as there are insufficient stocks to support this supply issue.
- Consider reserving available supplies of diamorphine 10mg injection for priority areas.
- Morphine 10mg injection (Hameln) will be available to cover the diamorphine 5mg injection shortfall and should be considered first line. Continue to order morphine 10mg injection from Martindale in line with historic demand. Martindale CANNOT support increased orders.
- Please only order to cover existing demand and shortfall. Do not stock pile as this will lead to issues with other Trusts accessing stock. Please consider how you will manage having two morphine 10mg injection presentations in your departments.
- Please let your regional procurement specialist know of any local issues or if you are considering using an alternative other than morphine.
- If your Trust supports any local hospices with diamorphine injection, please discuss with your regional procurement lead who will review your allocation.

Voriconazole 200mg injection

- Pfizer, sole supplier of this product, currently have very limited supplies of voriconazole 200mg injection until mid-July 2019.
- Limited stock remains at wholesalers. Once the wholesaler stock is exhausted within NHS Trusts please contact your regional procurement specialist who may be able to facilitate stock sharing between Trusts.
- 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.

Adrenaline 1:1000 1mL ampoules

- Martindale are currently out of stock of adrenaline 1:1000 1mL ampoules with a resupply date of 7<sup>th</sup> June 2019.
- Hameln have confirmed that during the period where Martindale are out of stock, they are able to supply to the whole market.
- If Hameln stock is required hospitals should place orders directly with the manufacturer. Hameln will provide the wholesalers with stock for use within primary care.

## Orals

Actiq (fentanyl) lozenges

- Teva are experiencing supply issues with several strengths of Actiq lozenges with no supplies of the 200mcg or 400mcg strength available until mid-July. 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/>

COMMERCIAL-SENSITIVE

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.
- 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>

Bezalip (bezafibrate) 200mg tablets

- Teva, sole suppliers, are currently out of stock of bezafibrate 200mg tablets until mid/end July 2019.
- A clinical memo from UKMI will be published on the SPS website shortly.

Cardura (doxazosin) XL tablets

- Pfizer have a supply issue with of Cardura XL 4mg and 8mg tablets. Further stock is expected at the end of 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.

Constella (Linaclotide) 290microgram capsules

- Allergan, the sole supplier of Constella are experiencing a short-term European wide supply issue as a result of packaging difficulties at their primary and secondary sites.
- Allergan anticipate new supplies to become available at the end of June 2019.
- We are aware that parallel imports are available, and Pharmacies should be able to source supplies through their usual routes.

Epanutin (phenytoin) 30mg/5ml oral suspension

- DHSC are aware of a supply issue with Epanutin oral suspension by Pfizer.
- 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](mailto:safetyalerts@mhra.gov.uk) and requesting this facility.
- Please see below for a link to the CAS alert:  
<https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102868>

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 of mid-September.

#### COMMERCIAL-SENSITIVE

- They manufacture Heminerin (Clomethiazole) 31.5mg/ml syrup, however, there is insufficient supplies to meet any additional demand.
- A clinical memo from UKMI will be published on the SPS website shortly.

#### Hiprex (methenamine) 1g tablets

- Mylan, the sole supplier, have a delay in the delivery of methenamine 1g tablets.
- Stock should be available to order by Friday 7<sup>th</sup> June.

#### Hypovase (prazosin) 0.5mg tablets

- Pfizer are currently out of stock of Hypovase 0.5mg tablets until w/c 24<sup>th</sup> June 2019.
- Hypovase 1mg tablets are available; each 1mg tablet is scored and can be halved.

#### Megace (megestrol) 160mg tablets

- SOBI, sole distributors of megestrol tablets in the UK are out of stock until 31<sup>st</sup> July.
- National clinical experts have confirmed there are several other products available to treat the licensed indication but, if appropriate, unlicensed supplies of megestrol can be used.
- Unlicensed megestrol 160mg tablets are available from some specialist importers although lead times vary.
- Unlicensed megestrol 40mg tablets are also obtainable as an unlicensed import with several importers currently holding stock.
- A very limited supply of megestrol 160mg tablets is available for those patients for whom an alternative option is unsuitable. Pharmacies should contact Alloga directly on 01773 510123.

#### Microgynon 30 (ethinylestradiol 30 mcg/levonorgestrel 150mcg) tablets

- Bayer have since notified DHSC that following production improvements Microgynon 30 tablets are not expected to experience supply shortages and will be available at pharmacies as usual for the foreseeable future. Wholesalers were replenished from 31<sup>st</sup> May 2019.
- Please see the attached *Dear Healthcare Professional* letter for more information.

#### 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, Elevin 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.

## Others

#### Dalacin (clindamycin) 2% vaginal cream

- Pfizer, sole supplier of clindamycin 2% vaginal cream, are out of stock until mid-July due to delays in packaging.
- A clinical memo from UKMI will be published on the SPS website shortly.

## COMMERCIAL-SENSITIVE

### Instanyl (fentanyl) nasal spray

- Takeda are currently out of stock of all strengths of Instanyl nasal spray with resupply date as follows: 50mcg end June; 100mcg mid-July; 200mcg mid-September.
- 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/>

### Sancuso (granisetron) transdermal patches 3.1mg/24hours

- Kyowa Kirin, the sole supplier of granisetron patches have a supply issue due to delays in serialising the product.
- New stock is expected to be available w/c 10<sup>th</sup> June 2019.
- Limited supplies currently remain within the NHS and Trusts should consider stock sharing where appropriate.

## Ongoing Issues

### Injectables

#### Ancotil (flucytosine) injection

- Mylan, the sole supplier of flucytosine, have experienced a manufacturing delay with this product.
- They are currently out of stock; further stock is expected at the end of June 2019.
- There is stock availability within the NHS and information has been shared with regional procurement specialists to request they facilitate sharing between Trusts if stock is required urgently for a patient.
- Specialist importers have confirmed that they have sourced unlicensed stock and some specialist importers currently have stock available.

#### Arsenic acid

- Teva have advised of issues with Trisenox. Further supply is expected by the end of June 2019.
- Teva has decided to import into the UK an equivalent formulation containing 1mg/ml of arsenic trioxide (known as Phenasen by Phebra Pty Ltd) which is a licensed product from Australia but will be classified as an unlicensed product in the UK. This unlicensed product should be ordered directly from Teva.
- Further details can be found in the attached DHCP letter.
- Flexipharma Austrading Limited (FAL) have recently received MHRA approval for a new arsenic trioxide product and will be marketing under the name arsenic trioxide phebra. It is a vial presentation which is a generic of the originator product. This product was previously supplied under its Australian tradename/registration. Stock of this product is now available from Mawdsleys wholesaler.

## COMMERCIAL-SENSITIVE

### Dimercaprol 50mg/ml injection

- Advanz Pharma, sole supplier of this product, have advised that dimercaprol injection will be unavailable until July 2019.
- See the link below for advice by RCEM/NPIS on antidote availability in Emergency Departments: <http://scanmail.trustwave.com/?c=8248&d=k6Xu3H1CL5IR-wsS7AOdJI7vHz4ZQXW-N1bfd1XHWa&u=https%3a%2f%2fwww%2esps%2enhs%2euk%2farticles%2fregional-medicines-optimisation-committee-antidotes-and-rums-position-statement%2f>
- NHS Trusts should contact the NPIS for clinical advice if required.

### EpiPen and EpiPen Junior

- The supply situation for EpiPen and EpiPen Junior continues to improve, and further stock is due in the coming months.
- All preparations of EpiPen, Emerade and Jext adult and junior are currently available via wholesalers.
- 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/>

### 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 by early July 2019.
- 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.

### Fentanyl 50mcg/ml 2ml injection

- There have been recent issues affecting fentanyl injection:
  - Advanz remain out of stock until mid-June 2019.
  - Martindale are currently in stock with very limited supplies but are expecting further supplies w/c 10<sup>th</sup> June.

### Fludarabine 50mg/2ml injection

- Teva have a supply issue with fludarabine solution for injection and expect to have limited supplies until the next delivery in August due to API issues.
- Current 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.



## COMMERCIAL-SENSITIVE

### 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.

Manufacturer	Presentation	Stock Availability
Bayer Plc	Gadovist 1mmol/ml solution for injection 10ml PFS	Currently <b>OOS</b> until the next delivery that is scheduled to arrive in July*.
Bayer Plc	Gadovist 1mmol/ml solution for injection 15ml vials	Currently <b>in-stock</b> . It is anticipated that current stock levels will be sufficient to maintain an in-stock status until the next planned delivery in August*.
Bayer Plc	Gadovist 1mmol/ml solution for injection 5ml PFS	Currently <b>OOS</b> until the early August*.
Bayer Plc	Gadovist 1mmol/ml solution for injection 7.5ml PFS	Currently <b>OOS</b> . The next delivery is scheduled for mid-August*.
Bayer Plc	Magnevist 2mmol/l solution for injection 20 ml PFS	Currently <b>OOS</b> . Next delivery is due mid-July. However, anticipated stock quantities lead to the expectation that each delivery will be consumed by back-orders. Therefore, supply will continue to be significantly interrupted/reduced until at least Q3 2019.
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 vial; 17ml PFS; 20ml vial	All presentations in stock and Bracco have enough stock to support the shortage

\* Overall, it is anticipated that restricted supply will be likely to continue through Q2/Q3 2019, due to production problems.

### Idarubicin injection

- Pfizer are out of stock of idarubicin 5mg and 10mg injection due to a quality issue.
- Pfizer are working to bring an alternative ready to use formulation from Australia into the UK. Further communications will be issued to secondary care once we have more information about this product.
- We have been working with the importers who have confirmed that limited supplies are available from Europe and USA – hospitals requiring stock should place orders NOW for unlicensed imports as lead times will vary.
- Hospitals who have surplus stock have been asked to consider sharing supplies locally.
- The licensed powder for injection product should be available during July 2019.

## COMMERCIAL-SENSITIVE

### Midazolam injection

- The following midazolam presentation continues to have supply issues: Midazolam 1mg/ml solution for injection 5mg/5ml ampoules.
- There has been a delay in the Accord stock of the 5mg/5ml and we are also anticipating a further issue with Hameln supplies of the 5mg/5ml presentation.
  - Accord expect further supplies by the end of June.
  - Hameln expect further supplies w/c 17<sup>th</sup> June.
- We have confirmed that there is sufficient stock of **Midazolam (5mg/ml) 10mg/2ml** ampoules to support demand for the duration of this supply issue from Hameln and Accord.
- Other strengths are available, but suppliers have confirmed they cannot support this shortage with any other remaining presentations of midazolam injection as there is insufficient stock available to support an increase in demand.
- **We acknowledge this is a high-risk supply issue as per the Rapid Response Report published in 2008 regarding reducing the risk of overdose with midazolam injection in adults and the associated Never Event. The Rapid Response Report and Never Event framework can be found at the following links: [SPS website & Never Event framework](#)**

#### Local action required:

- Review remaining stock holdings of midazolam injection.
- In collaboration with the local Medication Safety Officer and relevant clinical leads, organisations need to undertake local risk assessment to reduce the risk of overdose. Please consider local actions in the following order:
  1. Risk assess supply of remaining stocks of midazolam injection; consider ring fencing supply to highest risk clinical area
  2. Collaborate and share stock locally where possible.
  3. Where appropriate, please consider alternative drugs for different clinical indications; especially conscious sedation.
  4. **Last line option:** If midazolam (5mg/ml) 10mg in 2ml is the only suitable alternative then a local risk assessment should be undertaken, and risk mitigation actions need to be considered; for example: named patient supply only, raising staff awareness that high strength midazolam is in use (e.g. use of posters / additional labelling). Consider additional checks when preparing and administering, ensure only one strength of midazolam is available in a clinical area (to avoid confusion). Please **do not** switch to any of the other remaining presentations of midazolam injection as there is insufficient stock available to support an increase in demand.
- **As is standard practice, please ensure that flumazenil injection is readily available in all areas where midazolam is used.**
- Please review local protocols and ensure that all those affected are aware of this issue and that particular consideration is given to mitigating the risks associated with switching to alternative higher strength midazolam presentations.

### Mivacron (mivacurium chloride) injection

- Aspen Pharma will be out of stock of 20mg/10ml Mivacron from 6<sup>th</sup> June 2019 to 9<sup>th</sup> August 2019
- Limited supplies of short-dated Mivacron 10mg/5ml ampoules currently remain available through Movianto. Expiry date is October 2019.
- Future deliveries are expected in July (5ml amps) and August (10ml amps).
- There are alternative non-depolarising neuromuscular blocking drugs in the benzyisoquinolinium group available on the market. Please consult local anaesthetists for advice on switching between agents.

## COMMERCIAL-SENSITIVE

### Neurobloc (Botulinum Toxin Type B)

- Neurobloc (Botulinum Toxin Type B) will not be available until late August/early September 2019 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.

### Pentamidine 300mg in 5mL injection

- Sanofi anticipate there will be a short term out of stock period of this product. Stock will be available 7<sup>th</sup> June 2019.
- Information about this issue has been cascaded to regional leads by NHS England Commercial Medicines Unit and information about availability of unlicensed imports has been shared with regional procurement leads.
- Trusts are asked to review current stock holdings to determine if stock will be required during the short term out of stock period and to place orders with specialist importers for the unlicensed product if stock is required during the out of stock period.

### 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.

### Urokinase injection

- Further to our previous communications on urokinase injection, Syner-med have now confirmed that all three urokinase strengths, 10,000unit, 25,000unit and 100,000 unit, are now **out of stock** and anticipated resupply dates are provided below:
  - 10,000IU – further stock available late September;
  - 25,000IU –further stock available mid-July;
  - 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](mailto:customerservice@kimal.co.uk) and copy [louise.kelly@kimal.co.uk](mailto:louise.kelly@kimal.co.uk)

## Orals

### Adalat (nifedipine) tablets/capsules

- As previously communicated, there are ongoing supply issues with the Adalat range. Generic supplies are available. Please see the attached letter from Bayer and the shortages memo from UKMi:

## COMMERCIAL-SENSITIVE

<https://www.sps.nhs.uk/articles/shortage-of-adalat-nifedipine/>

### Bumetanide 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 the end of July/early August 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 mid/late 2019.
- The affected products are:
  - Carbagen 200mg immediate release tablets – unavailable until mid-2019
  - Carbagen 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/>

### Cycloserine 250mg capsules

- King Pharmaceuticals have been supplying cycloserine 250mg tablets which expire on 31<sup>st</sup> May 2019.
- There has been a delay in supplies, but King have confirmed that new stock will be available 11<sup>th</sup> June 2019.
- We are working with King Pharmaceuticals to expedite the supply of cycloserine capsules and further updates will be shared once available.
- Some specialist importers are currently in stock of an unlicensed product. Contact your regional procurement leads for further information.

### 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.

## COMMERCIAL-SENSITIVE

### 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.

#### *Elleste Range*

- Mylan, the sole manufacturer of the Elleste HRT product line has reported that some of the Elleste range (Elleste Solo 1mg, 2mg; Elleste Duet Conti; Elleste Duet 1mg; Elleste Solo MX 40micrograms, 80micrograms patches) are currently unavailable due to manufacturing issues.
- The resupply date for the Elleste range is now expected to be the end of June 2019.
- 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	Out of stock	Progynova 1mg	estradiol hemihydrate	In Stock
			Zumenon 1mg		In Stock
Elleste Solo 2mg	estradiol hemihydrate	Out of Stock	Progynova 2mg	estradiol hemihydrate	In Stock
			Zumenon 2mg		In Stock
Elleste Duet Conti	estradiol 2mg/ norethisterone 1mg	Out of Stock	Kliefem	estradiol 2mg/ norethisterone 1mg	In Stock
Elleste Duet 1mg	estradiol 1mg/ norethisterone 1mg	Out of Stock	NovoFem	estradiol 1mg/ norethisterone 1mg	In Stock

#### *Labetalol tablets*

- There are two suppliers of labetalol tablets in the UK; Mylan and Recipharm.
  - Mylan have had a delay in resupply due to an internal delay in serialisation of FMD packs, further stock of the 100mg and 400mg tablets is expected end of June. The 200mg strength is available.
  - Recipharm have experienced an issue with the active pharmaceutical ingredient and are currently unable to provide a resupply date.
- Prescribers should be aware that no new patients should be commenced on labetalol during this time as there are currently very limited stocks available.

## COMMERCIAL-SENSITIVE

- Patients who do not have sufficient supplies of 100mg/400mg tablets to last until the resupply date and who are unable to obtain supplies of labetalol will need to be switched to an appropriate alternative treatment during this time.
- Please see link below to a memo developed by UK Medicines Information with input from national experts at NHSE and NHSI, which advises on management options for patients, including the use of alternative anti-hypertensives during pregnancy. <https://www.sps.nhs.uk/articles/shortage-of-labetalol-tablets/>
- Manufacturers of both nifedipine modified release and methyldopa can support additional demand on their products during this time.
- Different versions of modified-release preparations may not have the same clinical effect. Prescribers should liaise with their community pharmacy to determine which brands of nifedipine modified release tablets are currently available in your area.
- The manufacturers of carvedilol and metoprolol have indicated they would be unable to meet demand if patients were switched to these products. Manufacturers of bisoprolol, atenolol and propranolol have indicated they have capacity to support additional demand.
- Specialist importers have identified unlicensed stock they can bring into the UK from abroad. Lead times for these products vary between 7 and 21 days.

### 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.

### Lofexidine tablets

- Britannia, sole supplier, are no longer supplying BritLofex (lofexidine) tablets due to manufacturing problems (see attached letter).
- Britannia does not yet know the resupply date for the next delivery of BritLofex tablets, but the out of stock period is likely to continue for several months. This is due to the transfer of the product to a new manufacturer. We have been in discussion with specialist importer companies and they have been unable to source supplies from abroad.
- UKMI have prepared the following shortages memo, which has now been published on the SPS website:  
<https://www.sps.nhs.uk/articles/shortage-of-lofexidine-hydrochloride-tablets-200-microgram-britoflex/>

### Metopirone 250mg capsules

- HRA Pharma, the sole supplier in the UK of metopirone 250mg capsules, are experiencing manufacturing issues and as a result are out of stock until July 2019
- This has been communicated to the Endocrinology group at NHS England and should now have been disseminated through their networks.

### 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.

## COMMERCIAL-SENSITIVE

- 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/>
- 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.

### Olena (fluoxetine) 20mg dispersible tablets

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

### Questran Powder for Oral Suspension/Questran Light (colestyramine) 4g sachets

- Bristol-Myers Squibb (BMS) are out of stock of Questran Powder 4g sachets and will be receiving no more deliveries before the planned divestment of this product to Cheplapharm on 31<sup>st</sup> July 2019 (see attached letter for further information).
- Emergency supply measures are already in place via Alliance Healthcare for Questran Light sachets and supplies will be sufficient to support both products, if a switch is deemed clinically appropriate.
- This process will remain in place until further notice to avoid a total out of stock situation. Contact Alliance Healthcare for further information on the emergency supply process.

### Sandimmun (ciclosporin) capsules

- Novartis have a supply issue affecting Sandimmun capsules due to a manufacturing site transfer.
- All strengths are currently out of stock, resupply is expected mid-June 2019.
- An unlicensed supply of all strengths has been sourced from the Italian market to meet the gap during this period and is available through Clinigen.
- Pharmacies can order stock through Clinigen at: Churchfield Road, Weybridge, KT13 8DB, Tel: 01932 824 100, Fax: 01932 824 300 [ukcustomerservice@clinigengroup.com](mailto:ukcustomerservice@clinigengroup.com)
- Novartis have issued a letter (attached) to customers

### Sinemet (co-careldopa) tablets

- Ongoing issues with the supply of Sinemet from MSD due to capacity constraints at their manufacturing facility - please see attached company letter.
- The latest update on the current supply position is:
  - **Sinemet 25/250mg** - back in stock.
  - **Sinemet 12.5/50mg** - currently out of stock; further stock expected at the middle of June;
  - **Sinemet Controlled Release 50/200mg** - currently out of stock; further stock is expected mid-June.
- DHSC has been working with generic suppliers and can confirm generic co-careldopa supplies in the above strengths will be available to support.
- All other Sinemet preparations are unaffected and remain available.
- DHSC are continuing to work with MSD and generic manufacturers to manage the overall supply position over the coming months and will provide updates as information becomes available.
- **MSD have informed DHSC that some of their Sinemet tablet range will have a change in appearance. Further information on this change in appearance can be found in the attached letter from MSD.**



## COMMERCIAL-SENSITIVE

### Stemetil (prochlorperazine) 5mg in 5ml oral syrup

- Sanofi are out of stock of Stemetil oral syrup until 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/>

### Thorens (colecalfiferol) 10,000i.u./ml oral drops

- Galen are out of stock of Thorens 10,000i.u./ml oral drops until w/c 12<sup>th</sup> July 2019.
- Several other strength colecalciferol oral drops remain available from alternative suppliers.
- Please see the link below for UKMI advice on alternate preparations:  
<https://www.sps.nhs.uk/articles/shortage-of-thorens-colecalciferol-10-000-i-u-ml-oral-drops/>

### Tizanidine 4mg tablets

- There is an ongoing supply issue affecting tizanidine 4mg tablets.
- Niche has limited supplies of the 4mg strength with further supplies expected w/c 3<sup>rd</sup> June 2019.
- Teva has limited supplies of the 4mg tablets available through Alliance with a further delivery planned at the end of June 2019.
- Supplies of 2mg tablets are currently available.

### Trifluoperazine tablets

- There have been ongoing manufacturing issues affecting trifluoperazine 1mg and 5mg tablets causing long term issues with no current date for resupply.
- 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.

## 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.



## COMMERCIAL-SENSITIVE

- 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

**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.msd-uk.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.

### Pneumococcal Polysaccharide Vaccine (PPV23):

- MSD are the sole UK supplier of this vaccine and although under restriction, supplies of the vials and PFS are currently available.
- MSD has introduced a limited quantity of a prefilled syringe (PFS) presentation of PPV23 under the brand name PNEUMOVAX® 23 to supplement the current supply of vials. A combination of growing global demand for pneumococcal polysaccharide vaccines, alongside manufacturing constraints, have led to regular interruptions in supply of PPV to the UK since 2017. The introduction of a PFS presentation of PPV is intended to support the continuity of supply and to help address public health need.
- Pneumovax® 23 in the PFS presentation can be ordered in the same way as the PPV in vials through MSD's distribution partner AAH online at <http://www.aah.co.uk> or by phone on 0344 561 8899.
- For more information about the vaccine, please refer to the Summary of Product Characteristics (SmPC).
- PHE's recommendations and guidance to GPs published in February's edition of PHE's Vaccine Update Bulletin (Page 7), continue to apply.

### Rabipur (Rabies vaccine)

- GSK is currently experiencing a supply delay with their Rabies vaccine, Rabipur, due to manufacturing constraints.
- Limited supplies are currently available and likely to continue through the first half of 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>

COMMERCIAL-SENSITIVE

## Discontinuations

### Diflucan (fluconazole) 200mg/100ml solution for infusion (Pfizer)

- Being discontinued with immediate effect following supply issue
- Low volume product
- Alternate products remain available from a number of suppliers

### Lartruvo (olaratumab) (Lilly)

- EMA revoked license due to lack of therapeutic efficacy:  
<https://www.ema.europa.eu/en/medicines/human/referrals/lartruvo>

### Memantine initiation pack (Accord)

- Being discontinued in June 2019
- Alternate strengths and initiation packs remain available from other suppliers

### 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.

### Refolinate (calcium folinate) 30mg/10ml injection (Pfizer)

- Being discontinued with immediate effect
- Hospira continue to market a generic product of the same strength

### Zeridame SR (tramadol) prolonged release tablets (Accord)

- Being discontinued in June 2019
- Low volume product
- Alternate branded tramadol MR products remain available

## Resolved (date resolved)

- Fusidic Acid 1% Viscous Eye Drops 04/6/19)
- Gastrografin (5/19)
- Iopidine (apraclonidine hydrochloride) 0.5% eye drops (22/5/19)
- Methadone 1mg/ml oral solution (sugar free) (3/6/19)
- Microgynon 30 tablets

#### COMMERCIAL-SENSITIVE

- Qlaira tablets (21/5/19)
- Rifadin (rifampicin) 300mg capsules (16/5/19)
- Sabril (vigabatrin) 500mg tablets (06/19)
- Sinemet (co-careldopa) 10/100mg tablets (17/5/19)
- Vibramycin D (doxycycline) dispersible tablets (20/5/19)
- Zolmitriptan 2.5mg orodispersible tablets (1/5/19)
- Xanax (alprazolam) 250mcg tablets (28/5/19)