

**Supply issues update for primary care November/December 2018** - this report has been produced by the Department of Health and Social Care (DHSC) Medicine Supply team. We aim to update this report on a monthly basis for the PRESCQIPP network to provide an update on current primary care medicine supply issues that we are working on. Please share with all relevant colleagues and networks in primary care.

## **Information provided w/c 10<sup>th</sup> December 2018**

### **New issues**

#### **Sinthrome 1mg tablets**

- DHSC have been informed of a supply issue with Sinthrome (acenocoumarol) 1mg tablets.
- Norgine are currently out of stock but wholesalers should have limited supplies.
- Norgine have advised that further stock is expected next week.

#### **Diamorphine Injection (Wockhardt)**

- DHSC have been made aware of a manufacturing issue from one of the suppliers of diamorphine 5mg and 10mg injection.
- There are currently two suppliers of diamorphine injection in the UK; Accord and Wockhardt. Recently Wockhardt have informed us that they have experienced a manufacturing issue which will lead to an intermittent supply issue of 5mg injection over the next 2 months followed by a full out of stock period of both strengths (5mg and 10mg) from January to early February 2019.
- We have contacted Accord and they have confirmed that they can support both primary and secondary care use over this period providing pharmacies continue to order in line with forecasted demand.
- Martindale and Hameln are aware of the diamorphine injection issue and have confirmed they have sufficient Morphine 10mg injection stock to cover normal demand.
- Pharmacies should continue to order all strengths of diamorphine in line with historical demand and are asked not to stockpile

#### **Valsartan**

- The MHRA recalled batches of Teva and Mylan valsartan and valsartan/hydrochlorothiazide in late November 2018.
- DHSC have confirmed that alternative generic suppliers currently have stock of unaffected valsartan and valsartan/hydrochlorothiazide.
- The recall notice can be accessed here: <https://www.gov.uk/drug-device-alerts/class-2-medicines-recall-teva-uk-limited-and-mylan-recall-of-some-valsartan-containing-products>

#### **Pethidine 50mg injection**

- DHSC have been informed of a supply issue with pethidine 50mg injection.
- Martindale are experiencing a manufacturing issue and are currently unable to supply pethidine 50mg injection until their next delivery which is expected late January 2019
- Concordia have confirmed that they have supplies available during this period. Until recently these were reserved for hospitals only but Concordia have now taken steps to ensure that these are available for primary care pharmacies to also order. Supplies can be obtained from Alliance.
- Please only order in line with normal demand to ensure that these supplies remain available for all to order.
- The 100mg injection remains available to order via the usual routes from Alliance and AAH.

#### **Bricanyl Turbohaler (terbutaline 500microgram turbohaler)**

- Astra Zeneca have informed DHSC about a supply issue affecting Bricanyl Turbohaler
- There will be small deliveries expected in late November and in December but normal supply will not resume until end of January 2019
- Astra Zeneca have provided a Dear HCP letter which can be found below

- UKMI have produced a memo which details clinical management strategies, this can be viewed on the following link: <https://www.sps.nhs.uk/articles/shortage-of-bricanyl-turbohaler-terbutaline/>
- Salbutamol products are available from a range of suppliers if patients are required to be switched during this period of short supply. Patients will require retraining if they are required to be switched to a different device



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### **Kwells (hyoscine hydrobromide 300microgram)**

- Bayer have notified DHSC of a supply issue with Kwells (hyoscine hydrobromide 300mcg) and is due back w/c 10<sup>th</sup> December 2018. The issues are due to some regulatory issues with the artwork.
- The Kwells junior (hyoscine hydrobromide 150mcg) is currently available, however there may be an increase in usage due to the 300mcg not being available and this may encounter supply issues.
- Teva have advised that they have good supplies of Joy-rides (hyoscine hydrobromide 150mcg) tablets based on normal demand. However, Teva has advised that there is a possibility they may encounter supply issues if there is a high demand on their products and therefore pharmacies are asked to only order the stock they require.

### **Bactroban nasal ointment**

- GSK have informed us that they are out of stock of this product due to an unforeseen increase in demand. Further stock is expected to be available by the w/c 17<sup>th</sup> December.
- Please refer to previous UKMI shortages memo, which provides advice on clinical alternatives. This is available at the following link:  
<https://www.sps.nhs.uk/articles/shortage-of-bactroban-mupirocin-nasal-ointment/>
- We have been in discussion with the suppliers of the alternatives, who are aware of GSK's issues and have advised that supplies of the following products are all available:
  - Naseptin Nasal Cream- available via the wholesalers: AAH, Alliance Healthcare and Well Pharmacy
  - Prontoderm – available via NHS supply Chain and wholesalers: AAH and Phoenix.
  - Octensian Nasal- available via NHS supply Chain and wholesalers: AAH, Alliance and Phoenix.

### **Pivmecillinam tablets**

- Due to the recent divestment of Selexid (pivmecillinam) tablets from Leo Pharma to Karo Pharma, there have been some recent supply issues with this product.
- Selexid supplies have now returned to normal and available from Alliance Healthcare.
- Aurobindo have also been experiencing a long-term supply issue with generic pivmecillinam tablets
- Resupply is expected during December 2018, however date is yet to be confirmed.

## **Ongoing issues**

### **Sinemet (co-careldopa) tablets**

- Ongoing issues with the supply of Sinemet from MSD- please see attached company letter
- The latest update we have on the current supply position is:
  - **Sinemet 12.5mg/50mg** - Further deliveries arrived mid-November and further deliveries expected imminently
  - **Sinemet Plus 25mg/100mg** – product currently out of stock but further deliveries are expected early December
  - **Sinemet 25mg/250mg** - MSD are currently out of stock, further deliveries are expected in January 2019
  - All other Sinemet preparations are unaffected
- DHSC has been working with generic suppliers on this issue and can confirm generic co-careldopa supplies in all the above strengths will be available to support the intermittent supply constraints

- DHSC are continuing to work with MSD and generic manufacturers to manage the overall supply position over the coming months and will provide an update when more information is available
- MSD have provided information to Parkinson's UK which can be accessed on their website via the following link: <https://www.parkinsons.org.uk/news/manufacturing-capacity-causes-shortage-sinemet>



MSD HCP letter.pdf

**Dalteparin supply issue update (Pfizer)**

- Pfizer have contacted NHS England and DHSC to provide an updated position on the key dalteparin presentations they have been experiencing problems with, detailed in the table below:

Presentation	Supply Status
2,500 units	Expected in UK w/c 10 Dec 18
5,000 units	Good Supply
7,500 units	Expected in UK w/c 10 Dec 18
10,000unit Graduated Dose Syringe	Limited stocks due to high demand, expected national out of stock by 30 Nov. Expected resupply date w/c 17 Dec 18
10,000 units Amp	Limited stocks due to high demand, expected national out of stock by 30 Nov. Expected resupply date w/c 17 Dec 18

- Pfizer have been asked to provide weekly updates and notify us immediately if the position changes.
- NHS England/ DHSC will continue to work with suppliers of alternative LMWH's and provide them with this updated supply information. Please find below advice which was circulated in October to help support local management plans.
- Detailed below is a list of the suppliers of other LMWH, who can support through to December. They are ranked with the supplier with greatest capacity sited at the top and we will continue to work alternative suppliers and update networks if there are changes in availability.
- Previous guidance about low molecular weight heparin is available on the SPS website: <https://www.sps.nhs.uk/articles/comparative-table-of-low-molecular-weight-heparins/>
- Local pharmacies are advised to work with their local secondary care trust to understand whether they are affected by this issue.
- If the local Trust is affected by this issue then primary care providers should understand which product/preparation they are using. All patients prescribed a LMWH should be counselled on the product they receive and understand how to administer the injection.

		Brand	Company
1	Supplier with the most stock available	Inhixa (Enoxaparin)	Techdow
2	Stock available	Arovi (Enoxaparin)	Rovi Biotech
3	Very limited capacity	Arixtra (Fondaparinux)	Aspen
4	No capacity	Innohep (Tinzaparin)	Leo

5	No capacity	Clexane (Enoxaparin)	Sanofi
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### Tambocor (flecainide) 200mg modified release tablets

- Teva are experiencing a supply issue affecting Tambocor (flecainide) 200mg modified release tablets due to a recent change in ownership that has resulted in a disruption to supply.
- Generic presentations of Flecainide 50mg and 100mg immediate release tablets remain available.
- Resupply for Tambocor (flecainide) 200mg modified release tablets is anticipated in 2019.

### EpiPen and EpiPen Junior

- There have been ongoing supply issues affecting EpiPen, supplied by Mylan for several months. The issue is due to manufacturing delays from Mylan's contract manufacturer, Meridian Medical Technologies, a Pfizer company in the US. Stabilising supply is taking longer than anticipated and is affecting countries globally.
- Initially the delays affected the 0.3mg preparation of EpiPen, however these have extended to the EpiPen Junior 0.15mg device.
- In the UK there are two alternative adrenaline auto-injector devices available, Emerade, supplied by Bausch and Lomb and Jext, supplied by ALK. Both companies manufacture adult and paediatric presentations of adrenaline auto-injectors. Both companies are aware of the supply disruptions affecting EpiPen and EpiPen Junior and have been working with their supply chains to increase supplies to the UK for the remainder of this year.
- Overall supply update for all presentations can be found below.
- On Friday 28<sup>th</sup> Sep, DHSC issued a supply disruption alert about EpiPen and EpiPen Junior and an update to the original alert was provided on 15<sup>th</sup> October which included a letter to parents/guardians, most recent alert and letter attached.



### 0.3mg Adrenaline Auto-injectors:

- Currently supplies are available of EpiPen 0.3mg via a stock management process. Pharmacies are allocated stock on a prescription-only basis and can place orders for up to a maximum of two EpiPen 0.3mg Auto-Injectors per prescription.
- Supplies of Emerade and Jext are currently available, and further supplies are scheduled for December.
- Emerade also supply a 0.5mg adrenaline auto-injector which is currently available.
- Mylan have received approval from the MHRA to extend the use of specific batch numbers of EpiPen 0.3mg auto-injectors, beyond the labelled expiry date by four months. Further information about these batches can be found: <http://www.epipen.co.uk/>
- ALK, the manufacturers of Jext, have recently obtained acceptance from the MHRA to extend the use of specific lot numbers of both the adult and paediatric device. Further information regarding these batches is contained in the letter below.



### 0.15mg Adrenaline Auto-injectors:

- Stock of EpiPen Junior is now available and can be obtained via a prescription management protocol. Pharmacies are allocated stock on a prescription-only basis and can place orders for up to a maximum of two EpiPen Junior 0.15mg auto-injectors per prescription. Information about this process is available on the EpiPen website under the 'Instruction to Pharmacists' section: <http://www.epipen.co.uk/>
- Supplies of both Jext and Emerade 0.15mg adrenaline auto-injectors are currently available and stock of these adrenaline auto-injectors can be obtained from wholesalers. Jext and Emerade are no longer subject

to wholesaler prescription validation. Wholesalers have placed caps on orders but these are in line with caps in place prior to the prescription management protocol, please contact wholesalers for further information.

- Pharmacies are urged not to over order during this time to avoid future supply problems and stocks are being monitored closely
- The supply situation for EpiPen Juniors is expected to improve by the end of the year and therefore the situation is likely to remain constrained until this time.
- ALK, the manufacturers of Jext, have obtained acceptance from the MHRA to extend the use of specific lot numbers of both the adult and paediatric device (see letter attached above for further information)

### **Clomipramine**

- Teva and Mylan are the only UK suppliers and are experiencing ongoing supply problems due to API issues
- 10mg capsules – Teva and Mylan both have stock available
- 25mg capsules – both out of stock, Mylan have advised resupply is due early December and Teva have advised a resupply is due in January 2019.
- 50mg capsules – Mylan are currently out of stock and due back in December and Teva currently have stock available and further stocks due in January 2019.

### **Promazine tablets**

- Teva are the sole supplier and are experiencing ongoing supply issues.
- Currently the 50mg tablet is out of stock with further supplies due imminently.
- Supplies of 25mg tablet remain.
- Rosemont have advised that the oral liquid preparation remains available in both 25mg/5ml and 50mg/5ml.

### **Adalat (nifedipine) all products**

- Letter from Bayer attached below
- There continues to be a temporary interruption to the supply of some Adalat presentations, with Bayer UK intending to re-supply the market at a later date than previously advised.
- There will be some out of stock periods for some preparations and long-term discontinuations of the following products:
  - Adalat 5mg capsules – discontinued after February 2019
  - Adalat 10mg capsules – discontinued after March 2019
  - Adalat Retard 10mg modified release tablets – discontinued after November 2018
- The below letter also lists the other preparations of Adalat (nifedipine) that remain available to order as well as contact details for healthcare professionals to obtain further advice and support.



Adalat DoH  
communication Oct

- Supplies of other nifedipine capsules and tablets that remain available currently, including;
  - Adipine (Chiesi)
  - Coracten (UCB)
  - Nifedipress (Dexcel)
  - Tensipine (Genus)
- UKMI have issued a shortages memo, which provides advice on alternatives, this is available on the SPS website via the following link: <https://www.sps.nhs.uk/articles/shortage-of-adalat-nifedipine/>
- Please do pass on information about this shortage to relevant clinical specialities.

### **Imigran (sumatriptan) injection**

- Ongoing issues with GSK's branded sumatriptan injection, Imigran.
- Supplies of both Imigran injection initiation packs and Imigran injection refill packs have now been exhausted.
- Resupply is not expected until Q1 2019 (January-March 2019)
- Generic supplies of sumatriptan injection in both initiation and refill packs are available from Sun Pharma/Ranbaxy – this product is 'sumatriptan 6 mg/0.5 ml solution for injection'

- Sun Pharma/Ranbaxy have confirmed that they are able to support the additional demand during this time.

### Lofexidine tablets

- Britannia are no longer supplying Britloflex (lofexidine) tablets due to manufacturing problems.
- Britannia is the sole supplier of this product to the UK.
- Britannia does not yet know the resupply date for the next delivery of Britloflex tablets, but the out of stock period is likely to last several months. This is due to the transfer of the product to a new manufacturer. We have been in discussion with the specialist importer companies about this and they have been unable to source supplies from abroad, as this product is not used in many other countries.
- 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-britloflex/>



Britloflex Temporary  
Discontinuation Notifi

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

- Sanofi have very limited stock available of Stemetil oral syrup,
- Stocks are likely to last until approximately early December 2018 with next delivery not due until mid- 2019.
- Other presentations of Prochlorperazine which will continue to remain available 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, this has now been published on the SPS website:
- <https://www.sps.nhs.uk/articles/shortage-of-stemetil-prochlorperazine-5mg-5ml-syrup/>

### Menadiol tablets

- Alliance, the sole supplier, has advised that there has been a further delay and stock is not expected until December 2018- date has yet to be confirmed.
- They are now supplying an unlicensed special which is the same formulation as the licensed product. Please find attached information sheet which was drawn up about the special product. This product is available to order from Alcura



Menadiol  
Diphosphate Informal

- Other specialist importers are also able to source unlicensed supplies.
- UKMI have drafted a shortages memo, which will provide advice on alternatives, this is available on the SPS website: <https://www.sps.nhs.uk/articles/shortage-of-menadiol-diphosphate-tablets-10mg/>
- Please do pass on information about this shortage to relevant clinical specialities including paediatrics.

### Acetazolamide MR

- Diamox MR – Concordia have advised resupply not due until late December 2018
- Eytazox Capsules 250mg M/R - Teva have advised that supplies are available.
- Immediate release acetazolamide 250mg tablets are available from both Teva and Concordia.

### Trimovate cream

- The product was divested from GSK to Ennogen, but Ennogen will not be in stock until January 2019.
- Ennogen are importing Trimovate cream as an unlicensed product and are now distributing this product.
- A copy of the communication letter with ordering details is attached.



### **Trifluoperazine tablets**

- There have been ongoing long term supply issues affecting trifluoperazine 1mg and 5mg tablets due to manufacturing issues with the active ingredient.
- Supplies will not improve until 2019 (date to be confirmed).
- Concordia and Rosemont have trifluoperazine as a liquid formulations and good supplies are available.
- We are also aware that unlicensed supplies of the 1mg and 5mg tablet are available from both Ennogen and a number of specialist importer companies. Under the medicines legislation, doctors can prescribe unlicensed products for their patients if they think it appropriate, but do so entirely on their own responsibility. Pharmacies can obtain unlicensed supplies via these specialist companies or Ennogen.

### **Zaditen (ketotifen) 300ml (1.38mg in 5 ml oral solution)**

- CD Pharma are currently out of stock of Zaditen oral solution 300ml (no date available for resupply).
- In the interim, they can provide alternative 100 ml packs for Zaditen Syrup (Origin Polish market), which is now available at Alloga.
- The MHRA has approved a variation for CD Pharma to supply this product, so it is considered licensed.
- The UK stock will be available once all Polish stock has been exhausted, expected to be early to mid-2019.
- Please find attached the information letter for further info.
- Zaditen 1mg tablets are not affected by this issue and remain readily available.



Final letter to  
distributors for Zadite

### **Metronidazole suppositories**

- Sanofi have had recent supply issues of the 1g product.
- Currently the 1g are expected back into stock January 2019
- They are the sole licensed supplier of this product.
- UKMI have discussed with specialists and advised that metronidazole should be administered using alternative routes (oral and IV presentations).

### **Eye drops/ treatments:**

#### **Bausch & Lomb**

- Prednisolone minims are currently on back order due to an API issue. Stock is expected to be delivered early December but this is not expected to clear all back orders.

#### **Allergan**

- Nevanac e/d x 3ml – stock expected early December.
- Duotrav e/d x 2.5ml – stock expected early December.
- Cilodex ear drops x 5ml – stock expected early December.

#### **Allergan**

- **Lacri-Lube supplies**- out of stock for the rest of the year due to a manufacturing issue.
- 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 (marketing authorisation holder) who distribute the product through Focus Pharmaceuticals have advised about the discontinuation of Betnesol Eye Ointment 0.1% w/w x 3g towards the end of March
- RPH Pharmaceuticals will be launching a generic Betamethasone Eye Ointment 0.1% w/w x 3g and are currently expecting stock in early 2019

## Resolved

- Ativan (lorazepam 4mg/mL)
- Epanutin (phenytoin) 30mg/5ml oral suspension
- Salofalk (mesalazine) 500mg suppositories – Dr. Falk Pharma
- Epilim Chronosphere 250mg
- Diazepam 5mg/ml Emulsion for injection (Diazemuls)
- Furosemide 40mg tablets
- Metronidazole 400mg tablets

## 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#2018>

### Hepatitis B Vaccines

- MSD have recently informed us that their supplies of the adult vaccine, HBVAXPRO 10mcg vaccine will go out of stock imminently. Resupply is not expected until mid-2020
- We have been working with GSK who have reassured us they are confident they can support the increased demand during this time.
- GSK have good supplies of all hepatitis B vaccine-

### Pneumococcal Polysaccharide Vaccine (PPV23):

- MSD are the sole UK supplier of this vaccine and currently have limited supplies available
- Further supplies are expected in December 2018
- MSD is introducing a limited quantity of a prefilled syringe presentation (PFS) of PPV under the brand name PNEUMOVAX® 23 to supplement the current supply of vials from December 2018. 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. Customers need an AAH account to place an order.
- For more information about the vaccine, please refer to the Summary of Product Characteristics (SmPC).
- PHE's guidance to GPs and recommendations published in February edition of PHE's Vaccine Update Bulletin (Page 7) on how to manage patients if unable to obtain PPV vaccine continue to apply.



PPV vaccine  
shortage PHE letter t

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

- GSK are out of stock of Menveo until late 2018 (date has not yet been confirmed)



- Pfizer have confirmed they are in stock of Nimenrix and currently able to support increased demand

## **Discontinuations**

### **Cilest (norgestimate and ethinylestradiol) tablets (Janssen- Cilag) -**

- Being discontinued from the UK market in July 2019 due to commercial reasons. Alternate branded norgestimate and ethinylestradiol products – Ciliq and Lizinna - remain available from other suppliers. The company is advising HCP's not to start any new patients on Cilest and to transfer patients over to alternate oral contraceptives. Company letter attached below.



UK Cilest

### **Desitin**

- Desitrend (levetiracetam) oral solution discontinued with immediate effect. Levetiracetam oral solution remains available from several alternate suppliers.

### **Almogran (almotriptan) 6-tablet pack (Almirall)**

- Being discontinued in December 2018, however, the 3-tablet pack will remain available.

### **Noristerat (noresthisterone) 200mg injection (Bayer)**

- Being discontinued with immediate effect with stock expected to last until Jan/Feb 2019.

### **Pro-Viron (mesterolone) tablets (Bayer)**

- Being discontinued with immediate effect.

### **Dolmatil (sulpiride) 200mg & 400mg tablets (Sanofi)**

- Being discontinued with immediate effect, supplies are expected to be depleted in October. However, generic sulpiride tablets remain available from other manufacturers.

### **Hypurin Bovine insulin (Wockhardt): Update**

- All the latest information about the discontinuation of bovine insulin can be found on the Wockhardt website: <http://www.wockhardt.co.uk/our-products/bovine-insulin-patient-information.aspx>

### **Duavive (conjugated oestrogens & bazedoxifene) (Pfizer)**

- Being discontinued in December 2019 due to commercial reasons