

Supply issues update for primary care January 2019

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 28th January 2019

New issues

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 (the manufacturers of Carbagen) have informed DHSC that the following preparations of Carbagen (carbamazepine) tablet will be unavailable until mid-late 2019.
- The affected products are listed below:
 - 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 which is the alternative brand of carbamazepine, tablets have confirmed 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 during this period. The memo can be found at the following link:
<https://www.sps.nhs.uk/articles/shortage-of-carbagen-carbamazepine-tablets/>
- Clinicians and pharmacists should identify potentially affected patients as soon as possible and ensure they are managed appropriately.

**There are clear indications that clinically relevant differences between different manufacturers' products might occur, even when the pharmaceutical forms are the same and bioequivalence has been shown.*

Clexane 40mg injection

- Sanofi informed NHS England and DHSC that there has been a quality issue with their most recent batch of Clexane 40mg injection that was due to arrive w/c January 14th.
- There was an out of stock period from mid-end of January 2019, however, further stock is now available.
- **Clexane (Sanofi) Imported stock – available from 23rd January 2019**
 - Over the past 2 weeks Sanofi have imported Clexane 40mg stock from Italy to help cover the shortfall in stock. This product is imported under a batch specific variation to the UK and is therefore classed as licensed in the UK.
 - This product is currently available to order via the usual routes.
 - The most important difference between the Italian and UK preparations is the difference in the needle guard device. To deploy the Preventis needle shield on the Italian syringes, users will need to firmly push the plunger after completing the injection. The user will hear an audible “click” to confirm the activation of the protective sleeve and the protective sleeve will automatically cover the needle.

- Patients and HCPs will need to be trained on this new device; instructions for use can also be found within the PIL. This product will NOT be over-labelled in English but an English PIL will be included in the pack.
- Sanofi have provided information on the differences in these products and these materials can be found at the following link:
<https://www.medicines.org.uk/emc/product/4499/rmms>

Further Clexane is now available and so alternative products should not be required, however, we have provided the information below in case helpful:

Alternative products

We have been in contact with the suppliers of enoxaparin biosimilar agents and the following information is available:

Inhixa 4,000 IU (40mg) in 0.4ml solution for injection pre-filled syringe (supplied by Techdow)

- Techdow supply Inhixa (enoxaparin) and have confirmed that they have sufficient stock of Inhixa 40mg injection to cover the additional demand:
<https://www.medicines.org.uk/emc/product/784/smpc>
- If you wish to switch Clexane 40mg to Inhixa please see attached support / training materials and link to online video: <https://www.youtube.com/watch?v=E8AytPojtVI>
- For further support and to arrange a visit with a field director who can provide training on how to use Inhixa please contact: selina.temperton@uk.techdow.com 07376280709_or jo.phillips@uk.techdow.com 07540979066.
- Orders for product can be placed via wholesalers.

Arovi 4,000 IU (40mg) in 0.4ml pre-filled syringe (supplied by Rovi Biotech)

- Rovi Biotech supply Arovi (enoxaparin) and have confirmed that they have sufficient Rovi 40mg injection to cover additional demand in primary care.
- If you wish to switch Clexane 40mg to Arovi please see attached supporting / educational material and link to further online material:
<https://www.rovi.es/en/biosimilar-de-enoxaparina>
- For any queries or to order training material please contact: Blanca Esteban, besteban@rovi.com 0203 642 06 77.
- Orders for Arovi can be placed via Alliance Healthcare.

- We would suggest GPs and pharmacies work closely to discuss local management options.

Madopar (co-beneldopa) Update

- Roche, the manufacturer of Madopar (co-beneldopa), are currently experiencing supply difficulties with some of the Madopar range. This is due to an unforeseen increase in demand on their Madopar products throughout 2018.
- Supplies of some Madopar presentations, may be constrained during January. The situation is expected to improve in February.
 - **Madopar 125mg Hard Capsules** – Stock is due week commencing 28th January.
 - **Madopar 62.5mg Dispersible Tablets** – will be out of stock mid-January for three weeks.
 - **Madopar 125mg Dispersible Tablets** – stock is now available following supply issues in December.
 - **Madopar 125mg Controlled Release Capsules** – back in stock and available at wholesalers.
 - Other Madopar presentations remain unaffected at this time

- If patients are having difficulties obtaining supplies of Madopar we would recommend they see a clinician to discuss alternative treatment options.
- Please be assured that we are continuing to work closely with the manufacturer and others to try to resolve these issues and improve the situation as quickly as possible.

Naproxen

- DHSC has been made aware of difficulty in obtaining supplies of naproxen 250mg and 500mg tablets.
- DHSC is working closely with all manufacturers of this product to ensure there are sufficient supplies available to meet historic demand.
- There should now be adequate supplies of both naproxen 250mg and 500mg tablets to meet normal demand and further stocks are being made available over the coming weeks.
- DHSC is working with the manufacturers to expedite future deliveries to ensure stock is available for both primary and secondary care. Further stock is expected in the coming weeks and the situation is improving.

Isoniazid 100mg tablets

- Recipharm currently have no stock available and are changing their API source.
- Morningside have had limited stock available over the past few weeks but stock will become available week commencing 4th February.
- Morningside will be able to supply the whole market during this time.
- DHSC will continue to monitor the situation and if stocks become limited will look to speak with the specialist importers.

Metronidazole 400mg tablets

- DHSC is aware of recent supply issues with metronidazole 400mg tablets.
- There are currently supplies available and further supplies are being made available week commencing 21st January and DHSC are monitoring the situation closely.
- Metronidazole 200mg tablets are available.

Lofepamine 70mg tablets

- DHSC were made aware of a slight interruption of supply to lofepramine 70mg tablets at the beginning of January.
- Creo Pharma have confirmed that stock is now available to all wholesalers to meet demand.
- Creo Pharma have informed DHSC they are expecting further deliveries in January and the stock they are receiving is sufficient to meet historic demand.
- Accord are expecting new stock to become available in February 2019.
- Teva may have some stock available.

Ongoing Issues

Nimodipine

- DHSC/CMU have been made aware of an impending supply problem with nimodipine 30mg tablets.
- Bayer, the sole licensed supplier of this product, have experienced delays in manufacturing at their product site in Germany (see attached letter for further details).
- Supplies currently remain available for emergency orders directly from Bayer.
- However, stock is expected to be depleted from end December. Bayer are working hard to resolve this issue and although are unable to provide a confirmed resupply date they expect stock to be available early in 2019, by mid-February at the latest.

We have been in contact with specialist importer companies and they have confirmed that supplies can be sourced of unlicensed nimodipine.

Sinthrome (acenocoumarol) 1mg tablets

- Sinthrome is currently available to order.
- Norgine are expecting further deliveries at the beginning of February however there may be a one week gap in supply until the next delivery arrives week commencing 4th February.

Pivmecillinam tablets

- Leo Pharma have divested Selexid (pivmecillinam) tablets to Karo Pharma, this product will still be supplied via Alliance Healthcare.
- There was a recent interruption in supply during the divestment but Karo Pharma have confirmed that stock is being delivered week commencing 21st January.
- Aurobindo currently have stock available but may be limited and further deliveries are expected in February.

Diamorphine Injection (Wockhardt)

- DHSC have been made aware of a manufacturing issue from one of our 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.
- Pharmacies should continue to order all strengths of diamorphine in line with historical demand and are asked not to stockpile

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.
- Further supplies are currently expected by the 3rd week of January 2019.
- However, Concordia have confirmed that they have supplies available. 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.

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** - Stock is currently available and further stocks are expected over the coming weeks.
 - **Sinemet Plus 25mg/100mg** – Stock is currently available and further stocks are expected over the coming weeks.

- **Sinemet 25mg/250mg** - MSD are currently out of stock, further deliveries are expected at the end of 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 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 28 th January 2019
5,000 units	In stock
7,500 units	In stock
10,000unit Graduated Dose Syringe	In stock
10,000 units Amp	In stock

- 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/>

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

The supply situation for EpiPen and EpiPen Juniors continues to improve and further stock is due in the coming months, the latest position for adrenaline auto-injectors is as follows:

0.3mg Adrenaline Auto-injectors:

- EpiPen 0.3mg is currently available from wholesalers.

- Supplies of Emerade and Jext are also available, and further deliveries are scheduled for January and February.
- Emerade also supply a 0.5mg adrenaline auto-injector which is currently available.

0.15mg Adrenaline Auto-injectors:

- Stock of EpiPen Junior is now available via a prescription validation process. 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 continues to improve and further stock is due in the coming months.

Clomipramine

- Teva and Mylan are the only UK suppliers and are experiencing ongoing supply problems due to API issues
- 10mg capsules – Teva are currently out of stock, they are expecting further deliveries in March. Mylan are out of stock but have stock arriving in February 2019.
- 25mg capsules – Teva are currently out of stock but will be releasing stock week commencing 21st January. Mylan are out of stock advised they currently have no dates for resupply.
- 50mg capsules – Teva and Mylan are currently in stock.

Adalat (nifedipine)

- 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 from February 2019. Bayer were the sole licensed UK supplier of this product. We have been working with potential alternative manufacturers and are working to get another licensed supply to the UK market. We have had a positive response and it is currently estimated that supplies could be available April – May 2019. We have also been in contact with the specialist importers and can confirm that unlicensed supplies have been sourced.
 - Adalat 10mg capsules – discontinued after March 2019
 - Adalat Retard 10mg modified release tablets – discontinued after November 2018
 - Adalat Retard 20mg modified release tablets – discontinued August 2018
 - Adalat LA 20mg, 30mg and 60mg prolonged release – out of stock until 2021.
- 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.
- Supplies of other nifedipine capsules and tablets remain available currently, including;
 - Adipine (Chiesi)
 - Coracten (UCB)

- Nifedipress (Dexcel)
- Tensipine (Genus)
- We are in contact with the suppliers of all of these alternatives and they are working to ensure that supplies remain available and to expedite future deliveries where possible.
- 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.



Adalat DoH Sto

Imigran (sumatriptan) injection:

- We have been made aware of a manufacturing issue affecting supplies of GSK's branded sumatriptan injection, Imigran.
- GSK have confirmed the treatment pack is due back in stock early February but the refill is not expected until July 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 Britlofex (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 Britlofex 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->



Britlofex Temporary
Discontinuation Notifi

[microgram-britoflex/](https://www.sps.nhs.uk/articles/shortage-of-lofexidine-hydrochloride-tablets-200-microgram-britoflex/)

Stemetil (prochlorperazine) 5mg in 5ml oral syrup

- Sanofi have informed DHSC that there is very limited stock available of Stemetil oral syrup,
- Stocks are likely to last until approximately late November 2018 with next delivery not due until the middle of 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 stock is not expected until March 2019.
- 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 Information

- 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.

Trifluoperazine tablets

- There have been ongoing supply issues affecting trifluoperazine 1mg and 5mg tablets.
- Supplies will not improve until some point in 2019 due to manufacturing issues with the active ingredient, therefore there are long term issues affecting the tablets.
- 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 week commencing 28th 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

- There is a short-term back order of Viscotears but this is expected to be cleared in early February.

Allergan

- **Lacri-Lube supplies**- out of stock due to a manufacturing issue.
- 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 (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 2019.

Resolved

- **Bactroban nasal ointment**
- **Bricanyl Turbohaler**
- **Questran 4g Sachet Powder for Oral suspension**
- **Promazine 50mg 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 are out of stock HBVAXPRO 10mcg vaccine with 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 vaccines

Pneumococcal Polysaccharide Vaccine (PPV23):

- MSD are the sole UK supplier of this vaccine and although still under restriction, supplies have improved.
- MSD has introduced a limited quantity of a prefilled syringe presentation (PFS) of PPV 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. 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 mid 2019 (date has not yet been confirmed)
- Pfizer have confirmed they are in stock of Nimenrix and currently able to support increased demand.

Discontinuations

Zovirax (acyclovir) eye ointment (GSK)

- Being discontinued globally in June 2019 due to repeated challenges in guaranteeing a sustainable product supply. There are no other acyclovir eye ointments on the market but an alternative licensed product Virgan (ganciclovir) is available. This is the link to the webpage with further information: <https://gskpro.com/en-gb/products/zovirax/>
- UKMi have produced a memo giving advice on possible alternative treatments, the memo can be found on the following link: <https://www.sps.nhs.uk/articles/shortage-of-aciclovir/>
- Thea Pharmaceuticals are aware of this discontinuation and have confirmed they can meet demand for Zovirax eye ointment with their Virgan (ganciclovir) eye gel.

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, suppliers 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