

Medicines Shortage Notification

RE: Supply problems with medicines for ADHD

Summary

There are supply disruptions affecting the following medications:

Methylphenidate

- Equasym XL® 10, 20, and 30mg capsules
- Xaggitin XL® 18 and 36mg prolonged-release tablets
- Concerta XL® 54mg prolonged-release tablets
- Xenidate XL® 27mg prolonged-release tablets

Lisdexamphetamine

- Elvanse® 20, 30, 40, 50, 60 and 70mg capsules
- Elvanse® Adult 30, 50 and 70mg capsules

Guanfacine

- Intuniv® 1, 2, 3 and 4mg prolonged-release tablets

Atomoxetine

- All strengths of atomoxetine capsules

The supply disruption is caused by a combination of manufacturing issues and increased global demand.

Other ADHD products remain available but stocks are not sufficient to meet the increased demand caused by other shortages.

Supply disruption is expected to resolve at various dates between October and December 2023.

Action

- No new patients to be initiated on products affected by this shortage until supply issues resolve.
- Patients calling for advice should be informed of current stock situation and a management plan should be agreed between the patient and prescriber.
- No new requests for shared care between SFT and primary care until supply issues resolve.

Clinical information on switching between products is given below.

Methylphenidate

- All long-acting methylphenidate (MPH) preparations include an immediate-release component as well as a modified-release component.
- Preparations differ in their immediate release (IR) and extended release (ER) release profiles.
- Data from head-to-head studies comparing long-acting MPH formulations^{1, 2} suggest that clinical equivalence is most closely related to the IR component of the release mechanism, rather than the ER component.
- Therefore, the IR component should be used as a reference when switching between long-acting MPH formulations.
- Note that switching between formulations can result in changes in symptom management at different time periods during the day. Patients should be reviewed after the switch and doses adjusted if required.

How to switch between preparations

1. Identify the new preparation to switch to, using table 1.
2. Select the dose to switch to by matching (as closely as possible) the IR component of the old and new preparations, using tables 2 - 4.

Table 1. MPH preparations affected by the shortage, and options for switching

Preparation affected by shortage	Switch options
Equasym XL [®] 10, 20, and 30mg capsules	Medikinet XL [®] MPH IR
Xaggitin XL [®] 18 and 36mg prolonged-release tablets	Affenid XL [®] Concerta XL [®] Delmosart XL [®] Matoride XL [®] Xenidate XL [®]
Concerta XL [®] 54mg prolonged-release tablets	Affenid XL [®] Delmosart XL [®] Matoride XL [®] Xaggitin XL [®] Xenidate XL [®]
Xenidate XL [®] 27mg prolonged-release tablets	Affenid XL [®] Concerta XL [®] Delmosart XL [®] Xaggitin XL [®]

Table 2. Equasym XL[®] release characteristics¹

Equasym XL [®]		
Total daily dose	Immediate release component	Slow release component
	0 - 4 hours	4 - 8hours
10mg/day	3mg	7mg
20mg/day	6mg	14mg
30mg/day	9mg	21mg
40mg/day	12mg	28mg
50mg/day	15mg	35mg
60mg/day	18mg	42mg

Table 3. Medikinet XL^{®1} and bioequivalent generic preparation release characteristics

Medikinet XL [®] , Metyrol XL [®]		
Total daily dose	Immediate release component	Slow release component
	0 - 4 hours	4 - 8hours
5mg/day	2.5mg	2.5mg
10mg/day	5mg	5mg
20mg/day	10mg	10mg
30mg/day	15mg	15mg
40mg/day	20mg	20mg
50mg/day	25mg	25mg
60mg/day	30mg	30mg

Table 4. Concerta XL[®] and bioequivalent generic preparations release characteristics¹

Affenid XL [®] , Concerta XL [®] , Delmosart XL [®] , Matoride XL [®] , Xaggitin XL [®] , Xenidate XL [®]		
Total daily dose	Immediate release component	Slow release component
	0 - 4 hours	4 - 12hours
18mg/day	4mg	14mg
27mg/day	6mg	21mg
36mg/day	8mg	28mg
45mg/day	10mg	35mg
54mg/day	12mg	42mg
63mg/day	14mg	49mg
72mg/day	16mg	56mg

Worked example

- Current preparation: Equasym XL[®] 20mg/day
- Using table 1, switching to: Medikinet XL[®]
- Using table 2, IR component of current preparation = 6mg
- Using table 4, closest match for current IR component = 5mg, contained in **Medikinet XL[®] 10mg** preparation.

Lisdexamphetamine

- Lisdexamphetamine is a prodrug of dexamphetamine. It is broken down in red blood cells so that dexamphetamine is gradually made available.
- The dexamphetamine portion of lisdexamphetamine is complexed with the amino acid lysine, and in this form is inactive until activated by red blood cells. It is therefore unlikely to be abused for recreational or dependency-driven purposes, compared with dexamphetamine.
- In the event of unavailability of lisdexamphetamine, patients may be switched to dexamphetamine. However, if there is a risk of abuse or diversion of dexamphetamine, an alternative medication (eg. MPH XL) may be considered instead.

Table 5. Suggested switches from lisdexamphetamine to dexamphetamine

Preparation affected	Switch to dexamphetamine
Elvanse® 20mg capsules	Dexamfetamine sulphate 5mg in divided doses
Elvanse® 30mg capsules	Dexamfetamine sulphate 7.5mg in divided doses
Elvanse® 40mg capsules	Dexamfetamine sulphate 10mg in divided doses
Elvanse® 50mg capsules	Dexamfetamine sulphate 15mg in divided doses
Elvanse® 60mg capsules	Dexamfetamine sulphate 17.5mg in divided doses
Elvanse® 70mg capsules	Dexamfetamine sulphate 20mg in divided doses and monitor for need to adjust dose further (maximum daily dose in children and adolescents is usually 20mg, although doses of 40mg may be necessary in rare cases)
Elvanse® Adult 30, 50 and 70mg capsules	As above, but note the need to enquire for current or history of substance use and assess risk of diversion

Guanfacine

- Guanfacine is an alpha-2-agonist, and sometimes used as an alternative non-stimulant medication to atomoxetine.
- There are no alternative guanfacine preparations available. A different treatment will need to be sought, based on the patient's ADHD medication history and medical history.
- Guanfacine should not be stopped abruptly because of the risk of rebound hypertension. Hypertensive encephalopathy has been very rarely reported on abrupt cessation of treatment. Contact patients prescribed guanfacine and advise them to reduce their dose gradually if their stock of medication at home allows. Ideal tapering is to reduce in decrements of 1mg every 3 – 7 days. For example, for a patient prescribed 4mg Intuniv® tablets, with a stock of 3mg and 1mg tablets at home: reduce the dose to 3mg, then 2mg, then 1mg. Intuniv® tablets cannot be split.
- If it is not possible to reduce slowly, monitor BP and HR on stopping. The hypotensive effect of guanfacine may take about 2 – 4 days to resolve^{3,4}. Rebound hypertension may occur, and has been reported to persist in some cases⁵. This is usually asymptomatic and clinically insignificant^{5,6}. Monitor BP and HR at day 2, and again at day 4. If blood pressure is raised at day 4, measure again at weekly intervals until normal. If there are signs of clinically significant rebound hypertension, seek medical advice.

Atomoxetine

Recommendations to help manage the supply issues (predicted to resolve mid-October 2023):

If one pharmacy is unable to supply atomoxetine, try a different pharmacy.

- Community pharmacies may have stock on their shelves of different strengths. Some pharmacies are tied to ordering from one wholesaler whereas others (such as independent pharmacies) can order from several wholesalers. Advise patients to first try other pharmacies in their local area to see if supplies are available. This may allow them to continue treatment until the supply disruption resolves. Limited stock of most strengths remains available from one manufacturer, but wholesaler stock levels are likely to fluctuate on a daily basis.

Adjust the dose slightly (if appropriate) – a new prescription will be required.

- If a community pharmacy only has stock of a particular strength(s), as a short-term measure it may be necessary to consider prescribing whichever capsule strengths are available to make up a dose that is as close as possible to the dose that a patient responds to (this would be determined on an individual case by case basis weighing up pros and cons, including taking into account any issues with tolerability).

Only continue atomoxetine (Strattera®) liquid (4mg/ml) for patients already prescribed this formulation.

- Strattera liquid remains available and can be continued in those already receiving it. However, a wholesale switch for people currently taking capsules to the liquid formulation is not recommended as it is unlikely the supply chain would be able to meet the demand.

If a patient is unable to secure a supply after the above recommendations have been followed, consider the following:

What impact would a short break in treatment have?

- Atomoxetine is not associated with withdrawal symptoms if it is stopped suddenly. It can therefore be discontinued temporarily without the need for dose tapering.
- Once it is possible to restart atomoxetine, depending on the gap in treatment, achieving a therapeutic response may take several weeks.

If a short break in treatment would have more than a minimal clinical impact, consider the following options:

- Stimulant medication
 - What was the response and tolerability to any previously tried ADHD medication?
 - Would short term use of a previously used stimulant medication be appropriate/safe?
- FOR SFT PRESCRIBERS ONLY: Prescribe a short supply of atomoxetine on a Hospital Prescription Order (HPO)
 - SFT has limited supplies of atomoxetine at YDH dispensary. This varies *day to day*.
 - Stock holding is not sufficient to cover the current supply shortage for all patients.

- This option should therefore only be considered when there are concerns about the impact of the return of ADHD symptoms during a brief break in treatment.
- An HPO should be sent to the dispensary by email (process detailed below)
- **The patient should also be advised to continue to try and source supply via FP10 from their local pharmacy because stock levels are fluctuating.**

Process to order via HPO

- Community prescriber to prescribe required dose of atomoxetine on Rio
- Print PDF of a hospital prescription order (HPO) as per Word document below and email it to Pharmacy.Orders@SomersetFT.nhs.uk
- On the PDF of the HPO add a text box and include:
 - **cost centre** (i.e. CAMHS West, CAMHS East, Adult ADHD, Adult CMHS, paediatrics)
 - **delivery location** closest to patient; the options are Taunton CMHT (Foundation House), Bridgwater CMHT (Glanville House), Wells CMHT (The Bridge) or Yeovil CMHT (Magnolia Court)
- N.B. Allow **5 working days** for ordering and delivery



How do I print and
send a HPO to YDH pl

Further information

- [National Patient Safety Alert](#)
- Extended-release methylphenidate: a review of the pharmacokinetic profiles of available products, [Specialist Pharmacy Service](#)
- Attention deficit hyperactivity disorder: diagnosis and management, [NICE](#)
- Manufacturer's information about individual products, [electronic medicines compendium](#)
- To access the usual responsibilities of prescribers of these medications please see the shared care protocol on the Somerset ICB Medicines Management shared care page [Shared Care and PGDs - NHS Somerset ICB](#)

References

1. Coghill D, et al. Long-acting methylphenidate formulations in the treatment of attention-deficit/hyperactivity disorder: a systematic review of head-to-head studies. *BMC Psychiatry* 2013,13:237
2. Sonuga-Barke EJ, et al. Efficacy of two once-daily methylphenidate formulations compared across dose levels at different times of the day: preliminary indications from a secondary analysis of the COMACS study data. *BMC Psychiatry* 2004, 4:28.
3. Zamboulis C, et al. Withdrawal of guanfacine after long-term treatment in essential hypertension. Observations on blood pressure and plasma and urinary noradrenaline. *Eur J Clin Pharmacol.* 1981, 19(1)
4. Reid JL, et al. Guanfacine: effects of long-term treatment and withdrawal. *Br J Clin Pharmacol* 1980, 10(suppl 1)
5. Newcorn JH, et al. Extended-release guanfacine hydrochloride in 16 – 17 year olds with ADHD: a randomised-withdrawal maintenance of efficacy study. *J Child Psychol & Psych.* 2016, 57:6
6. Kisicki JC, et al. Phase I, double-blind, randomised, placebo-controlled, dose-escalation study of the effects on blood-pressure of abrupt cessation versus taper down of guanfacine extended-release tablets in adults aged 19 – 24 years. *Clinical Therapeutics.* 2007, 29(9)

ADHD Resources

- www.adhdadult.uk
- www.adhd.co.uk
- The ADHD Adults podcast (Dr James Brown, Dr Alex Connor) [Home - The ADHD Adults](#)
- Jessica McCabe: This is what it's really like to live with ADHD [Jessica McCabe: This is what it's really like to live with ADHD | TED Talk](#)
- <https://www.additudemag.com/>
- <https://adhduk.co.uk/>
- www.somersetrecoverycollege.co.uk
- www.somersetft.nhs.uk/somerset-talking-therapies
- www.gov.uk/access-to-work

Contact details for additional support e.g. for patients you feel are high risk or vulnerable:

Paediatric patients (up to age 18 only): ADHDNursing@somersetft.nhs.uk

Adult ADHD (age 18 and over): adhdinquiries@somersetft.nhs.uk

Medicines Management: medicinesmanagement@somersetft.nhs.uk