Management of ADHD medication shortages: advice for primary care

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There are widespread shortages of ADHD medications and patients could experience a break in their treatment whilst stocks return to normal.

Patients are not restricted to using their nominated pharmacy. They may need to obtain stock from another pharmacy, this can be done by using the prescription token/barcode AND the pharmacy releasing the prescription back to the spine.

LYPFT has produced patient information which will be updated regularly on the LYPFT ADHD page of our website at <https://www.leedsandyorkpft.nhs.uk/our-services/adult-attention-deficit-hyperactivity-disorder-adhd-service/>.

Patients should be advised to use their remaining supply sparingly and to consider a drug holiday if appropriate, if further supplies cannot be sourced. NOTE: it is not advised to abruptly stop or start guanfacine m/r (Intuniv®)

Behavioural management is already consistently advocated. Omitting medication on weekends and non-school days is possible and routinely practiced. It can prolong supply for the days that it is most necessary.

Searches to identify affected patients can be found in the clinical systems (searches will need importing from Leeds ICB Central 27491 reporting unit in EMIS): Leeds ICB > Medicines Optimisation Team > Prescribing Support Medicines Safety >

NatPSA ALL Methylphenidate XL preps on rpt

NatPSA Guanfacine tabs on rpt

NatPSA Lisdexamfetamine caps on rpt

NatPSA Methylphenidate XL branded tablets on rpt

NatPSA Equasym XL capsules on rpt

# **Key Messages for Primary Care:**

1. **No new initiations:**

Prescribers should not initiate new patients on products affected by this shortage until the supply issues resolve. This will be regularly reviewed at West Yorkshire level and further changes/updates will be communicated.

1. **Identification of patients:**

Identify all patients currently prescribed these products (searches have been made available in clinical systems), and send a text message to all patients with link to Comms on West Yorkshire HCP Website (this will be updated as new guidance and stock updates are made available)

1. **Medication specific advice:**

a) Guanfacine: Patients should be advised to taper the dose prior to stopping, by no more than 1mg every 3 days where supplies allow this. The patient may require an acute prescription of 1mg/2mg strength tablets to allow them to taper their dose – PRESCRIBE THE MINIMUM QUANTITY OF TABLETS REQUIRED (see below).

If it is not possible to reduce slowly, monitor BP and HR on stopping (see below).

Patients who are required to discontinue Guanfacine abruptly should be advised to 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, this should be monitored according to existing protocols until normal (see below).

b) Lisdexamfetamine: Patients should be encouraged to taper the dose prior to stopping. Patients maintained on doses of lisdexamfetamine greater than 50mg/day should be advised to reduce to 50mg/day at which point it can be discontinued. For patients prescribed 60mg or 70mg capsules, this may require an acute prescription of 3 x 50mg capsules, then stop. Alternatively, higher dose capsules can be dissolved in water (see below).

c) Methylphenidate MR Tablets: recommendation for primary care to switch patients on branded MR Methylphenidate TABLETS to an alternative brand(see below).

d) Methyphenidate XL **Capsules** are not bioequivalent.

Patients may consider a switch in formulation if their usual preparation is unavailable. To switch between different XL preparations please refer to the comparison tables (see below)

1. **Seeking specialist Advice:**

Where primary care clinicians have concerns about individual patient management they should contact specialist services for advice and guidance. e.g. management of patients at risk from severe symptoms following withdrawal. Many patients in Leeds will be under Shared Care agreements with other providers. LYPFT only provides patient specific guidance for those patients under the Leeds service. For those patients under Shared Care with other providers we ask that you revert to that provider for advice and guidance.

Primary care clinicians must be aware that the ability of specialist services to assist will be limited by both capacity and limited pharmacological options. The specialist team will only be able to review patients who are under Shared Care with NHS services (if Shared Care is with a private provider, then revert to them for guidance) and for those who the absence of medication would be expected to result in a significant risk or harm to themselves or others (e.g. serious self-harm, severe aggression leading to injuries or the Police being called).

Referrals for supply should **not** be made as hospitals do not have access to additional supplies of these medicines.

# **Guidance On Alternatives, Switching, And Reinitiation**

**Methylphenidate: Product specific guidance**

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| **Preparation affected by shortage** | **Switch options** |
| Equasym XL® 10, 20, and 30mg capsules | Limited parallel imports of methylphenidate (Equasym XL) modified release capsules remain available but cannot support an uplift in demand. There is no bioequivalent, but the dose can be converted to another long-acting methylphenidate preparation (see below). |
| 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® |

Where there is not a direct equivalent product the patient should be advised that they can manage the supply by dosing only on days where they have planned activity i.e. work / school and omitting doses on weekends / holidays.

Switching patients to immediate release methylphenidate requires supervision of the efficacy and tolerability of the switching regime, due to the volume of people affected it is not possible for the ADHD team to provide this supervision for all patients. Primary care cannot switch to equivalent forms of immediate release products due to the skill requirement and resource implications.

There is no bioequivalent alternative to Equasym. Equasym differs from Concerta (and its bioequivalents) in that it has slightly less of the long-acting component. As such, switching from Equasym to Concerta (or a bioequivalent) may result in issues with insomnia. Patients should be informed about this by the community pharmacy and advised to be alert to this side effect and to consider taking the medication earlier than usual. An alternative is to switch to Medikinet which is less likely to cause insomnia, but it provides less symptom coverage through the day (as it has less of a long-acting component than Equasym). This information should be provided by the community pharmacist to enable the patient to make an informed decision.

To switch from Equasym to an alternative long-acting form of methylphenidate please refer to the tables below. First identify the immediate release component of the prescribed dose of Equasym and then match to the closest match for the long-acting alternative. E.g. if the patient is prescribed Equasym XL 20mg/day, the IR component of the preparation is 6mg, this would correspond to a dose of Concerta (or its bioequivalent) of 27mg/day. Alternatively, for the same dose of Equasym, a 10mg/day dose of Medikinet would be appropriate.

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| **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 |

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| **Concerta XL® and its bioequivalents (Affenid 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 |

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| **Medikinet 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 |

Where a patient has needed to either switch away from their original product there should be a discussion planned regarding return to their original product (in the first instance this can be done with the community pharmacist).

Where this is a brand switch for one of the XL tablets as outlined above the brand can be switched back without issue.

Where a patient has had a treatment break greater than 4 days, they should build the dose up according to BNF guidance (see table below), with the aim of reestablishing the previous dose. Monitoring should be undertaken as specified in the shared care guidance and other medication reviewed to ensure no new medication has been added that may interact. This can be done safety within primary care if resources and skills are available. Failing that, the patient can be referred to the specialist service for reinitiation but due to the limited resources this will result in a lengthy delay in reinitiation.

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| **Medication** | **Reinitiation** |
| Concerta XL and its bioequivalents (Affenid XL®  Xaggitin XL®  Delmosart XL®  Matoride XL®  Xenidate XL® | Initially 18 mg once daily, dose to be taken in the morning; increased at weekly intervals by 18mg until the original maintenance dose is achieved. Once stable check blood pressure and pulse. BP, pulse, and weight, should be recorded at baseline. |
| Equasym XL® | Initially 10 mg once daily, dose to be taken in the morning before breakfast; increased gradually at weekly intervals by 10mg. until the original maintenance dose is achieved. Once stable check blood pressure and pulse. BP, pulse, and weight, should be recorded at baseline. |
| Medikinet XL® | Initially 10 mg once daily, dose to be taken in the morning with breakfast; adjusted at weekly intervals by 10mg until the original maintenance dose is achieved. Once stable check blood pressure and pulse. BP, pulse, and weight, should be recorded at baseline. |

**Lisdexamfetamine**

Lisdexamfetamine is a prodrug of dexamphetamine. It is broken down in red blood cells so that dexamphetamine is gradually made available.

The dexamphetamine portion of Lisdexamfetamine 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.

There is no bioequivalent formulation available for lisdexamfetamine. Switching to methylphenidate alternatives requires specialist input and it is not anticipated that this would be achievable for patients given the resources required. Additionally, switching to methylphenidate from lisdexamfetamine is often not clinically appropriate. There is no accurate conversion factor to enable switching to the immediate release alternative dexamfetamine. Again, this would require specialist input, and this is not achievable due to the resource implications.

As there is not a direct equivalent product the patient should be advised that they can manage the supply by dosing only on days where they have planned activity i.e. work / school and omitting doses on weekends / holidays.

Some patients may tolerate abrupt withdrawal from higher doses (above 50mg) of lisdexamfetamine whereas others may experience symptoms of withdrawal (fatigue and low mood). Patients maintained on doses of lisdexamfetamine greater than 50mg/day should be advised to taper the dose prior to stopping where supplies allow this. Patients maintained on lisdexamfetamine should be advised to taper the level of medication by no more than 20mg every 3 to 7 days until they reach a dose of 50mg at which point it can be discontinued. Where tapering is not possible patients can be advised to dissolve the contents of the capsule in water, drink half and discard the rest. If this is done for 3-7 days then the risk of withdrawal symptoms will be reduced.

The following specialist importers have confirmed they can source unlicensed imports of lisdexamfetamine (Vyvanse) capsules (please note there may be other companies that can also source supplies and lead times vary):

* + Alium
  + Target

Where a patient has had a treatment break greater than 4 days, they should build the dose up according to BNF guidance, with the aim of reestablishing the previous dose. Medication must be reviewed to ensure no new medication has been added in the interim period that may interact. This can be done safety within primary care if resources and skills are available. Failing that, the patient can be referred to the specialist service for reinitiation but due to the limited resources this will result in a lengthy delay in reinitiation.

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| **Medication** | **Reinitiation** |
| Lisdexamfetamine (Elvanse ®) | Initially 30 mg once daily, increased in steps of 20 mg every week until the original maintenance dose is achieved. Once stable check blood pressure and pulse. BP, pulse, and weight should be recorded at baseline.  (BP and pulse do not need to be checked before and after each dose change for people who have previously been established on a maintenance dose where treatment has ceased for less than 12 months and there is no significant change to their physical health status). |

**Guanfacine**

Guanfacine is an alpha-2-agonist, and sometimes used as an alternative non-stimulant medication to atomoxetine.

There are no bioequivalents to guanfacine. Given the limited alternative options and considering the fact that the majority of patients on guanfacine will already have failed or been unable to tolerate other products it is likely that there will be no alternatives and patients will need to wait until stock levels return.

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. Most patients with this diagnosis have blood pressures in excess of 220/120 mm Hg. 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. e.g.

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| Current prescription | Recommended tapering regime | Supplies required |
| Intuniv® 4mg OD | Intuniv® 3mg for 3 days then  Intuniv® 2mg for 3 days then  Intuniv® 1mg for 3 days then  Stop treatment | 6 x 2mg tablets  6 x 1mg tablets |
| Intuniv® 3mg OD | Intuniv® 2mg for 3 days then  Intuniv® 1mg for 3 days then  Stop treatment | 3 x 2mg tablets  3 x 1mg tablets |
| Intuniv® 2mg OD | Intuniv® 1mg for 3 days then  Stop treatment | 3 x 1mg tablets |
| Intuniv® 1mg OD | Stop treatment | Nil |

If it is not possible to taper doses, monitor BP and HR on stopping. The hypotensive effect of guanfacine may take about 2 – 4 days to resolve3,4. Rebound hypertension may occur, and has been reported to persist in some cases5. This is usually asymptomatic and clinically insignificant5,6.

Patients who are required to discontinue Guanfacine abruptly should be advised by the community pharmacist to monitor BP and HR at day 2, and again at day 4, patients with blood pressures over 140/90 mmHg (either the systolic or the diastolic) should be referred to primary care for further monitoring. If blood pressure is raised at day 4 (but not over 140/90 mmHg), measure again at weekly intervals until normal. If there are signs of clinically significant rebound hypertension (altered mental status, visual abnormalities, headache, or seizures), the pharmacist should alert primary care as per the existing protocols.

The following specialist importers have confirmed they can source unlicensed guanfacine prolonged-release tablets, lead times may vary (please note there may be other companies that can also source supplies):

* Smartway
* Genetech
* Target
* Alium

Where a patient has had a treatment break greater than 4 days, they should build the dose up according to BNF guidance (see table below), with the aim of reestablishing the previous dose. Medication must be reviewed to ensure no new medication has been added in the interim period that may interact. This can be done safety within primary care if resources and skills are available. Failing that, the patient can be referred to the specialist service for reinitiation but due to the limited resources this will result in a lengthy delay in reinitiation.

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| **Medication** | **Reinitiation** |
| Guanfacine | Initially 1 mg once daily; adjusted in steps of 1 mg every week until the original maintenance dose is achieved. Once stable check blood pressure and pulse. BP, pulse, and weight should be recorded at baseline.  (BP and pulse do not need to be checked before and after each dose change for people who have previously been established on a maintenance dose where treatment has ceased for less than 12 months and there is no significant change to their physical health status). |

**Atomoxetine**

Atomoxetine is a selective norepinephrine reuptake inhibitor (SNRI). There have been supply issues with atomoxetine over recent months.

Atomoxetine can be discontinued without side effects, but ADHD symptoms are likely to return.

Patients initiated on atomoxetine usually will have either have failed to respond to stimulants (methylphenidate / dexamfetamine) or will have had reasons that prohibited them from the use of stimulants. As such, those unable to source atomoxetine will have very limited options.

Where a patient has had a treatment break greater than 4 days, they should build the dose up according to BNF guidance (see table below), with the aim of reestablishing the previous dose. Medication must be reviewed to ensure no new medication has been added in the interim period that may interact. This can be done safety within primary care if resources and skills are available. Failing that, the patient can be referred to the specialist service for reinitiation but due to the limited resources this will result in a lengthy delay in reinitiation.

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| **Medication** | **Reinitiation** |
| Atomoxetine | Initially 40 mg daily for 7 days, dose is increased weekly by 40mg until the original maintenance dose is achieved. Once stable check blood pressure and pulse.  (BP and pulse do not need to be checked before and after each dose change for people who have previously been established on a maintenance dose where treatment has ceased for less than 12 months and there is no significant change to their physical health status). |