

American Association
of Psychiatric Pharmacists



AAPP Pharmacist Toolkit: Addressing Stimulant Shortages

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This toolkit is intended to highlight both the evidence base available as well as strategies of clinical decision making used by expert clinicians. The content reflects the views and practice of the authors as substantiated with evidence-based facts as well as opinion and experience. The opinions and recommendations in this document reflect those of the authors and do not necessarily reflect those of their employers or AAPP.

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Background

Stimulants (e.g., methylphenidate and amphetamine salts) are effective medications for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children, adolescents, and adults.^{1,2} Questions regarding increased prescribing of stimulants in the setting of the COVID-19 Pandemic, national emergency in child and adolescent mental health, and online prescribing platforms continuing to emerge in clinical practice.^{3,4} In the setting of a stimulant shortage, psychiatric pharmacists may be asked to identify alternative stimulant options for patients when a stimulant product becomes unavailable. Given class differences in mechanism of action (e.g., methylphenidate versus amphetamine salt), pharmacokinetic differences among formulations, and varying release technologies (e.g., OROS, SODAS), finding an ideal alternative product can be challenging.

This toolkit is intended to provide an evidence-based guide for thoughtfully converting from one stimulant product formulation to another.

General Dosing Considerations

Table 1. Stimulant Class Comparisons⁵

| | Methylphenidate | Amphetamine |
|--------------------------------------|--|---|
| Mechanism of Action | <ul style="list-style-type: none"> Allosterically block presynaptic DAT and NET Inhibit monoamine oxidase D-isomer more potent than L-isomer on both NET and DAT binding <ul style="list-style-type: none"> Unless otherwise noted, MPH formulations are all 1:1 D-MPH to L-MPH | <ul style="list-style-type: none"> Competitive inhibitor/ pseudosubstrate of presynaptic DAT and NET Inhibit monoamine oxidase (more potently than MPH) Competitive inhibitor of DA/NE vesicular transporter (VMAT2) at high doses D-isomer more potent DAT binding L-isomer equally potent DAT/NET binding <ul style="list-style-type: none"> MAS: 3:1 D-AMP to L-AMP |
| Metabolism | <ul style="list-style-type: none"> Hydrolysis via carboxylesterase-1 (CES-1) in the liver | <ul style="list-style-type: none"> Hepatically via CYP2D6 in the liver |
| General Dosing Considerations | <ul style="list-style-type: none"> D-MPH twice as potent as methylphenidate products MPH pediatric weight-based dosing: 0.3-2 mg/kg/day D-MPH pediatric weight-based dosing: 0.3-1 mg/kg/day | <ul style="list-style-type: none"> Twice as potent as MPH MAS: Pediatric weight-based dosing: 0.3-1 mg/kg/day Clinically significant drug interactions: CYP2D6 inhibitors (e.g., fluoxetine, bupropion) |

AMP = amphetamine; CYP = cytochrome P450; D-AMP = dextroamphetamine; DAT = dopamine transporter; DMPH = dexmethylphenidate; NET = norepinephrine transporter; MAS = mixed amphetamine salts; MPH = methylphenidate.

Table 2. Stimulant Dose Conversions⁶⁻⁸

| Product Base | Treatment Plan | Recommendation | |
|--------------------------------|---|--|---|
| Mixed Amphetamine Salts | Adderall IR → Adderall XR | <ul style="list-style-type: none"> • Same total daily dose of Adderall XR, taken once daily (i.e., 5 mg BID IR → 10 mg daily) • Adderall IR tablets can be crushed/split • Adderall XR capsules (50%IR/50%ER beads) can be opened and contents sprinkled onto applesauce. Consume entire contents immediately, do not chew or crush beads | |
| | Adderall XR → Adzenys XR ODT | Adderall XR 5 mg | Adzenys XR 3.1 mg |
| | | Adderall XR 10 mg | Adzenys XR 6.3 mg |
| | | Adderall XR 15 mg | Adzenys XR 9.4 mg |
| | | Adderall XR 20 mg | Adzenys XR 12.5 mg |
| | | Adderall XR 25 mg | Adzenys XR 15.7 mg |
| | Adderall XR 30 mg | Adzenys XR 18.8 mg | <ul style="list-style-type: none"> • 50%IR/50%ER composition • Orange/Citrus flavor |
| | All MAS products (except Adderall XR) → Adzenys XR ODT | <ul style="list-style-type: none"> • Discontinue previous treatment and titrate Adzenys XR using titration schedule in package insert • Do not substitute other amphetamine products on a mg:mg basis | |
| All MAS products → Adzenys ER | <ul style="list-style-type: none"> • Do not substitute on a mg/mg basis due to differences in PK profiles | | |
| All MAS products → Dyanavel XR | <ul style="list-style-type: none"> • Discontinue previous treatment and titrate Dyanavel XR using titration schedule in package insert • Do not substitute other amphetamine products on a mg:mg basis • Dyanavel XR tablets may be chewed or swallowed whole; scored tablets (5 mg) may be cut. • Suspension is bubblegum flavored | | |
| All MAS products → Evekeo | <ul style="list-style-type: none"> • No direct conversion, discontinue previous treatment and titrate Evekeo using titration schedule • No information is available regarding crushing/splitting Evekeo tablets | | |

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| | | <ul style="list-style-type: none"> • ODT-tablets should be dissolved on the tongue without chewing or crushing; not flavored |
| | Adderall XR →LDX | Adderall XR 10mg LDX 30 mg |
| | | Adderall XR 20mg LDX 50 mg |
| | | Adderall XR 30mg LDX 70 mg |
| | <ul style="list-style-type: none"> • LDX capsules may be opened and mixed with yogurt, water, or orange juice. A thin film containing inactive ingredients may remain in the container following consumption | |
| | All MAS products →Mydayis | <ul style="list-style-type: none"> • Do not substitute on a mg/mg basis due to differences in PK profiles • Capsules may be opened, and contents sprinkled. Do not chew beads |
| Dextroamphetamine | Dexedrine IR → SR | <ul style="list-style-type: none"> • Same total daily dose, taken once daily • Dexedrine IR tablets can be crushed/split • Dexedrine SR spansule (50%IR/50%ER beads) can be opened and sprinkled on applesauce. Consume entire contents immediately, do not chew or crush beads |
| | All D-AMP products →LDX | <ul style="list-style-type: none"> • Discontinue previous stimulant product, and titrate as outlined in package insert |
| | All D-AMP products → Xelstrym | <ul style="list-style-type: none"> • Do not substitute for other AMP products on a mg:mg basis because of different AMP base compositions and differing PK profiles • From the Xelstrym manufacturer PI: <ul style="list-style-type: none"> ○ 4.5 mg/9-hour patch contains 5 mg D-AMP ○ 9 mg/9-hour patch contains 10 mg D-AMP ○ 13.5 mg/9-hour patch contains 15 mg D-AMP ○ 18 mg/9-hour patch contains 20 mg D-AMP |

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| Methylphenidates | Ritalin IR → Ritalin LA | <ul style="list-style-type: none"> • Same total daily dose of Methylphenidate LA, taken once daily (i.e., 5 mg IR BID → 10 mg LA daily) • Ritalin LA (50%IR/50%ER) capsules may be opened and contents sprinkled onto applesauce. Consume entire contents immediately, do not chew or crush beads | | |
| | Ritalin SR → Ritalin LA | <ul style="list-style-type: none"> • Direct conversion on a mg:mg basis (i.e., 20 mg SR → 20 mg LA) | | |
| | MPH IR (Ritalin IR) → methylphenidate ER (Concerta, Relexxii) | Methylphenidate IR 5 mg BID or TID | MPH ER 18 mg daily | |
| | | Methylphenidate IR 10 mg BID or TID | MPH ER 36 mg daily | |
| | | Methylphenidate IR 15 mg BID or TID | MPH ER 54 mg daily | |
| | | Methylphenidate IR 20 mg BID or TID | MPH ER 72 mg daily | |
| | | <ul style="list-style-type: none"> • MPH IR tablets can be crushed/split | <ul style="list-style-type: none"> • MPH ER cannot be crushed/split | |
| | MPH products → Daytrana patch | <ul style="list-style-type: none"> • Follow normal titration schedule; cannot convert on a mg per mg basis • From the Daytrana manufacturer PI: <ul style="list-style-type: none"> ○ 10 mg/9-hour patch contains 27.5 mg MPH ○ 15 mg/9-hour patch contains 41.3 mg MPH ○ 20 mg/9-hour patch contains 55 mg MPH • 30 mg/9-hour patch contains 82.5 mg MPH | | |
| MPH products → QuilliChew XR | <ul style="list-style-type: none"> • Discontinue previous treatment and titrate QuilliChew XR using titration schedule in package insert • Do not substitute other methylphenidate products on a mg:mg basis • Chewable tablets (30%IR/70%ER composition) are cherry flavor and can be chewed or swallowed whole | | | |
| MPH products → Quillivant XR | <ul style="list-style-type: none"> • No direct conversion available, given differences in PK profiles • Follow normal titration schedule; cannot convert on a mg:mg basis | | | |

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| | | <ul style="list-style-type: none"> Oral suspension (20%IR/80%ER composition) must be shaken before each dose and is banana flavored |
| | Metadate CD → Metadate ER | <ul style="list-style-type: none"> No direct conversion available, given differences in PK profiles CD: faster onset of action, reaches peak more quickly, capsule (30% IR/70% XR beads) contents can be opened and sprinkled. Consume entire contents immediately, do not chew or crush beads ER: wax matrix, with less reliable absorption. Tablets cannot be crushed/split |
| | MPH products → Cotempla XR ODT | <ul style="list-style-type: none"> No direct conversion available, given differences in PK profiles Follow normal titration schedule; cannot convert on a mg per mg basis Orally disintegrating tablet (25% IR/75% XR) is grape flavored |
| | MPH products → Jornay PM | <ul style="list-style-type: none"> Do not substitute Jornay PM for other methylphenidate products on a mg per mg basis Other methylphenidate products have different pharmacokinetic profiles from Jornay PM and may have different methylphenidate base composition |
| Dexmethylphenidate | MPH IR → D-MPH IR | <ul style="list-style-type: none"> Half the current total daily dose of MPH IR (i.e., MPH 5 mg BID → D-MPH 2.5 mg BID) MPH IR, D-MPH IR tablets can be crushed/split |
| | MPH IR → D-MPH XR | <ul style="list-style-type: none"> Half of the current total daily dose of MPH (i.e., MPH 5 mg BID → D-MPH 5 mg daily) D-MPH XR capsule (50%IR/50% enteric coated DR beads) contents can be opened and sprinkled. Consume entire contents immediately, do not chew or crush beads |
| | D-MPH IR → D-MPH XR | <ul style="list-style-type: none"> Same total daily dose of dexmethylphenidate XR given once daily (i.e., 5 mg BID IR → 10 mg daily) |
| | MPH products → Azstarys (D-MPH and serdexmethylphenidate) | <ul style="list-style-type: none"> To avoid substitution errors and overdosage, do not substitute for other methylphenidate products on a mg:mg basis |

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|--|--|
| | <ul style="list-style-type: none"> Azstarys capsule (30%IR D-MPH/70% serdexmethylphenidate) contents can be opened and sprinkled onto 2 tablespoons of applesauce or into 2 ounces of water. Consume entire contents within 10 minutes. |
|--|--|

AMP=amphetamine; CD = controlled delivery; D-AMP = dextroamphetamine; ER/XR = extended release; IR = immediate release; LA = long acting; MAS = mixed amphetamine salts; MPH = methylphenidate; ODT = orally disintegrating tablet; PK = pharmacokinetics; SR = sustained release

Other Important Considerations

Refer to package inserts for initial dosing and recommended titrations for each medication⁸

When in doubt, start with lower dose of medication and titrate to effect. Take into consideration relative potency of the stimulant product (e.g., methylphenidate vs amphetamine), onset and duration of effect, potential for drug interactions (e.g., CYP2D6 inhibitors and amphetamine), and practical administration factors (e.g., capsules that can be opened and sprinkled vs tablets that can be crushed/split).

When switching between Concerta products, remember that generics manufactured by Actavis are bioequivalent to brand name Concerta (osmotic controlled release oral delivery system (OROS). (AB equivalence rating). Generics: Mallinckrodt, Kremers are not equivalent to the brand name and do not have the same OROS delivery mechanism. (BX equivalence rating).⁹

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