Novel Formulations of ADHD Medications: Stimulant Selection and Management

Ann C. Childress, M.D.

Attention-deficit hyperactivity disorder (ADHD) is the most commonly diagnosed psychiatric disorder in children and adolescents in the United States. In 2016, approximately 3.8 million U.S. children ages 2 to 17 years with ADHD were being treated with medication. There are approximately 30 different amphetamine (AMPH) and methylphenidate (MPH) formulations on the market. These include immediate-release and extended-release compounds. The extended-release formulations contain various ratios of immediate-release and extended-release components, which determine the pharmacokinetic (PK) profile. For stimulants, the PK and pharmacodynamic (PD) profiles are tightly linked, and the immediate-release and extended-release percentages influence onset and duration of drug effects. Choosing the right stimulant medication for a patient depends on an understanding of the PK/PD profile, the time of day that symptoms are most impairing, the need for morning and evening symptom control and individual patient preferences.

Focus 2021; 19:31–38; doi: 10.1176/appi.focus.20200032

Attention-deficit hyperactivity disorder (ADHD) is the most commonly diagnosed psychiatric disorder in children, and symptoms often continue into adulthood (1–3). Among U.S. children ages 2 to 17, approximately 6.1 million (9.4%) were estimated to have been diagnosed as having ADHD on the basis of the 2016 National Survey of Children's Health (4). Of these, 62.0% (approximately 3.8 million) with current ADHD symptoms were taking medication. The estimated prevalence of ADHD among U.S. adults is 4.4% (3). The prevalence of adult ADHD medication use in the total U.S. population was 1.48% in 2010—the highest in the world (5).

Several professional societies in the United States, including the American Academy of Pediatrics (AAP), the American Academy of Child and Adolescent Psychiatry (AACAP), and the Society for Developmental and Behavioral Pediatrics (SDBP), have released guidelines for the treatment of ADHD in children and adolescents. Although organizations in other countries, such as the National Institute for Health Care and Excellence, have also published ADHD treatment guidelines, this article focuses on recommendations for treatment and medications available in the United States (6).

Key action statement 5b in the recent AAP "Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of ADHD in Children and Adolescents" states that elementary school– and middle school–age children should be treated with a U.S. Food and Drug Administration (FDA)–approved medication, along with parent training in behavior management (7). Key action statement 5c states that adolescents should be prescribed FDA-approved medications for ADHD, with the adolescent's assent, and encourages the primary care provider to also prescribe evidence-based training or behavioral interventions along with appropriate educational interventions. For preschool-age children (ages 4 to <6), key action statement 5a recommends evidence-based parent training in behavior management. If parent training in behavior management is not available or is available and not effective, treatment with methylphenidate is recommended.

The SDBP issued a practice guideline for the assessment and treatment of complex ADHD in children and adolescents in February 2020 (8). It recommends evidence-based treatments for ADHD and coexisting conditions.

Although the AACAP "Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder " was published more than a decade ago, it is still relevant (9). It recommends initial pharmacological treatment with an FDA-approved medication.

FDA-approved medications include stimulants and nonstimulants. Stimulants include amphetamine (AMPH) and methylphenidate (MPH). Nonstimulants include atomoxetine, guanfacine extended release, and clonidine extended release (10–14).

DRUG REVIEW

Stimulants are by far the most widely prescribed medications for the treatment of ADHD in the United States (15).

Thus this article focuses on the use of stimulants to treat ADHD, specifically how to target specific patient needs. Although osmotic-release oral system (OROS) MPH (Concerta), mixed amphetamine salts (Adderall), mixed amphetamine salts extended release (Adderall XR), and lisdexamfetamine (Vyvanse) have the largest market share in the United States, stimulant formulations prescribed less frequently should also be considered when treating individual patients (15).

Approximately 30 stimulants are FDA-approved for the treatment of ADHD, and 12 of these have been approved since 2010. New stimulant formulations approved since 2010 include MPH extended-release oral suspension (Quillivant XR), MPH extended-release chewable tablets (QuilliChew ER), racemic AMPH (Evekeo), racemic AMPH orally disintegrating tablets (Evekeo ODT), multilayer-release MPH (Aptensio XR), AMPH extended-release oral suspension 2.5 mg/mL (Dyanavel XR), MPH extended-release orally disintegrating tablet (Cotempla XR-ODT), AMPH extended-release orally disintegrating tablets (Adzenys XR-ODT), AMPH extended-release oral suspension 1.25 mg/mL (Adzenys ER), mixed amphetamine salts 16 hour (Mydayis), MPH delayed-release and extended-release (Jornay PM), and MPH multilayer-release 16 hour (Adhansia XR) (16–26). AMPH immediate release (Zenzedi) is not a new formulation but includes multiple dextroamphetamine doses not previously available (27). Medications approved since 2000 are listed in Tables 1 and 2.

Stimulant formulations not mentioned above include racemic MPH controlled delivery (Metadate CD), MPH long acting (Ritalin LA), Methylin, and Methylin ER (28–30). Methylin is an oral suspension of MPH immediate-release formulation, and Methylin ER is bioequivalent to Ritalin SR. Ritalin SR has been shown to have efficacy from approximately 1 hour to 9 hours after dosing (31). MPH transdermal system (Daytrana), a patch placed on the hip that delivers MPH through the skin, is also marketed (32). Dexmethylphenidate, the *d*-threo enantiomer of racemic MPH, is marketed as Focalin, dexmethylphenidate extended release (Focalin XR), and multiple generics (33, 34).

Stimulants exhibit a strong concentration-response relationship for both efficacy and safety (35–37). For this reason, different formulations with different pharmacokinetic profiles developed from the same active component (AMPH or MPH) may have differing onset and duration of effect.

How to Choose a Stimulant Formulation

With the vast number of medications available to treat ADHD, selecting an initial pharmacological treatment may seem complex. However, the array of available medications allows the clinician to tailor treatment to individual patient needs. When choosing an initial therapy for ADHD, one should first consider that stimulants are in general more effective than nonstimulants (38). Other factors, such as the time of day when a patient is most symptomatic, the ability to swallow a tablet or capsule, concern about abuse or diversion either with the patient or a household member, and patient or parent preference, should also be considered. Daytime functioning or evening commitments should also influence the formulation choice. In general, when choosing a stimulant, an extended-release formulation should be chosen in lieu of an immediate-release formulation to improve adherence and decrease the risk of misuse (39, 40).

A recent meta-analysis of efficacy and tolerability of ADHD medications in children, adolescents, and adults favored the use of MPH in children and adolescents and AMPH in adults as initial pharmacological treatment for ADHD (41). FDA-approved drugs evaluated also included guanfacine extended release and atomoxetine.

Is the Patient Able to Swallow Tablets or Capsules?

Although the extended-release stimulant capsule formulations can be opened and sprinkled on applesauce for patients who cannot or prefer not to swallow a capsule whole, this maneuver is more difficult than it sounds. Capsules must be opened carefully to avoid spilling the contents, and it is important that the patient not chew the contents to avoid premature release of the drug (dose dumping). For patients who cannot or will not swallow an intact tablet or capsule, it may be more practical to choose an extended-release suspension in a chewable or orally disintegrating tablet formulation. It is important to consider patient and parent preference, including taste, when choosing a preparation. For example, teens may prefer not to take a suspension. Suspensions may also be less transportable than tablets or capsules, and MPH extended-release oral suspension is dispensed in a glass bottle that can break if dropped.

Oral suspensions can be easily titrated with just one prescription. The directions contained in the package inserts allow quick titration to optimal dose: MPH extended-release oral suspension (10–20 mg weekly), AMPH extended-release oral suspension 1.25 mg/mL (3.1–6.3 mg weekly), and AMPH extended-release oral suspension 2.5 mg/mL (2.5–10 mg every 4 to 7 days), so that patients can escalate to an effective dose within 1 month of starting medication. In contrast, for patients who have difficulty tolerating stimulant increases with tablets or capsules, the medication can be titrated very slowly with an oral suspension. Dosage can easily be adjusted by less than a mL to allow time for attenuation of adverse effects.

How to Achieve Optimal Response

Dose optimization of medication is important when treating ADHD. In double-blind, placebo-controlled clinical studies using one stimulant, 25%−35% of subjects were considered nonresponders (9). However, in crossover studies comparing AMPH with MPH, 68%−97% of subjects responded to at least one class of stimulants and 12%−71% responded to both (42).

How, then, does a clinician maximize the opportunity for response? A standardized scale should be used to obtain baseline and follow-up ADHD symptom ratings. For children, adolescents, and adults, several scales are available. A

TABLE 1. Extended-release methylphenidate formulations approved since 2000 for the treatment of attention-deficit hyperactivity disorder

Formulation	Dose form	Onset of effect[a]	Maximum duration of effect[a]	Initial dose	Dosing
Methylphenidate multilayer release, extended release (Adhansia XR)	25-, 35-, 45-, 55-, 70-, 85-mg capsules	1.0 hour	16 hours	25 mg	25–85 mg; increase 10–15 mg every 5 days
Methylphenidate multilayer release (Aptensio XR)	10-, 15-, 20-, 30-, 40-, 50-, 60-mg capsules	1.0 hour	12 hours	10 mg	10–60 mg; increase by 10 mg every 7 days
Osmotic-release oral system methylphenidate (Concerta)	18-, 27-, 36-, 54-mg tablets	1.0 hour	12.5 hours	18 mg	18–54 mg for children; 18–72 mg for adolescents and adults (not to exceed 2 mg/kg/day)
Methylphenidate extended release, orally disintegrating tablet (Cotempla XR-ODT)	8.6-, 17.3-, 25.9-mg tablets	1.0 hour	12 hours	17.3 mg	17.3–51.8 mg; increase 8.6–17.3 mg/day every 7 days
Methylphenidate transdermal system (Daytrana)	10-, 15-, 20-, 30-mg patches	2.0 hours	12 hours (when worn for 9 hours)	10 mg	10–30 mg
Dexmethylphenidate extended release (Focalin XR)	5-, 10-, 15-, 20-, 25-, 30-, 35-, 40-mg capsules	0.5 hour	12 hours	5 mg for children; 10 mg for adults	5–30 mg for children; 10–40 mg for adults
Methylphenidate delayed release/extended release (Jornay PM)	20-, 40-, 60-, 80-, 100-mg capsules	10 hours after dosing	23 hours after dosing	20 mg	20–100 mg; increase 20 mg weekly
Methylphenidate controlled delivery (Metadate CD)	10-, 20-, 30-, 40-, 50-, 60-mg capsules	1.5 hours	7.5–12 hours (depending on dose)	20 mg	10–60 mg
Methylphenidate extended release, oral suspension (Quillivant XR)	Extended-release suspension 25 mg/5 mL	0.75 hour	12 hours	20 mg	20–60 mg; increase 10–20 mg every 7 days
Methylphenidate extended release, chewable tablet (QuilliChew ER)	20 mg-, 30 mg-, 40-mg tablets	2.0 hours	8 hours	20 mg	20–60 mg; increase 10–20 mg every 7 days
Long-acting methylphenidate (Ritalin)	10-, 20-, 30-, 40-mg capsules	30 minutes	12 hours (depending on dose)	10–20 mg	10–60 mg

[a] Data for onset and duration of effect may not be in the Food and Drug Administration–approved label.

clinician should choose one for children and adolescents and another for adults to use regularly. Most laboratory classroom studies used an open-label, dose-optimization design prior to the double-blind, placebo-controlled classroom period. For several studies, a 30% improvement on an ADHD rating scale and a Clinical Global Impression improvement score of 1 (very much improved) or 2 (much improved) were considered minimal criteria for optimal response. Many protocols allowed further dose increases if tolerability was acceptable and subjects could benefit from an increased dose. If subjects had difficulty tolerating the higher dose, a dose reduction was allowed. Additionally, if subjects could not achieve the above criteria, they were discontinued from the trial. These criteria should be considered when treating patients in clinical practice. If a patient is unable to reach or tolerate an optimal dose in practice, the drug should be discontinued and another formulation prescribed.

Target Specific Times of Day

Early-morning efficacy. The time of day when symptoms are most impairing can be targeted with stimulant formulations. If a child or adult has severe problems in the morning that cause difficulty preparing for school or work, a medication that is effective in the morning can be chosen. For example, delayed-release/extended-release MPH is formulated to have delayed onset of effect for approximately 10 hours after ingestion and is designed for patients to take in the evening and have onset of effect upon awakening the next morning. Data

TABLE 2. Intermediate- and extended-release amphetamine formulations approved since 2000 for the treatment of attention-deficit hyperactivity disorder

Formulation	Dose form	Onset of effect[a]	Maximum duration of effect[a]	Initial dose	Dosing
Mixed amphetamine salts, extended release (Adderall XR)	5-, 10-, 15-, 20-, 25-, 30-mg capsules	1.5 hours	12 hours (depending on dose)	10 mg for ages 6–17; 20 mg for adults	5–30 mg for ages 6–12; 5–20 mg for ages 13–17; 20 mg for adults
Extended-release amphetamine, orally disintegrating tablets (Adzenys XR ODT)	3.1-, 6.3-, 9.4-, 12.5-, 15.7-, 18.8-mg tablets	Bioequivalent to Adderall XR	Bioequivalent to Adderall XR	6.3 mg for ages 6–17; 12.5 mg for adults	6.3–18.8 mg for ages 6–12; 6.3–12.5 mg for ages 13–17; 12.5 mg for adults
Extended-release amphetamine, suspension (Adzenys ER)	1.25-mg/mL extended-release suspension	Bioequivalent to Adderall XR	Bioequivalent to Adderall XR	6.3 mg for ages 6–17; 12.5 mg for adults	6.3–18.8 mg for ages 6–12; 6.3–12.5 mg for ages 13–17; 12.5 mg for adults
Amphetamine, extended release, oral suspension (Dyanavel XR)	2.5-mg/mL extended-release suspension	30 minutes	13 hours	2.5–5 mg for ages 6 and older	2.5–20 mg for ages 6 and older; increase 2.5–5 mg every 4–7 days
Racemic amphetamine (Evekeo)	5-, 10-mg tablets	45 minutes	10 hours	2.5 mg for ages 3 and older; 5 mg for ages 6 and older	5–40 mg divided daily or twice daily for ages 6 and older
Racemic amphetamine, orally disintegrating tablets (Evekeo ODT)	5-, 10-, 15-, 20-mg tablets	Bioequivalent to Evekeo	Bioequivalent to Evekeo	5 mg daily or twice daily	Increase 5 mg weekly; maximum dose not listed in label
Mixed amphetamine salts, extra-long extended release (Mydayis)	12.5-, 25-, 37.5-, 50-mg capsules	2.0 hours	16 hours	12.5 mg for ages 13 and older	12.5–25 mg for ages 13–17; 12.5–50 mg for adults
Lisdexamfetamine (Vyvanse)	10-, 20-, 30-, 40-, 50-, 60-, 70-mg capsules; 10-, 20-, 30-, 40-, 50-, 60-mg chewable tablets	1.5 hours	14 hours in adults; 13 hours in children	30 mg	30–70 mg; increase 10–20 mg weekly

[a] Data for onset and duration of effect may not be in the Food and Drug Administration–approved label.

from two studies enrolling subjects ages 6 to 12 years who had morning impairment showed significant improvement in completing the morning routine. A laboratory classroom study demonstrated that the drug was effective, compared with placebo, during the school day and into the evening. An important consideration with delayed-release/extended-release MPH is dosing. The relative bioavailability of delayed-release/extended-release MPH is 73.9%, compared with immediate-release MPH (43). At the end of a 6-week, open-label, dose-optimization period in one study, the mean daily optimized dose was 66.2 mg (SD=19.56) (44). Although the FDA-recommended starting dose is 20 mg, most patients will not achieve optimal symptom control until higher doses are prescribed. For example, a patient taking 72 mg of OROS-MPH may need to take 100 mg of delayed-release/extended-release MPH.

For patients with early-morning impairment who prefer not to take medication in the evening, two extended-release formulations have demonstrated onset of efficacy at 30 minutes after dosing. These include dexmethylphenidate extended-release and AMPH extended-release oral suspension 2.5 mg/mL (45, 46). Additionally, MPH extended-release oral suspension has onset of effect at 45 minutes after dosing (47). Onset of effect is influenced by the percentage of immediate-release compound in different formulations. For example, OROS-MPH is composed of 22% immediate-release MPH, whereas MPH controlled delivery contains 30% immediate-release MPH and MPH long acting and dexmethylphenidate extended release have a 50% immediate-release component. Although MPH extended-release oral suspension contains approximately 20% MPH immediate release and 80% MPH extended release, there are thousands of MPH particles in each dose. The extended-release particles are covered by a proprietary coating of various thicknesses to achieve early onset and extended duration of effect (47).

OROS-MPH has 22% MPH immediate-release coating on the tablet, and the label states that OROS-MPH did not have significant change from placebo in a laboratory classroom

trial until 2 hours after dosing (13). A head-to-head trial between OROS-MPH and MPH controlled delivery demonstrated that OROS-MPH has an earlier onset of effect, with an effect size of 0.52 at 1.5 hours postdose (48). A later trial, measuring time points from 1 hour to 12.5 hours after dosing, demonstrated onset of efficacy at 1 hour and duration of effect to 12.5 hours, compared with placebo (49).

Another option is to apply the MPH transdermal system to the hip before the patient awakens; however, this approach requires a caregiver to be up early to apply the patch because it takes about 2 hours to onset of effect (50). Because it is recommended to wear the patch for no more than 9 hours, application early in the morning would likely require removal and proper disposal by the child at school. For example, if the MPH transdermal system is applied at 0400, it should be removed at 1300. Because more than 50% of MPH drug content remains in the patch after removal at 9 hours, the potential for misuse exists for discarded patches (51).

Evening efficacy. Multiple marketed extended-release formulations have been shown to be effective 12 hours postdose, as measured in a laboratory classroom, after the drug has been optimized over several weeks. It is important to remember that drug effects are compared with placebo effects in the laboratory classroom trials. In an examination of one such effect—dexmethylphenidate 20 mg at 12 hours—ratings were similar to predose but significantly better than placebo ratings. This is an example of a statistically significant but not clinically relevant outcome. Consequently, many patients may require the addition of an afternoon immediate-release formulation to achieve noticeable efficacy at 12 hours and beyond.

To avoid use of multiple medications for patients who require a longer duration of effect, one MPH extended-release and three AMPH extended-release formulations are available. Laboratory classroom studies in adults demonstrated duration of effect of up to 16 hours for dose-optimized MPH extended-release and mixed amphetamine salts extended-release formulations (52, 53). The duration of effect for lisdexamfetamine in laboratory classroom trials was shown to be 13 hours in children ages 6 to 12 and 14 hours in adults (54, 55). In another laboratory classroom trial, AMPH extended-release oral suspension 2.5 mg/mL also showed efficacy to 13 hours (56).

Because lisdexamfetamine is a prodrug and the *l*-lysine has to be cleaved from the dextro-amphetamine for the drug to become active, its onset of effect is delayed. In a laboratory classroom study in children ages 6 to 12, onset of effect occurred approximately 1.5 hours after ingestion (55). In the mixed amphetamine salts 16-hour trials, the first onset of effect was measured at 2 hours after dosing in an adolescent laboratory classroom (57).

In addition to differences in onset and duration of effect, formulations differ in the time of peak efficacy and the amount of interpatient variability. Many of the extended-release properties depend on pH in different segments of the gastrointestinal (GI) tract. GI transit time can influence release of the extended-release portion of the drug and shorten or lengthen the duration of efficacy. Food can delay onset of effects for many formulations and shorten it for others (37). For example, administration with a high-fat meal delayed time to maximum concentration (Tmax) by 1 hour for OROS-MPH and by 2.5 hours for mixed amphetamine salts extended release and shortened Tmax by 30 minutes for MPH extended-release orally disintegrating tablet (37). Maximum concentration of the active moiety may also be decreased when administered with a high-fat meal.

Few head-to-head studies have evaluated extended-release stimulants. In two studies comparing dexmethylphenidate extended release with OROS-MPH, the dexmethylphenidate extended-release formulation had a faster onset of effect, whereas OROS-MPH showed greater effect at 10–12 hours (58, 59). When controlled-delivery MPH was compared with OROS-MPH, both were significantly better statistically, compared with placebo, from 1.5 to 7.5 hours (48). The MPH controlled-delivery effect was statistically better, compared with OROS-MPH, at 1.5–4.5 hours, whereas the OROS-MPH effect was statistically better, compared with MPH controlled delivery, at 12 hours (48). Direct comparisons of other MPH products have not been conducted.

Extend Duration of Effect

When prescribing a stimulant, it is important to understand that increasing the dose can prolong duration of efficacy. This is illustrated by the trial comparing 20 mg dexmethylphenidate extended release with 30 mg dexmethylphenidate extended release. Attempted and correct scores on a math test were higher for the patients on the 30 mg dose at 10–12 hours (60). Mixed amphetamine salts extended release is another example. In the mixed amphetamine salts extended-release laboratory classroom trials, onset of effect was seen by 1.5 hours after dosing (61). However, only the 20- and 30-mg doses were effective at 10.5 and 12 hours after dosing. Although extended duration of effect is seen in trials, it may not be seen clinically. If a patient is tolerating a specific dose of medication but the dose is not fully optimized, increasing the dose may be a consideration. Adverse effects should be queried before and after the dose increase to ensure that an attempt at extending the efficacy does not make the drug side effects intolerable.

Single-Isomer Versus Racemic Formulation

Another consideration in treatment is whether to use a single isomer or a racemic formulation. With MPH, the *d*-threo-enantiomer preferentially crosses the blood-brain barrier. Plasma concentrations are ten to 40 times higher than those of the *l*-enantiomer (62). When dexmethylphenidate is used, the dose used is half of the racemic drug. Theoretically, one might expect fewer adverse effects with the single *d*-enantiomer; however, no data available support this notion—adverse effects are similar for dexmethylphenidate and racemic MPH in clinical trials.

In contrast, for AMPH, both the both the *d*- and *l*- isomers are effective in treating ADHD (63). Both isomers increase the extracellular concentrations of dopamine and norepinephrine in the brain. Currently, only *d*-AMPH and *d,l*-AMPH preparations are on the market. The *d,l*-AMPH preparations contain *d*- and *l*-isomers in a ratio of 50:50 (racemic AMPH and racemic AMPH orally disintegrating tablets) or in a ratio of 3:1 (mixed amphetamine salts, AMPH extended-release oral suspension, AMPH extended-release orally disintegrating tablet, and AMPH extended-release oral suspension) (14, 64–66). AMPH extended-release orally disintegrating tablets and AMPH extended-release oral suspension 1.25 mg/mL are bioequivalent to mixed amphetamine salts extended release; however, AMPH extended-release orally disintegrating tablets and AMPH extended-release oral suspension do not contain salt molecules, and their doses are described only as AMPH base.

In 2013, the FDA began to require all newly approved stimulant formulations to express dose of the active moiety rather than the salt form (67). Although the directive was meant to decrease confusion, the goal has not been accomplished. For example, mixed amphetamine salts extended-release 30 mg is equivalent to 18.8-mg AMPH extended-release orally disintegrating tablets or AMPH extended-release oral suspension 1.25 mg/mL, and MPH hydrochloride 30 mg is equivalent to 25.9-mg MPH extended-release orally disintegrating tablets (68, 69). Multiplying the dose of MPH hydrochloride extended-release products by 0.8647 will result in the appropriate dose of MPH extended-release orally disintegrating tablets. Because the conversion factor for AMPH extended-release orally disintegrating tablets depends on the molecular weight of the AMPH salt and because marketed AMPH products vary in their salt composition, the reader is referred to the table in Engelking et al. (67) for the appropriate conversion factors.

Regarding the AMPH orally disintegrating tablets and AMPH extended-release suspension 1.25 mg/mL, 50% of AMPH microparticles are coated for delayed release and 50% are left uncoated for the immediate-release component (69). Although bioequivalent to mixed amphetamine salts extended release, the properties of the orally disintegrating tablets and suspension dosage forms may make these formulations more tolerable for individual patients. With mixed amphetamine salts extended release, half of the drug is released immediately and half approximately 4 hours later (64). AMPH extended-release oral suspension 2.5 mg/mL is bioequivalent to two doses of mixed amphetamine salts extended release dosed 4 hours apart but is also formulated with immediate-release and extended-release microparticles and no salt—and doses are described in mg of AMPH base.

Racemic AMPH is intermediate acting. A single dose measured in a laboratory classroom demonstrated onset and duration of effect at 45 minutes and 10 hours, respectively (70). Racemic AMPH orally disintegrating tablets are bioequivalent to racemic AMPH and are expected to have similar onset and duration, but this formulation has not been evaluated in a laboratory classroom (71). These drugs are often dosed twice daily, 4 to 6 hours apart (67, 72).

Dextro-AMPH is marketed in multiple immediate-release preparations and also as the extended-release prodrug lisdexamfetamine. The immediate-release formulation of dextro-AMPH is dosed two to three times daily (73, 74).

CONCLUSIONS

Multiple MPH and AMPH drugs are available for the treatment of ADHD, and the pharmacokinetic and pharmacodynamic properties of various formulations are tightly linked. Choosing the most appropriate medication depends on time of day when symptom control is needed, tolerability, and individual preferences. Small differences in the ratio of immediate-release to extended-release drug may translate to significant differences in onset and duration of effect. It is important have a thorough understanding of the entire ADHD armamentarium to provide the best care for patients.

AUTHOR AND ARTICLE INFORMATION

Center for Psychiatry and Behavioral Medicine, Inc., Las Vegas. Send correspondence to Dr. Childress (drann87@aol.com).

Dr. Childress reports receipt of research or writing support, participation on advisory boards, and service as a consultant or speaker for Adlon Therapeutics, Aevi Genomic Medicine, Akili Interactive, Allergan, Arbor Pharmaceuticals, Cingulate Therapeutics, Emalex Biosciences, Ironshore Pharmaceuticals, Jazz Pharmaceuticals, KemPharm, Lundbeck, Neos Therapeutics, Neurovance, NLS Pharma, Otsuka, Pearson, Pfizer, Purdue Pharma, Rhodes Pharmaceuticals, Sunovion, Supernus Pharmaceuticals, Takeda, and Tris Pharma.

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