

# PERSPECTIVE ON THE **RX** PIPELINE

Understanding changes in the medication market and their impact on cost and care.

EnvisionRx continuously monitors the drug pipeline. As treatment options change, we evaluate and share our perspective on the clinical benefits, cost-effectiveness and overall impact to payers and patients. Our Perspective on the Rx Pipeline report provides ongoing actionable insights from our team of clinical experts and the steps we are taking to protect and improve plan performance.

## Included in this Edition

- ▶ It's Time to Pay Attention to the Growing Pipeline of Attention Deficit Hyperactivity Disorder (ADHD) Medications

# ADHD

## It's Time to Pay Attention to the Growing Pipeline of Attention Deficit Hyperactivity Disorder (ADHD) Medications

### PIPELINE STAGE



### TIMING

When will payers be impacted?



### CLINICAL EFFECTIVENESS

Compared to available options, is this drug better for treatment?



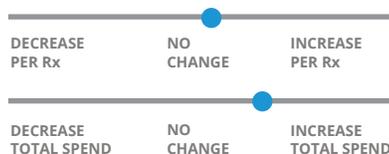
### PATIENT EXPERIENCE

Will this positively or negatively impact members?



### PAYER IMPACT

How will this influence Rx spend?



### Situation Summary

Attention Deficit Hyperactivity Disorder (ADHD) is a condition that mainly affects children and young adults, and the prevalence of the condition is on the rise with 10.2% of the U.S. population impacted in 2015-2016, compared to only 6.1% in 1997-1998.<sup>[1]</sup> While not as common, currently 4.4% of adults ages 18 to 44 in the U.S. are diagnosed with ADHD as well.<sup>[2]</sup>

**Treatment for ADHD:** When treating ADHD, a step-wise approach is utilized and many factors, such as age, gender and severity weigh into the management of this condition. Medications are not often first-line treatment options. According to the American Academy of Pediatrics' ADHD clinical practice guidelines, behavioral therapy is recommended prior to medication for preschool-aged children. Pharmacotherapy can be used in conjunction with behavioral therapy for children six years of age and older.<sup>[3]</sup>

The most common treatment for ADHD is stimulants, such as amphetamines (Adderall) or methylphenidate (Ritalin). The efficacy of stimulants was demonstrated in a recent study of 379 children that found approximately 70% of the subjects responded to a stimulant, making them the preferred therapy.<sup>[4]</sup>

With any medication, especially in children, there are considerations when choosing the right treatment, and side effects is one of those factors. Stimulants are controlled substances with side effects, including decreased appetite, cardiovascular conditions, seizures, poor growth, abdominal pain, insomnia, aggression, headache, tics or psychosis.<sup>[1, 5]</sup>

The choice of which stimulant is usually patient specific based on dosing schedule, desired duration of effect and tolerability. Other considerations should include the age of the patient, the patient's ability to swallow tablets or capsules, abuse or diversion potential, and drug cost.<sup>[6]</sup>

Currently, non-stimulants such as Strattera® (atomoxetine), Kapvay™ (guafacine) and Intuniv® (clonidine) are options for patients where stimulants are contraindicated or have not resulted in symptom control, however, they tend to be less effective than stimulants for most patients.<sup>[3]</sup> While these

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medications are not controlled substances, there are still potential side effects, such as headache, drowsiness, decreased appetite, nausea and constipation.

**ADHD in Adults:** Studies show that ADHD persists into adulthood in approximately 30% to 60% of cases.<sup>[7]</sup> Adult onset ADHD may occur, but often is attributed to other conditions, such as mood disorders, anxiety or substance abuse. These conditions should be ruled out before starting therapy for ADHD if there is not a childhood history.<sup>[3]</sup> The preferred treatment for adults is also stimulants, however, atomoxetine is prescribed as well. Although off-label for the treatment of ADHD in adults, bupropion and tricyclic antidepressants (nortriptyline) have shown possible efficacy.<sup>[8, 9]</sup>

**Concerns with Stimulant Treatment Option:** While stimulants are successful in treating ADHD, they are controlled substances that can have adverse side effects, causing concerns for some parents, including the potential for abuse and addiction. Treating and managing ADHD may require trial and failure of a few therapies to find the ideal patient-centered care plan. Having additional treatment options available may give healthcare providers and parents options when selecting an appropriate therapy for the child.

**The Future of ADHD Therapy Focused on Adding More Non-Stimulant and Reformulation Options:**

There continues to be manufacturer research and product development in ADHD treatments. The drug pipeline is full of alternate dosage options for stimulants, several new non-stimulant options, as well as current medications seeking approval for ADHD. These repurposed options include omega-3 fatty acid supplementation, modafinil, Rexulti® (brexipiprazole), memantine and donepezil.

As more non-stimulant branded treatment options begin to emerge over the coming years, there could be an increase in spend and utilization over time. However, this potential increase is not just attributed to the development of non-stimulant medications. While there are several generic agents on the market today, there is still considerable use of brand-name products. This can be attributed to innovations in dosing schedules and delivery options being made available to patients. As an example, Jornay PM™ (methylphenidate), approved by the FDA in 2018 but not yet available in the market, is a delayed-release/extended-release medication dosed at nighttime for the next day.

Other approved ADHD treatments include Mydayis® (amphetamine salts), which offers 16-hour coverage compared to Adderall XR's (amphetamine salts) 12-hour coverage, and Cotempla XR-ODT® (methylphenidate ER), which offers an orally disintegrating, long-acting product for those six to 17 years of age.

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## The ADHD Drug Pipeline Includes:

Pipeline Drug Name	Generic Name	Stimulant or Non-Stimulant	Mechanism of Action	Stage	Clinical Insight
Dasotraline	Dasotraline	Non-Stimulant	Serotonin, norepinephrine and dopamine reuptake inhibitor (SNDRi)	Complete response issued, Phase III	In 2018, FDA requested more efficacy and tolerability data before possible approval.
SPN-810	Molindone Hydrochloride	Non-Stimulant	Dopamine receptor antagonist	Phase III	Intended to be used to help reduce aggression in children taking stimulants. Molindone was marketed as Moban® in the U.S. for the management of schizophrenia in the 1970s and has since been discontinued. <sup>[10]</sup>
SPN-812	Viloxazine Hydrochloride	Non-Stimulant	Norepinephrine reuptake inhibitor	Phase III	Viloxazine has been used since 1976 to treat depression in Europe, but has since been discontinued. <sup>[11]</sup>
AEVI-001	Fasoracetam	Non-Stimulant	Metabotropic glutamate receptor 5 (mGluR5) inhibitor	Phase III	Fasoracetam has a novel mechanism of action, a modulator of glutamate receptors. A published Phase I study showed improvement in symptoms for those with mGluR variant, but population size was limited. <sup>[12]</sup>
EB-1020	Centanafadine	Non-Stimulant	Serotonin, norepinephrine and dopamine reuptake inhibitor (SNDRi)	Phase III	Phase III trials compare centanafadine to placebo. Completion of the trial is estimated to be near May 2020. <sup>[13]</sup>
KP415	Serdexmethylphenidate	Stimulant	CNS stimulant	Phase III	Data suggests several potential clinically beneficial features of KP415 if approved, including a relatively rapid increase and higher overall levels of plasma d-methylphenidate compared to other formulations. KemPharm is examining if the drug may have once daily dosing potential and an improved onset of action. <sup>[14]</sup>
ORADUR®-Methylphenidate	Methylphenidate	Stimulant	CNS stimulant	Phase III	A once daily methylphenidate that may be tamper resistant to some forms of abuse, such as snorting, smoking, injecting, chewing and dissolving in drinks. <sup>[15]</sup>
AMPH ER	Amphetamine	Stimulant	CNS stimulant	Phase III	Current Phase III clinical trial is recruiting those 18 to 60 years of age to be randomized to AMPH ER or a placebo. <sup>[16]</sup>
Rexulti®	Brexipiprazole	Non-Stimulant	Atypical antipsychotic	Phase II	Currently indicated for adjunctive treatment of major depressive disorder and schizophrenia. <sup>[17]</sup>

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## PAYER ACTION PLAN

- **Apply Utilization Management Controls**

Since stimulants are the cornerstone for treatment of ADHD, EnvisionRx recommends that utilization management controls, such as quantity limits be implemented to prevent stockpiling and diversion of medications that could have the potential for abuse or misuse. Step therapy can also be utilized to increase generic utilization. For EnvisionRx clients enrolled in our standard utilization management programs, no action is needed, as we have already implemented the appropriate utilization management controls.

- **Monitor the Drug Pipeline**

As more ADHD therapy options become available, it is important to monitor the drug pipeline and update formulary strategies and utilization management controls as needed. For EnvisionRx clients, we will continue to watch this drug class and provide updates.

## Impact to the Pharmacy Care Experience

**Formulary:** EnvisionRx provides a balanced approach of stimulant and non-stimulant products on our formularies. There are a number of generic ADHD treatment options available. Those agents are preferred in our formularies to drive utilization of lower-costing alternatives.

We will continue to monitor the drug pipeline and as more ADHD treatment options are approved, our Pharmacy & Therapeutics committee will review these medications for safety and clinical efficacy, prior to an analysis of the pharmacoeconomic impact, to determine placement on our formularies.

**Plan Design:** To ensure that the right medication is given at the right time, EnvisionRx has implemented age restrictions for certain ADHD medications and applies quantity limits and refill thresholds to prevent inappropriate use of these controlled substances. We utilize step therapy to drive utilization of generic options as well.

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## Our Clinical Steering Committee

The Envision Clinical Steering Committee brings together leaders from across our national pharmacy care company to monitor the drug landscape, provide recommendations on how to address changes, and to ensure our clients and patients are prepared—in advance.

With any new development, we partner with our Pharmacy & Therapeutics (P&T) Committee and consult with our best-in-class specialty pharmacy, to provide a balanced perspective on the clinical effectiveness of all available options, the cost impact to our plan sponsors and patients, and the impact on the overall patient experience.



**Kel Riley, MD**  
*Chief Medical Officer*



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EnvisionRx is a Pharmacy Benefit Manager (PBM), providing affordable and effective prescription drug coverage for employers and health plans. Using its proprietary EnvisionCare model, EnvisionRx optimizes all aspects of the pharmacy care experience to consistently achieve better patient and plan outcomes.

