

UConn

AN ONGOING CE PROGRAM
of the University of Connecticut
School of Pharmacy

EDUCATIONAL OBJECTIVES

After completing the continuing education activity, pharmacists will be able to

- DESCRIBE autism spectrum disorder (ASD) and its manifestations
- LIST medications used to manage symptoms of ASD
- APPLY techniques to improve care in the pharmacy for patients with ASD and their caretakers

After completing the continuing education activity, pharmacy technicians will be able to

- DESCRIBE autism spectrum disorder (ASD) and its manifestations
- LIST medications used to manage symptoms of ASD
- RECOGNIZE situations in which they can help patients with ASD and their caretakers appropriately



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Pharmacists and pharmacy technicians are eligible to participate in this application-based activity and will receive up to 0.2 CEU (2 contact hours) for completing the activity, passing the post-test with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission

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Understanding Treatment Approaches for Autism Spectrum Disorder

TARGET AUDIENCE: Pharmacists and pharmacy technicians interested in behavioral health and the modalities used to manage behavioral conditions.

ABSTRACT: Our understanding of "autism" has evolved from the early 1900s when it was originally described as childhood schizophrenia. Although classified as an independent condition in the DSM-III in 1980, the DSM-V consolidated autistic disorder, Asperger syndrome, pervasive developmental disorder—not otherwise specified, and childhood disintegrative disorder into the term known as autism spectrum disorder (ASD). This has left many healthcare providers confused about the diagnosis and its treatment. Pharmacists and pharmacy technicians need tools so that they will be able to communicate with and help people who have ASD. In addition, they need to have science-based information about the treatments used in ASD, and the indications for which they are employed. It also introduces and expands upon the terms neurotypical and neurodiverse.

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INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by persistent challenges in social interaction and communication, and restricted, repetitive patterns of behavior, interests, or activities. "Autism" has evolved from the early 1900s, when it was originally described as childhood schizophrenia in the first and second editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM).¹ Autism was classified as an independent condition in the DSM-III in 1980. The DSM-IV in 1994 was the first to recognize autism as a spectrum

with various distinct diagnoses. In 2013, the DSM-V consolidated autistic disorder, Asperger syndrome, pervasive developmental disorder—not otherwise specified, and childhood disintegrative disorder into the term known as autism spectrum disorder.²

The change in terminology has left many healthcare providers unsure about how to talk with and about people who have ASD. Researchers from the United Kingdom surveyed 654 English-speaking adults with ASD around the world to determine their preferences.³ Regardless of country, participants tended to favor the terms autism, autistic person, is autistic, neurological/brain difference, differences, challenges, difficulties, neurotypical people, and neurotypicals. Thus, the researchers were unable to find a universally accepted vernacular to talk about autism.³ Perhaps the best way to determine how to describe a patient with ASD is to ask how they themselves prefer to discuss their condition.

The term neurotypical is closely related to the term neurodiverse, and the **SIDEBAR** (to the right) describes this relatively new term.

Prevalence rates of ASD are reported to be approximately 1% worldwide (i.e., affecting 1 in 100 people), with comparable figures observed in samples of children and adults.⁸ Prevalence estimates have increased over time and vary greatly within and across socioeconomic and demographic groups. ASD is diagnosed four times more often in males than females.²

PAUSE AND PONDER: How many symptoms of autism spectrum disorder can you list before you continue reading?

Diagnosing ASD

According to the DSM-V, diagnosis of ASD requires persistent deficits in all three areas of social communication and interaction, in addition to at least two of four types of restricted, repetitive behaviors. **Table 1** (on the next page) lists ASD's core characteristics and symptoms.

Symptoms must be present in early development, cause clinically significant impairment in functioning, and cannot be attributable to intellectual disability or developmental delay. Since ASD is a spectrum, symptoms, severity, and treatment response vary widely among children and adults. Severity is categorized into three levels, described in **Table 2** (on page 4).²

Prognosis

One concern for many people with ASD and their caregivers is long-term prognosis. A recent systematic review looked at data from 16 small studies (two randomized, 14 non-randomized).⁹ Only three of the included studies enrolled more than 100 participants, limiting the ability to draw conclu-

SIDEBAR: Neurodiversity⁴⁻⁷

Medical insight and social changes in the perception of developmental disorders and neurodevelopmental trajectories, including the autism spectrum, have led to a changing vocabulary and a deeper appreciation of what is “normal.” Increasingly, we understand that human development is neurodiverse, meaning all individuals develop and behave differently. The concept of neurodiversity promotes the idea that people who have neurological limitations also have strengths, and that accommodating their differences as early in life as possible can be beneficial to the individual and to society at large. This is an empathetic, humanistic, tolerant approach.

It's now clear that people with ASD are often skilled in working with systems and finding patterns in complex data or material. This makes them good candidates to work in technology and manufacturing if an employer can accommodate an individual's needs (e.g., quiet or dimly lit spaces, private or uncrowded work areas). People with dyslexia are often better than others at identifying peripheral or diffuse visual information or processing blurry visual scenes, making them excellent candidates for jobs that engage three-dimensional thinking (e.g., computer graphics, engineering, genetics, or molecular biology). Similarly, people with Williams syndrome (a rare genetic condition that affects physical features, development, and cardiovascular health), Down syndrome, and Prader-Willi syndrome (a rare genetic disorder causing weak muscles, poor feeding, and slow development in infants followed by constant hunger in childhood), tend to be more musical, more friendly, and more nurturing than others, respectively. Researchers have also connected specific strengths to other neurologic and intellectual disability diagnoses.

The origin of these strengths and limitations is probably linked to evolutionary adaptation. Being able to focus on patterns and systems, as seen in ASD, likely helped early humans in hunting and gathering societies. They were able to respond quickly to environmental stimuli and move in an appropriate direction when they identified potential prey. A famous quote comes from the autism activist Temple Grandin, who has autism. She has said, “Some guy with high functioning Asperger's developed the first stone spear; it wasn't developed by the social ones yakking around the campfire.”

The bottom line is that appreciating and respecting neurodiversity is kind and reasonable. Another quote from Temple Grandin explains it well: “Nature is cruel, but we don't have to be.”

sions, but researchers found that early intervention improved children's prognosis considerably.

Children who received intervention before 2 years of age were more likely to improve their cognition, social skills, and stereotyped behaviors than others. They needed less monitoring at

Table 1. Symptoms of ASD²

Social Communication Deficits	Restricted/Repetitive Behaviors
Deficits in social-emotional reciprocity <ul style="list-style-type: none"> ● Reduced sharing of interests ● Struggles with emotional recognition 	Stereotyped or repetitive motor movements, use of objects, or speech <ul style="list-style-type: none"> ● Arranging objects meticulously ● Echolalia (meaningless word repetition) ● Stereotypical movements like hand-flapping
Deficits in non-verbal communication <ul style="list-style-type: none"> ● Aversion to eye contact ● Abnormal body language/facial expressions 	Hypo- or hyper-reactivity to sensory input or unusual interest in sensory input <ul style="list-style-type: none"> ● Apparent indifference to pain/temperature ● Adverse response to sounds or textures ● Excessive smelling/touching of objects ● Visual fascination with lights or movement
Deficits in developing, maintaining, and understanding relationships <ul style="list-style-type: none"> ● Scripted speech/taking language literally ● Difficulty in sharing imaginative play ● Difficulty making friends ● Absence of interest in peers 	Highly restricted, fixated interests that are abnormal in intensity or focus <ul style="list-style-type: none"> ● Expecting others to share their interests ● Strong attachment to unusual objects
	Insistence on sameness, inflexibility in routines, or ritualized patterns of behavior <ul style="list-style-type: none"> ● Discomfort with change

school and were better able to function and integrate socially. These researchers noted that healthcare providers often fail to offer early intervention for four reasons⁹:

1. Many healthcare providers are unfamiliar with the necessary screening, diagnosis, and intervention tools for ASD
2. Early intervention involves many different strategies and is costly
3. Involving parents in early intervention programs is difficult
4. It's difficult to recognize ASD's signs in toddlers younger than 2 years

ASD CASE PRESENTATION

John, a 10-year-old boy with ASD, enters the community pharmacy with his mother to pick up his prescription for aripiprazole 10 mg tablets. His agitation due to the bright lights and loud chatter from other customers becomes immediately apparent to the pharmacy team. They notice several visible signs and hear auditory cues that indicate his discomfort and distress in the environment. John's body tenses up, with rigid posture and fidgety movements, and his hands are clenched tightly as he paces and rocks back and forth. His facial expressions—furrowed brows and widened eyes—convey distress, and his vocalizations include whimpers and "I don't like it here." Additionally, John exhibits repetitive behaviors such as hand-flapping and tapping his mother. He attempts to retreat from the situation by seeking refuge behind his mother. Understanding his sensitivity to sensory in-

put, the pharmacy team must respond with patience, empathy, and sensitivity to ensure John feels supported and safe during his visit. In addition, John's mother will appreciate empathy and accommodation.

Strategies for Support

Pharmacists can employ their medication expertise to help the healthcare team, families, and patients improve ASD management. As John's description indicates, patients with ASD are often sensitive to sensory input like noise, light, and crowded environments.¹⁰ Pharmacists should recognize how a pharmacy setup can affect patients, potentially hindering communication. Offering to move to a quiet, dimly lit, private space (e.g., the consultation or vaccination area) for counseling helps accommodate sensory sensitivities.

When communicating with patients with ASD, pharmacists should consider the patient's level of autonomy and assess the need to interact primarily with the patient or the caregiver. Communication strategies can include using simplified language, direct communication, and patients' names to engage them and aid comprehension. Providing training to pharmacy staff on ASD can help pharmacists and technicians to serve these patients better.¹⁰

Putting Strategies in Action

The pharmacist, Keith, addresses John by name, acknowledges his discomfort, and minimizes distractions to create a more calm-

ing environment to put John at ease. For example, “Hello, John. I’m your pharmacist, and my name is Keith. It’s noisy out here. Would you like to move to a quieter room?” A technician familiar with the patient can also make this suggestion as soon as the patient arrives.

Keith also involves caregivers in the discussion, ensures they understand the medication instructions, and addresses any concerns they may have. He also reassures them of his availability for further assistance by saying, “I’m glad we talked about your medications today. If you have questions, you can stop in or call. I’m generally here Tuesday through Saturday, and my coworker Suzanne covers when I’m not here.”

By implementing these strategies, community pharmacists and technicians can improve the patient care experience for individuals with ASD.¹⁰

ASD TREATMENT

ASD is complex, and treatment often involves a multidisciplinary approach targeting various symptoms and challenges.¹¹ Although there is no outright “cure,” effective interventions may enhance functioning of children and adults with ASD. Pillars of treatment include behavioral therapies, speech and language therapy, occupational therapy, educational support, and sometimes medication management.

Behavioral therapy (e.g., applied behavioral analysis) involves creating a structured behavioral plan to improve adaptive skills and reduce inappropriate behaviors by studying affected individuals' functional difficulties systematically. Speech and language therapy is an integral part of ASD treatment for many children. Speech therapy targets difficulty with social communication and language development, which are some of ASD's core symptoms. Language therapy may employ visual supports like picture cards, augmentative and alternative communication devices, and teaching sign language (e.g., American Sign Language). Occupational therapy focuses on enhancing individuals' ability to participate in everyday activities and improve their quality of life. It typically addresses sensory processing issues, motor skill development, self-care skills, social interaction, and coping strategies, aiming to promote independence and function in various environments.¹¹

ASD treatment involves a multidisciplinary care team comprising professionals such as specialists, psychologists, pediatricians, paraprofessionals, and educators; ideally, team members collaborate to address individuals' diverse needs and provide comprehensive support and intervention.¹¹

ASD Treatment Guidelines

Several treatment guidelines are available for ASD. The United Kingdom's National Institute for Health and Care Excellence

Table 2. Level of Severity of ASD²

Severity	Social Communication	Restricted/Repetitive Behaviors
Level 1 Requiring support	Noticeable impairments in social communication without support, difficulty initiating social interactions and exhibiting atypical or unsuccessful responses to social cues, possible decreased interest in social interactions <i>Example: Able to speak full sentences, engages in communications, but social conversation attempts are odd/unsuccessful</i>	Rigid behavior significantly disrupts functioning in various contexts, challenges transitioning between activities, difficulty with organization and planning
Level 2 Requiring substantial support	Marked deficits in verbal/nonverbal social communication skills, social impairments apparent even with support, limited initiation of social interactions, reduced/abnormal responses to social approaches from others <i>Example: Speaks simple sentences, interaction limited to narrow special interests, odd nonverbal communication</i>	Difficulty coping with change and showing obvious restricted/repetitive behaviors that interfere with functioning in multiple contexts, distress/difficulty switching focus
Level 3 Requiring very substantial support	Severe deficits in verbal/nonverbal social communication skills, severe impairments in functioning, very limited initiation of social interactions, minimal response to social cues from others <i>Example: Few words of intelligible speech, rarely initiates interaction, makes unusual approaches to meet needs only and responds to only very direct social approaches</i>	Inflexibility of behavior, extreme difficulty coping with change, restricted/repetitive behaviors significantly interfere with functioning in all contexts, great distress/difficulty changing focus or action



(NICE) has published ASD guidelines for both children under 19 years old and adults.^{12,13} The Canadian Pharmacists Journal published ASD practice guidelines specifically for pharmacists. The latter guideline outlines strategies for effective communication and discusses how the community pharmacy team can create a welcoming environment for people with autism and their caregivers.¹⁰

Community pharmacists and technicians often encounter patients with diverse needs, including those with ASD. To provide optimal care, it's crucial to understand patients' unique challenges and tailor services accordingly. Let's look at a case that highlights the importance of accommodating a patient with ASD in the pharmacy setting.

Pharmacologic Interventions

Pharmacotherapy for ASD primarily focuses on managing symptoms rather than directly targeting core features.⁸ However, many challenges exist in this area, including limited efficacy and evidence, adverse effects, individual variability, lack of targeted therapies, and long-term monitoring. Prescribers should consider that children with ASD often have heightened sensitivity to medication and are more prone to adverse reactions compared to neurotypical children. It is advisable to initiate pharmacologic treatment at lower doses and increase gradually based on response and tolerability. It's crucial to gather objective symptom measures from various sources both before and after intervention to assess treatment response accurately across different settings.⁸

Another major hurdle lies in addressing co-occurring disorders that often accompany ASD, such as attention-deficit/hyperactivity disorder (ADHD), anxiety, epilepsy, sleep disorders, and more. These additional conditions complicate treatment approaches, requiring tailored interventions to ad-

dress unique needs. Very limited evidence supports the effectiveness of many medications used to manage ASD symptoms.¹⁴

The lack of medications specifically targeting core ASD symptoms and the limited efficacy data for various medications present barriers to identifying effective treatment strategies. Addressing these challenges requires a comprehensive approach that integrates pharmacologic interventions with behavioral, educational, and supportive therapies personalized to the individual's specific needs and circumstances. Additionally, ongoing research is crucial to advance our understanding of ASD and develop more effective and targeted pharmacological treatments in the future.¹⁴

Most medications for ASD are used off-label and few United States Food and Drug Administration (FDA)-approved drugs are available for specific symptom management. Medications used may include atypical antipsychotics, stimulants, serotonergic drugs, alpha-2 adrenergic antagonists, anticonvulsants, and many others.¹⁴

Atypical Antipsychotics

Prescribers often use atypical antipsychotics for irritability associated with ASD. Currently, the FDA has approved only two medications for treatment of irritability associated with ASD: risperidone and aripiprazole.^{15,16} Both are atypical (second generation) antipsychotics and exert effects through dopamine, 5-HT (serotonin), alpha-adrenergic, and histaminergic receptors in the brain.

Clinical trials have demonstrated effectiveness of these drugs in reducing irritability and, to a lesser extent, repetitive behaviors. They share similar safety profiles, with common adverse effects including fatigue, increased appetite, gastrointestinal symptoms, hyperprolactinemia, weight gain, and sedation. Less common adverse effects include restlessness and akathisia (inability to remain still). Serious adverse effects such as dyslipidemia, hyperglycemia, metabolic syndrome, and extrapyramidal symptoms (e.g., involuntary movements, muscle stiffness, tremors) or drug-induced movement disorders have also been reported, necessitating close clinical and laboratory monitoring.¹⁴

Risperidone is FDA-approved for treatment of ASD-associated irritability in children and adolescents aged 5 to 16 years.¹⁵ Studies have demonstrated that risperidone may effectively improve core symptoms of ASD, including communication, social interaction, and repetitive behaviors. Non-core symptoms such as aggression, tantrums, and self-injurious behaviors also improved based on various behavioral rating scales. Risperidone is generally well-tolerated and safe, with the most common adverse effect being mild, self-limiting weight gain. In one small study of 97 children treated with risperidone over a 6-month period, participants gained an average of 5.4 kg over 24 weeks. At baseline, 59 of the 97 children (60.8%) had normal weight status. By week 24, only 25 of the remaining 85 children (29.4%) maintained normal weights.¹⁷ In adults with ASD, adverse cognitive effects have not

been observed in patients treated with risperidone for other psychiatric disorders. However, further exploration is needed regarding the efficacy of risperidone in adults with ASD.¹⁸

Aripiprazole is FDA-approved for treatment of ASD-associated irritability in pediatric patients 6 to 17 years old.¹⁶ Short-term studies have shown that aripiprazole can improve irritability, hyperactivity, and repetitive behaviors in children and adolescents with ASD compared to placebo. However, researchers have not observed improvement in lethargy or withdrawal symptoms. Aripiprazole use was associated with higher rates of movement disorders such as tremors and muscle rigidity. While aripiprazole may offer benefits, weight gain and neurological adverse effects like involuntary movements can limit its use. Regular monitoring of symptoms and adverse effects is recommended, and further research is needed to evaluate the long-term safety and effectiveness of aripiprazole in treating ASD.¹⁹

Other atypical antipsychotics occasionally used off-label for ASD include olanzapine, quetiapine, and ziprasidone. Providers generally avoid first generation antipsychotics due to the higher risk of movement-related adverse effects.¹⁴

Revisiting John's Case

John's ASD is graded at Level 2—needing substantial support. He requires a range of support services tailored to his individual needs to thrive. For instance, John may benefit from behavioral interventions aimed at addressing his irritability and other behavioral challenges associated with his autism. These interventions could include strategies to manage his sensory sensitivities, develop coping skills, and enhance social communication. Additionally, providing John with structured routines and visual supports, such as clear schedules and visual cues, can help him navigate daily activities more effectively and reduce anxiety. Given his sensitivity to sensory stimuli, providing sensory accommodations like a quiet space or sensory tools (e.g., noise-canceling headphones) can aid in regulating his sensory experiences and minimizing agitation.

Moreover, John's prescription for aripiprazole indicates the need for medication management to address his irritability. Keeping in mind that John is 10 years old and in a period of rapid growth, it's crucial for the pharmacy team to monitor his height and weight regularly. The pharmacy team must inquire about any recent changes in his behavior or symptoms. The reason: the two atypical antipsychotics approved for irritability have similarities and differences that are critical to recognize, and with weight changes, the dose may require adjustments. The pharmacy team can support John's family, particularly his mother, with referral to resources such as parent training programs and support groups that can help them navigate the challenges associated with caring for a child with ASD. John can receive the assistance he needs to thrive and lead a fulfilling life with these comprehensive supports in place.

PAUSE AND PONDER: How many children with ASD receive care from your pharmacy? What behaviors do you see and hear?

Stimulants

Clinicians often prescribe stimulants to manage hyperactivity and inattention in ASD and co-existing ADHD. Two main classes of stimulants are commonly used in ADHD: amphetamines and methylphenidate derivatives.¹⁴ Prior to initiating stimulant therapy, clinicians must evaluate patients' medical and family histories and conduct a comprehensive physical exam focused on cardiovascular health. Ongoing monitoring for common adverse effects, such as appetite changes and sleep disturbances, is imperative, and it is essential to assess adolescent patients for risk of substance use or misuse before treatment initiation.

Amphetamine formulations include amphetamine-dextroamphetamine, dextroamphetamine, amphetamine sulfate, amphetamine, and lisdexamfetamine. Research suggests that amphetamines tend to be slightly more effective in reducing ADHD symptoms than methylphenidate, but they are also less tolerable. In a systematic review of data from more than 10,000 neurotypical individuals (i.e., children, adolescents, and adults without ASD), researchers found that amphetamines were more efficacious in reducing ADHD symptoms, although they were less well-tolerated than both placebo and methylphenidate in children and adolescents.²⁰

Methylphenidate products come in various formulations including immediate- and extended-release tablets or capsules, a transdermal patch, an extended-release liquid, and orally disintegrating tablets. Short-term treatment with methylphenidate has shown some benefit in improving hyperactivity, inattention, and other ADHD symptoms in children with ASD, but studies are small. The largest has enrolled just 66 children.²¹ Nonetheless, no evidence showed improvement in core ASD symptoms or social interaction. Additionally, while some children with ASD responded positively to methylphenidate, a significant number experi-



enced adverse effects such as irritability, repetitive behaviors, insomnia, and reduced appetite.¹⁴

Alpha-2 Adrenergic Agonists

Alpha-2 adrenergic agonists—including guanfacine and clonidine—are commonly used in ADHD management for younger children. Evidence exists regarding the off-label use of alpha-2 adrenergic agonists in alleviating some symptoms of ASD, so some providers use them off label for this condition. Clinicians commonly prescribe these for children younger than 5 years old with ADHD or hyperarousal (intense, rapid, and often overwhelming emotional responses). These medications are also useful in cases when patients have poor responses to stimulants or selective norepinephrine reuptake inhibitors (e.g., atomoxetine) or when patients have significant co-occurring conditions like sleep issues that preclude stimulant use.

Research on the use of alpha-2-adrenergic agonists in ASD is limited to a few small studies.¹⁴ Guanfacine has been shown to be safe and effective in managing hyperactivity and impulsiveness in children with ASD. Common adverse effects of guanfacine include sedation, constipation, irritability, and aggression, but they are generally better tolerated than stimulant medications.¹⁴

PAUSE AND PONDER: What kinds of questions should you ask caregivers when they present a new prescription for a patient with ASD? What information do they need to know (but might not think about)?

Other Medications with Limited Supporting Data

Several medications have been explored with limited evidence in ASD management. These include various serotonergic medications (selective norepinephrine receptor inhibitors [SNRIs] and selective serotonin reuptake inhibitors [SSRIs]), anticonvulsants, gabapentin, and trazodone.

Researchers have looked at SNRIs and SSRIs to treat difficult behaviors in ASD. Venlafaxine has been proven beneficial as an adjunct treatment for self-injurious behaviors, aggression, and ADHD symptoms in children and adults with ASD, particularly when administered at doses lower than those typically used for

depression.²² Conversely, duloxetine (also an SNRI) did not demonstrate any additional advantages in addressing comorbid symptoms and behaviors associated with ASD when compared to alternative antidepressants.²²

SSRIs can be helpful in patients with comorbid anxiety, which is very common with ASD. However, clinical trials assessing the SSRIs citalopram and fluoxetine found them to have low tolerability and limited effectiveness in addressing repetitive behaviors.²³

Anticonvulsants, also known as antiepileptic drugs, are sometimes used off-label in the treatment of certain ASD symptoms. While these medications are primarily indicated for seizure management, they may also be prescribed to address co-occurring conditions such as epilepsy, aggression, irritability, and repetitive behaviors in individuals with ASD. Examples of anticonvulsants studied or used in ASD treatment include valproic acid (valproate), lamotrigine, levetiracetam, and topiramate.¹⁴ However, the evidence supporting anticonvulsants' efficacy in treating ASD symptoms remains limited, and healthcare professionals should consider the use of these drugs carefully and monitor closely for potential adverse effects and individual variability in response.¹⁴

Limited research suggests that carbamazepine, oxcarbazepine, levetiracetam, and topiramate may exacerbate hyperactivity, mood disturbances, psychotic symptoms, and other psychiatric or behavioral issues in individuals with ASD.²⁴ These effects appear most common with levetiracetam. Evidence is inconclusive on the role of anticonvulsants in ASD in the absence of epilepsy, but there always remains potential for specific cases. Further research is needed to better understand the safety and effectiveness of anticonvulsants in ASD treatment and to identify subgroups of individuals who may benefit most from this approach.

Off-label use of gabapentin and trazodone for ASD presents significant patient safety concerns. Despite lacking FDA approval for this indication, these drugs are increasingly prescribed, leading to adverse drug reactions.²⁵ Gabapentin is often used off-label to address anxiety and occasionally behavioral problems. Gabapentin can also cause central nervous system depression. Its use in ASD is poorly studied, with one study that enrolled just 23 children (mean age 7.2) with various neurologic diagnoses finding that 78% of children had improved sleep at doses of 5 mg/kg 30 to 40 minutes before bedtime.²⁶ However, further research is required to substantiate these findings.²⁶

Very limited evidence supports using trazodone to manage irritability, but many individuals with ASD still use it, as sleep disturbances are very common. Safety considerations exist, as trazodone poses risks of overdose-related complications, including arrhythmias, respiratory arrest, coma, and the rare but serious condition of priapism. Overprescribing of these medications is increasing and not backed by evidence, especially in ASD. Cau-



Table 3. Best Interventions for Children with ASD at the Pharmacy^{10,30,31}

Anticipate that you will provide care for patients with ASD and identify a calm area where you can counsel without noise or distraction
Accept that some parents do not want to take any more time in a store (pharmacy or not) than they must, and try to accommodate them
At every visit, ask if anything has changed since the last visit and record an updated height and weight (especially if the patient is on a medication dosed by weight)
If parents struggle with administering medications to children with ASD <ul style="list-style-type: none">● Provide tailored support and education, offer clear and concise medication instructions using visual aids and use simplified language● Recommend dosage forms like liquids or chewable tablets to ease administration challenges● Offer customized packaging options such as unit-dose blister packs or pre-filled syringes proactively to simplify dosing and organization● Help parents and caregivers create visual medication schedules or reward systems to reduce anxiety during medication administration
Encourage parents and caregivers to keep a diary of symptoms so they can monitor the patient's response to newly prescribed medications
Remember that stimulants, gabapentin, and trazodone have been linked to abuse and all families need to be reminded to store these drugs securely <ul style="list-style-type: none">● In some states, gabapentin is a controlled substance

tious prescribing practices and thorough patient education are needed to ensure the safety and well-being of individuals with ASD using gabapentin and trazodone.

As mentioned, sleep problems are common in children with ASD. In fact, between 40% and 80% of children with ASD develop them.²⁷ For many children, insomnia is the problem, but other children develop parasomnias (e.g., sleep talking, sleepwalking, sleep terrors), or circadian rhythm sleep-wake disorders. Prescribers have various options available to treat insomnia, but in autism, the largest body of work describes the use of melatonin to improve sleep onset and maintenance. Research suggests using lowest doses (1 to 2 mg) and titrating upward gradually.^{28,29}

John Develops Insomnia

Once again, John and his mother visit the pharmacy to fill a prescription. His mom says that although they have a very structured schedule and John's regular bedtime is 9:00 PM, John has difficulty falling asleep and is often awake and moving around in his room for long periods of time. His mom says, "Recently, it feels like he's awake all night long and his symptoms are worse when he doesn't get enough sleep. It's a vicious cycle." She looks exhausted; a key issue when children with ASD develop sleep disorders is that the entire family often loses sleep.

Mom also reports that her primary care provider has counseled her on ways to help John get to sleep, including discouraging behaviors that interrupt sleep, using positive reinforcement when John is actively trying to sleep, and employing relaxation techniques. She says that she moved his bedtime to 11:00 PM and he

has been a little bit sleepier. Her plan is to move John's bedtime 15 minutes earlier each week. Regardless, John and his entire family still need additional help with this issue. John's mother indicates that the prescriber told her to speak with the pharmacist so she can find the most reliable melatonin product. That's a prudent recommendation, since many supplements are mislabeled or unreliable.²⁸

PHARMACY IMPLICATIONS

Pharmacists, pharmacy technicians, and the community pharmacy setting serve as essential components of healthcare for patients with ASD and their families. The pharmacy team can address concerns, provide encouragement, and ensure parents and caregivers feel equipped to manage medication administration effectively. Pharmacists can provide counseling and technicians can offer support to help caregivers confidently manage medication regimens for patients with ASD, ensuring better adherence and improved healthcare outcomes. **Table 3** (above) lists important reminders for the pharmacy team.

Pharmacists are a valuable drug information resource and adept at assessing existing evidence to help patients with ASD and their families make well-informed decisions. Pharmacy involvement is invaluable in providing optimal care and support for this patient population.

The Future of Treating ASD

The future of pharmacologic treatment for ASD holds promise but also faces significant challenges. Continued research into ASD's underlying neurobiologic mechanisms may lead to the de-

velopment of more targeted interventions tailored to address specific symptoms and subtypes of the disorder. Additionally, advancements in genetic testing and biomarker identification could enable personalized treatment approaches, optimizing efficacy while minimizing adverse effects.

Large-scale clinical trials and collaborative research efforts to evaluate treatment effectiveness comprehensively are needed. Ultimately, the future of medication therapy for ASD will depend on the ability to integrate advancements with a nuanced understanding of individual differences and needs of patients with ASD.¹⁴

CONCLUSION

While progress has been made in understanding and treating ASD, significant challenges remain. A comprehensive approach combining behavioral interventions, therapies, and pharmacotherapy tailored to individual needs is essential for improving outcomes in individuals with ASD. Continued research efforts are necessary to develop more effective and evidence-based treatments for this complex disorder. Temple Grandin explains it well: “A treatment method or an educational method that will work for one child may not work for another child. The one common denominator for all of the young children is that early intervention does work, and it seems to improve the prognosis.”

Figure 1. Working Productively with Patients who have ASD

Best

- 1 **Be COMMUNITY CHAMPIONS** and disseminate information in April, which is World Autism Awareness month
- 2 **Ask about any difficulties administering medication**, and offer different dosage forms for patients who have difficulty with tablets or capsules
- 3 **Help parents and caregivers create visual medication schedules or reward systems** to reduce anxiety during medication administration

Better

- 1 **Use your counseling space** to provide a quiet place for patients with ASD to wait if necessary
- 2 **Discuss each medication's potential adverse effects** and if it is used for an off-label indication, be sure to explain what to expect
- 3 **Remind patients (or parents) to read labels carefully** and follow the directions exactly

Good

- 1 **Step up your vocabulary** so that you refer to patients appropriately
- 2 **Recognize social skills deficits and**
- 3 **Empathize with patients and their parents** when they present at the pharmacy and need help

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