

Application by the Prader-Willi Syndrome Association New Zealand Requesting Guanfacine ER (Intuniv) Funding Criteria for Prader-Willi Syndrome

To: Mental Health Specialist Advisory Committee (MHAC), Pharmac

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About PWSA(NZ)

Prader-Willi Syndrome Association New Zealand (PWSA NZ) is the national organisation supporting individuals and families affected by Prader-Willi syndrome (PWS). We provide advocacy, education and support services. We hold a Disability Information Advisory Services (DIAS) contract with DSS.

About Prader-Willi Syndrome

Prader-Willi syndrome is a rare, genetic neurodevelopmental disorder caused by the loss of gene expression on chromosome 15. It is a lifelong condition requiring ongoing medical, behavioural and social support. It affects multiple aspects of physical health, cognitive functioning, behaviour and emotional regulation. Many of the symptoms of PWS can be attributed to hypothalamic dysfunction, such as the dysregulation of metabolism, hunger, sleep, body temperature, stress responses and emotional control.

People living with PWS experience a complex combination of developmental delay, intellectual disability, hyperphagia, endocrine disorders, behavioural challenges and mental health vulnerabilities. Due to the rarity of the syndrome, a lack of clinical understanding about the complexities of the syndrome sometimes exists and patients can have difficulty accessing appropriate expertise. People living with PWS can also appear more capable than they are – communicating well, developing familiar routines and demonstrating a degree of independence in some settings, which can mask the significant executive functioning difficulties, reduced insight, cognitive rigidity and impaired judgement associated with the syndrome. Consequently, support needs are often underestimated, resulting in insufficient supports that can lead to crisis and place the individual, their family, and sometimes the wider community at risk.

The PWSA(NZ) database currently contains details of 153 individuals living with PWS, but we estimate that approximately 200 people are living with a Prader-Willi syndrome diagnosis in New Zealand.

1. The ADHD Connection

While some traditional literature describes ADHD as occurring in only some patients with PWS, modern psychiatric experts, such as Dr Deepan Singh (USA) [1] and [Dr Maryssa Portelli](#) (AUS), argue that ADHD is common in PWS, and many patients would meet the diagnostic criteria for ADHD if formally evaluated.

“Attention deficit/hyperactivity symptoms and insistence on sameness are common with patients with PWS and have an early age of onset. Butler et al. also reported that patients with the PWS deletion were more affected than patients with UPD. Particularly, patients with the larger typical PWS type I deletion had more behavioral problems than those with the smaller typical type II deletion....” Wigren M, Hansen S, 2005. [2]

In Prader-Willi syndrome, ADHD primarily manifests as severe inattention (difficulty sustaining focus, poor working memory, slow processing speed) combined with profound impulsivity (emotional outbursts, low frustration tolerance, skin picking, and food-seeking behaviours). [3, 4]

These traits are frequently masked by, or solely attributed to, intellectual disability, the behavioural phenotype of PWS, oppositional defiance, or autism-like rigidity.

Scientific literature demonstrates that significantly higher than typical rates of ADHD exist in people with intellectual disabilities in general, but despite this high rate of co-occurrence, ADHD frequently remains underdiagnosed or misdiagnosed due to overlapping symptoms and the clinical complexity of assessing behaviours. [5, 6, 7]

2. The Health Need in Prader-Willi Syndrome

Executive dysfunction in PWS, which can manifest as severe attention deficits, hyperactivity, and poor impulse control, serves as a primary driver of chronic instability. The ripple effects of these cognitive and behavioural difficulties create an urgent, unaddressed health and therapeutic need.

Attention deficits and impulsivity act as significant barriers to functional independence, cognitive development, and emotional well-being.

- **Disrupted Learning and Skill Acquisition:** Severe inattention makes it difficult to filter out environmental stimuli, anxiety, or internal ‘food noise’, significantly affecting focus in educational and vocational settings.
- **Emotional Dysregulation and Outbursts:** The impaired ability to self-monitor and self-regulate impulses means that when faced with minor frustrations, changes to routine, or delayed gratification, the individual’s immediate neurobehavioural response is often heightened emotional reactivity. This can often escalate into intense temper outbursts, oppositional behaviour, or physical aggression.
- **Compulsive and Self-Injurious Behaviours:** Impulsivity exacerbates repetitive and compulsive behaviours characteristic of PWS, most notably severe skin picking. Without the cognitive ‘brakes’ needed to interrupt the impulse due to difficulties in thought and activity switching, individuals may pick at wounds until they cause deep tissue damage. Unhealed open wounds are highly susceptible to bacteria and can frequently progress to serious infections in individuals with PWS, transforming a behavioural issue into a chronic medical risk. [8, 9]
- **Social Isolation and Peer Rejection:** Impulsive social interactions, an inability to read social cues, inappropriate behaviours and low frustration tolerance make building relationships extremely challenging. In schools, community settings, or recreational groups, the individual may be excluded, compounding their social isolation. The combination of inattention and impulsivity restricts the individual's ability to participate meaningfully in broader social environments.

When impulsive behaviours escalate to dysregulation and aggression, these episodes unfortunately often lead to life-altering, negative consequences for the individual, such as suspensions from school, permanent exclusions from enjoyed activities, or irreversible damage to relationships. Once calm, an individual may deeply regret their actions during an outburst, but the events cannot be undone.

Impact on the Patient’s Family, Whānau and Wider Society

The presence of attention deficits and impulsive behaviours can reshape the structure, routine, and mental health of the entire household.

- **Chronic Caregiver Stress:** Parents / guardians live in a state of hypervigilance. The propensity for rapid loss of emotional control and impulsive behaviours necessitates careful management of the environment to avoid and manage triggers. Daily tasks, such as getting dressed, transitions between activities, or grocery shopping, can become high-stress flashpoints. Strategies need to

be consistently applied, which means that anyone supporting the family also needs to have a good understanding of the person, the syndrome, and the strategies required. This limits respite opportunities. Studies consistently show that parental stress in PWS correlates directly with the severity of behavioural problems rather than the physical symptoms of the syndrome. The unpredictability of impulsive meltdowns generates pervasive anxiety within family members and can lead to high rates of burnout, marital strain, and social isolation. [10]

- **Sibling Trauma and Deprivation:** Siblings frequently navigate a home life characterised by unpredictability and emotional volatility. Because impulsive outbursts require intense management from parents, siblings may experience diminished parental attention. Outbursts can result in social isolation, and, in some cases, symptoms of trauma or post-traumatic stress disorder (PTSD). [11]
- **Financial and Domestic Strain:** Families are often forced to heavily modify their home environments and restrict routine activities to prevent impulsive or aggressive incidents. The intensive coordination of behavioural support, crisis intervention, and supervision can limit a parent's ability to maintain full-time employment, compounding financial pressures.
- **Strain on Educational, Vocational and Residential Services:** In classrooms and day programmes, hyperactive, impulsive and inattentive behaviours demand disproportionate resources. Educators and support staff must utilise continuous one-on-one interventions to maintain group safety and engagement. In classrooms and supported residential living situations, impulsive behaviours may negatively impact the well-being and safety of peers, housemates, teachers or support staff. Aggressive outbursts can also lead to schools having to frequently follow time consuming stand-down and suspension processes.
- **Crisis Care and Emergency Interventions:** When impulsive behaviours manifest as acute aggression or physical property damage, families are sometimes forced to rely on emergency services, ED departments, or inpatient psychiatric services. This reliance creates preventable utilisation of acute healthcare and community emergency resources.

Summary

Addressing the root executive and neurological deficits associated with attention and impulse control in Prader-Willi syndrome is not merely about aiming to suppress difficult behaviours. It is a fundamental health necessity for improving patient safety, learning ability, and quality of life for patients and their families, as well as facilitating stable, safe community participation.

3. Suitability - Why Guanfacine is Recommended for PWS

Guanfacine acts directly on the brain's prefrontal cortex. Several studies of brain activity have suggested differences in the prefrontal cortex in patients with PWS [12, 13, 14, 15]. In this area of the brain responsible for regulating attention and impulse control, guanfacine works by strengthening natural filtering function which, for individuals with PWS, can help to quieten background sensory overload and lower their baseline level of stress and anxiety. It appears to create a 'cognitive window', so that when faced with a trigger, the individual has a moment to process the event rather than immediately reacting, helping to reduce the frequency and severity of outbursts.

Limited Therapeutic Options

Due to genetic differences, underlying hypothalamic dysfunction and altered body composition / metabolism, people living with PWS can respond atypically to standard drug treatments [16]. They might be more affected by side effects, experience 'activation' from a medication, or a total lack of efficacy. Response to medications can be both individual and syndrome specific. Therefore, a range of psychiatric options are needed. There are currently no funded, tailored options specifically targeting the broader cluster of impulsivity, attention deficit, and temper outbursts / aggression in PWS.

SSRIs and Antipsychotics

The challenging behaviours characteristic of Prader-Willi syndrome often result in individuals being prescribed SSRIs and antipsychotic medications - both of which carry clinical risks for people with PWS.

SSRIs have been known to trigger behavioural activation such as increased agitation and hypomania, possibly due to altered serotonergic pathways in PWS. [17, 18]

Atypical antipsychotics, such as risperidone and aripiprazole, are frequently used for severe behavioural challenges, but carry a risk of weight gain, increased appetite, metabolic syndrome and other side effects [19, 20] which are unhelpful for someone who already requires reduced calorific intake and experiences hyperphagia. Since prevention of obesity and metabolic syndrome is paramount to improving the quality of life of patients with PWS, options that mitigate these side effects need to be explored.

Stimulant ADHD Medications

While standard stimulant medications are sometimes prescribed in PWS, they are generally avoided or used with caution, particularly if there is a risk of mania or psychosis. Stimulants can sometimes aggravate existing obsessive-compulsive behaviours, anxiety, or perseveration. They may worsen mood stability, irritability, insomnia, and can trigger manic-like states. [21, 22, 23]

Individual response to stimulants can vary greatly and is highly dose-dependent, but it is known that individuals with intellectual disabilities are generally less likely to experience therapeutic benefits and may be more likely to face adverse effects. [24, 25, 26]

“The pharmacological treatments currently recommended for use in adolescents and children include fast-acting psychostimulants (i.e., amphetamines, methylphenidate) and non-stimulants (i.e., atomoxetine [ATX], alpha-2 agonists). In contrast to the 2014 Japanese clinical guidelines, which recommend both stimulants and non-stimulants as first-line pharmacological treatment for children and adolescents (≥ 6 years) with ADHD, European and North American guidelines recommend stimulants as first-line pharmacological treatment, followed by non-stimulants, such as ATX or guanfacine extended-release (GXR), for those who do not respond to or cannot tolerate stimulants. In all settings, however, the presence of comorbidities adds complexity to the management of children and adolescents with ADHD, and certain medications may be preferred or contraindicated depending on the comorbidities that are present.” [27]

Comparison of Guanfacine with Other Non-Stimulant Options

When selecting a non-stimulant medication to treat executive dysfunction and behavioural symptoms in Prader-Willi syndrome, guanfacine (XR) offers distinct pharmacological advantages over the other options funded by Pharmac - atomoxetine and off-label clonidine.

Effect

Guanfacine and atomoxetine work through different neurochemical pathways in the brain. Guanfacine has a higher success rate at improving impulse control and reducing emotional dysregulation in PWS, whereas atomoxetine may worsen anxiety or agitation in some patients. [28, 29, 30] Clonidine's effect is thought to be due to decreased sympathetic outflow from the CNS. [31]

Tolerability

Guanfacine has minimal metabolic impact and its side effects are stable in XR form. Atomoxetine can cause higher rates of gastrointestinal issues, and clonidine carries more risk of hypotension and severe somnolence [32, 33, 34].

Dosing

The once-daily delivery of extended-release guanfacine prevents sharp peak and trough fluctuations; atomoxetine takes longer to take effect and the dose needs to be carefully increased to avoid mood instability, and clonidine often requires multi-dose daily scheduling.

In December 2024, [Dr Deepan Singh](#) provided us with the comments below on why he believes guanfacine is the preferred pharmaceutical option to atomoxetine and clonidine:

“Here are some benefits that GXR offers over other alternatives:

- 1) Offers consistent 24-hour coverage, reducing fluctuations in symptom control associated with short-acting alpha2-agonists such as clonidine. This extended coverage is especially beneficial in PWS, where behavioral issues, including aggression and impulsivity, can emerge unpredictably throughout the day.*
- 2) By increasing the functioning of the prefrontal cortex, guanfacine ER may reduce impulsivity, a core contributor to aggression and self-injurious behaviors like skin picking.*
- 3) GXR has a more favorable side effect profile, particularly with respect to sedation and blood pressure fluctuations, compared to short-acting alpha2-agonists. The gradual release minimizes peaks and troughs in drug concentration, lowering the risk of rebound symptoms such as irritability or hyperactivity when doses wear off.*
- 4) My studies and clinical experience suggest that guanfacine ER can significantly reduce aggressive outbursts and self-harming behaviors in individuals with neurodevelopmental disorders, including PWS. Skin picking, a hallmark of PWS, may improve through the medication’s calming and impulse-regulating effects.*
- 5) While atomoxetine is a norepinephrine reuptake inhibitor and has demonstrated benefits in attention-deficit/hyperactivity disorder (ADHD), it is less effective in addressing the behavioral dysregulation, aggression, and compulsivity that are prominent in PWS. Atomoxetine often requires several weeks to take effect, whereas improvements with guanfacine ER are often observed more rapidly.*
- 6) Short-acting clonidine or even short-acting guanfacine, can cause more sedation and requires multiple daily doses, increasing the risk of non-adherence and inconsistent symptom control.”*

4. Key Evidence

The clinical case for establishing funding criteria for guanfacine in PWS is spearheaded by the definitive 2025 randomised, double-blind, placebo-controlled trial led by child and adolescent psychiatrist, Dr Deepan Singh [[35](#)]. This trial evaluated 89 individuals with PWS (6 – 35 years) who presented with moderate to severe aggressive or self-injurious behaviours, and it provided robust, high-quality data over an 8-week double-blind phase followed by an 8-week open-label extension.

Key efficacy findings included:

- GXR treatment led to statistically significant reductions in severe aggression and agitation.
- Core behaviours associated with executive dysfunction and impulsivity also saw significant reduction (hyperactivity and noncompliance).
- Skin-picking lesions significantly decreased as measured by the Self-Injury Trauma (SIT) scale, demonstrating a reduction in response to GXR.

A Case Study

A case report published by Parikh et al highlights the classic trajectory of psychiatric comorbidities in PWS. The authors document an adolescent with PWS exhibiting severe mood dysregulation and ADHD symptoms. Multiple standard psychotropic treatments were tried, proving ineffective and causing unacceptable metabolic side effects (significant weight gain). The patient transitioned to guanfacine and achieved successful behavioural stabilisation and clinical improvement. [[36](#)]

This matches earlier foundational data from Dr Singh’s 2019 retrospective cohort study which found that GXR treatment led to marked improvements in skin-picking, agitation, and ADHD symptoms across patients who had previously tried other psychopharmacological treatments without success.

Dr Singh's 2019 Cohort Study – Improvements Reported with GXR [37]:

- ADHD symptoms: 93.7% experienced notable improvement in focus and impulsivity.
- Aggression and agitation: 82.3% experienced decreases in aggression.
- Self-injurious behaviour: 81.8% experienced improvement in skin picking.

Safety and Tolerability Profile

There were no serious side effects reported in the 2025 trial of guanfacine in PWS. Importantly, there was no abnormal weight gain. The most common side effect was mild, manageable sleepiness, but GXR was well tolerated overall. [35]

Clinicians report that side effects are typically mild, transient and manageable (such as initial mild somnolence). There are low discontinuation rates during long-term therapy.

5. Economic Offset

Funding guanfacine XR may provide a direct economic offset to the New Zealand health and social care sectors by potentially reducing the high expenditure associated with unmanaged behavioural crises:

- Reduced police callouts and custody requirements.
- Reduced need for emergency or wraparound social care for individuals and families.
- Reduced need for high-cost intensive support or forensic care placements.
- Reduced costs related to property damage in residential accommodation services and schools.
- Fewer incidents impacting others who may require medical treatment or time off work.

Funding guanfacine may also save health costs by potentially reducing ambulance callouts, acute psychiatric and emergency admissions, or prolonged admissions to assessment wards.

Funding guanfacine may reduce the need for health service treatments and hospitalisations for wound care and infection control.

6. Why Specific Funding Criteria for Prader-Willi Syndrome are Needed

In practice, Prader-Willi syndrome tends to function as an 'umbrella diagnosis' encompassing a wide spectrum of complex symptoms. Except for occasional diagnoses of ASD and ADHD, individual diagnoses relating to the range of cognitive and behavioural symptoms present are seldom made. Indeed, if tested, an individual with PWS may meet the diagnostic criteria for dyscalculia, executive dysfunction, and interoception dysfunction. They are also very likely to present with dyspraxia, apraxia of speech, APD, SPD, and ADHD. Additionally, some individuals also meet the criteria for OCD and ODD/PDA, and whilst there are many overlaps with PWS and ASD, up to approximately 25% will meet criteria for a dual diagnosis. However, patients are not usually referred for testing because of the umbrella diagnosis of PWS, and there are often long wait lists and costs involved.

As such, despite many PWS patients having symptoms of ADHD, they are frequently not tested. Whether testing occurs is also somewhat dependent on clinician knowledge and understanding of PWS, a clinically rare syndrome.

Diagnostic overshadowing and intellectual disability are also barriers to assessment in PWS and may make it difficult for physicians to distinguish between symptoms and investigate their underlying cause.

This is made more problematic by ADHD symptoms presenting atypically in PWS. When the DSM-5 criteria are applied, hyperactive symptoms, such as physical fidgeting or running around, are rarely prominent in PWS due to the underlying hypotonia and hypothalamic dysfunction.

It is essential that specific funding criteria for PWS are established so that:

- Patients and families do not have to attend another assessment to obtain an official ADHD diagnosis (in childhood or adulthood) if they present with behaviours that guanfacine has been proven to help. (Families already attend multiple health and social care appointments.)
- Diagnostic overshadowing is avoided, ensuring symptoms are not just dismissed as part of PWS.
- Patients are not at risk of symptoms being missed due to atypical presentation, or diagnostic difficulties due to intellectual disability.
- Clinicians are more aware of guanfacine as an accessible treatment option for PWS.
- Clinicians do not have to complete any additional paperwork to justify prescribing off-label.
- There are no additional financial and time costs involved for patients, families or clinicians.

We would like to see specific funding criteria for PWS allowing funded guanfacine to be prescribed for:

- ADHD symptoms in patients with PWS,
- Impulsive behaviours that are negatively affecting the individual's safety or quality of life, or that of their family,
- Severe agitation requiring pharmaceutical intervention,
- Aggressive behaviour requiring pharmaceutical intervention,
- Skin picking requiring pharmaceutical intervention.

Appendix

Patient voice stories of lived experience will accompany this application and will be submitted separately.

References

1. Chapter 8 - **Attention-Deficit/Hyperactivity Disorder in Prader-Willi Syndrome.** Neuro-behavioral Manifestations of Prader-Willi Syndrome: *A Guide for Clinicians and Caregivers* Edited by Deepan Singh, Cambridge University Press, 2022. DOI: <https://doi.org/10.1017/9781108886727.009>
2. Wigren M, Hansen S. **ADHD symptoms and insistence on sameness in Prader-Willi syndrome.** J Intellect Disabil Res. 2005 Jun;49(Pt 6):449-56. doi: [10.1111/j.1365-2788.2005.00690.x](https://doi.org/10.1111/j.1365-2788.2005.00690.x). PMID: 15882394.
3. Gross-Tsur V, Landau YE, Benarroch F, Wertman-Elad R, Shalev RS. **Cognition, attention, and behavior in Prader-Willi syndrome.** J Child Neurol. 2001 Apr;16(4):288-90. doi: [10.1177/088307380101600411](https://doi.org/10.1177/088307380101600411). PMID: 11332464.
4. Parikh P, Alphonse AA, Suthar HJ, Singh SK, Singh A, Oza M. **Integrated psychiatric management of Prader-Willi syndrome: a case report of disruptive mood dysregulation and ADHD.** Int J Community Med Public Health. 2025 Jun;12(7):3360-3. Available from: <https://www.ijcmph.com/index.php/ijcmph/article/view/14146>
5. Sawhney I, Perera B, Bassett P, Zia A, Alexander RT, Shankar R. **Attention-deficit hyperactivity disorder in people with intellectual disability: statistical approach to developing a bespoke screening tool.** BJPsych Open. 2021 Oct 4;7(6):e187. doi: [10.1192/bjo.2021.1023](https://doi.org/10.1192/bjo.2021.1023). PMID: 34602112; PMCID: PMC8503915.
6. Vega-Carrero, Mairim & Reyes-Gutiérrez, Yinaira & Díaz Guasp, María & Guzmán-Echevarría, Yazdel & Ocasio-Quñones, Idanara. (2026). **Treatment of ADHD in Children With Intellectual Disability: A Systematic Literature Review.** Journal of Pediatric Neuropsychology. [10.1037/jpn0000043](https://doi.org/10.1037/jpn0000043).

7. **Australian Evidence-Based Clinical Practice Guideline for ADHD, Oct 2022**, of which an overview was published in the Australian & New Zealand Journal of Psychiatry 2023
Identification: 1.1 High risk groups: adhdguideline.aadpa.com.au/identification/high-risk-groups/
8. Hustyi KM, Hammond JL, Rezvani AB, Hall SS. **An analysis of the topography, severity, potential sources of reinforcement, and treatments utilized for skin picking in Prader-Willi syndrome.** Res Dev Disabil. 2013 Sep;34(9):2890-9. doi: [10.1016/j.ridd.2013.06.014](https://doi.org/10.1016/j.ridd.2013.06.014). Epub 2013 Jun 27. PMID: 23810929.
9. **p.36 Self-Injurious Behavior**, Chapter 1 - Clinical and Genetic Findings with Natural History of Prader-Willi Syndrome. **p.150 Infections**, Chapter 5 – Medical Considerations Management of Prader-Willi Syndrome, Fourth Edition. Edited by Merlin G. Butler Phillip D. K. Lee, Barbara Y. Whitman, Springer Press 2022. <https://doi.org/10.1007/978-3-030-98171-6> via [Vanderbilt University](https://www.vanderbilt.edu/)
10. Micallef Pulè K, Hughes BM. **Anxiety, Depression and Stress in Parents and Siblings of People Who Have Prader-Willi Syndrome: Morbidity Prevalence and Mitigating Factors.** J Intellect Disabil Res. 2025 May;69(5):417-427. doi: [10.1111/jir.13223](https://doi.org/10.1111/jir.13223). Epub 2025 Feb 19. PMID: 39970479; PMCID: PMC11966354.
11. Bennett Murphy L, Thornton J, Thornton E. **Psychological adjustment of siblings of children with Prader-Willi syndrome.** J Intellect Dev Disabil. 2023 Jun;48(2):196-205. doi: [10.3109/13668250.2022.2132630](https://doi.org/10.3109/13668250.2022.2132630). Epub 2022 Nov 2. PMID: 39815905.
12. Honea RA, Holsen LM, Lepping RJ, Perea R, Butler MG, Brooks WM, Savage CR. **The neuroanatomy of genetic subtype differences in Prader-Willi syndrome.** Am J Med Genet B Neuropsychiatr Genet. 2012 Mar;159B(2):243-53. doi: [10.1002/ajmg.b.32022](https://doi.org/10.1002/ajmg.b.32022). PMID: 22241551; PMCID: PMC3296480.
13. Jauregi J, Arias C, Vegas O, Alén F, Martinez S, Copet P, Thuilleaux D. **A neuropsychological assessment of frontal cognitive functions in Prader-Willi syndrome.** J Intellect Disabil Res. 2007 May;51(Pt 5):350-65. doi: [10.1111/j.1365-2788.2006.00883.x](https://doi.org/10.1111/j.1365-2788.2006.00883.x). PMID: 17391252.
14. Yamada K, Suzuki K, Watanabe M. **Altered Functional Network Architecture of the Brain in Prader-Willi Syndrome.** Brain Connect. 2022 Mar;12(2):174-179. doi: [10.1089/brain.2020.0914](https://doi.org/10.1089/brain.2020.0914). Epub 2021 Jun 29. PMID: 34030490.
15. Woodcock KA, Humphreys GW, Oliver C, Hansen PC. **Neural correlates of task switching in paternal 15q11-q13 deletion Prader-Willi syndrome.** Brain Res. 2010 Dec 2;1363:128-42. doi: [10.1016/j.brainres.2010.09.093](https://doi.org/10.1016/j.brainres.2010.09.093). Epub 2010 Oct 1. PMID: 20920489.
16. Forster J, Duis J, Butler MG. **Pharmacodynamic Gene Testing in Prader-Willi Syndrome.** Front Genet. 2020 Nov 20;11:579609. doi: [10.3389/fgene.2020.579609](https://doi.org/10.3389/fgene.2020.579609). PMID: 33329716; PMCID: PMC7715001.
17. Forster J. **Sertraline-Induced Mood and Behavioral Activation in Two Adults With Prader-Willi Syndrome.** Case Rep Psychiatry. 2025 Jun 2;2025:9811985. doi: [10.1155/crps/9811985](https://doi.org/10.1155/crps/9811985). PMID: 40496034; PMCID: PMC12149475.

18. Pei-Ning Chiou, Li-Ping Tsai. **Psychopharmacological Treatment of Prader-Willi Syndrome.** Tzu Chi Medical Journal. 2010 March, vol 22 issue 1, pages 43-46. doi: [10.1016/S1016-3190\(10\)60035-3](https://doi.org/10.1016/S1016-3190(10)60035-3)
19. Almandil NB, Liu Y, Murray ML, Besag FM, Aitchison KJ, Wong IC. **Weight gain and other metabolic adverse effects associated with atypical antipsychotic treatment of children and adolescents: a systematic review and meta-analysis.** Paediatr Drugs. 2013 Apr;15(2):139-50. doi: [10.1007/s40272-013-0016-6](https://doi.org/10.1007/s40272-013-0016-6). PMID: 23519708.
20. Toren P, Ratner S, Laor N, Weizman A. **Benefit-risk assessment of atypical antipsychotics in the treatment of schizophrenia and comorbid disorders in children and adolescents.** Drug Saf. 2004;27(14):1135-56. doi: [10.2165/00002018-200427140-00005](https://doi.org/10.2165/00002018-200427140-00005). PMID: 15554747.
21. Kara T, Akaltun İ. **Newly Developed Skin Picking After Methylphenidate Treatment in Attention Deficit Hyperactivity Disorder: Possible Mechanisms.** Clin Neuropharmacol. 2018 Jan/Feb;41(1):28-30. doi: [10.1097/WNF.0000000000000262](https://doi.org/10.1097/WNF.0000000000000262). PMID: 29298167.
22. Handen BL, Feldman H, Gosling A, Breaux AM, McAuliffe S. **Adverse side effects of methylphenidate among mentally retarded children with ADHD.** J Am Acad Child Adolesc Psychiatry. 1991 Mar;30(2):241-5. doi: [10.1097/00004583-199103000-00012](https://doi.org/10.1097/00004583-199103000-00012). PMID: 2016228.
23. Thomson A, Maltezos S, Paliokosta E, Xenitidis K. **Amfetamine for attention deficit hyperactivity disorder in people with intellectual disabilities.** Cochrane Database Syst Rev. 2009 Jan 21;2009(1):CD007009. doi: [10.1002/14651858.CD007009.pub2](https://doi.org/10.1002/14651858.CD007009.pub2). PMID: 19160313; PMCID: PMC7388934.
24. Tarrant N, Roy M, Deb S, Odedra S, Retzer A, Roy A. **The effectiveness of methylphenidate in the management of Attention Deficit Hyperactivity Disorder (ADHD) in people with intellectual disabilities: A systematic review.** Res Dev Disabil. 2018 Dec;83:217-232. doi: [10.1016/j.ridd.2018.08.017](https://doi.org/10.1016/j.ridd.2018.08.017). Epub 2018 Sep 25. PMID: 30266025.
25. Handen BL, Sahl R, Hardan AY. **Guanfacine in children with autism and/or intellectual disabilities.** J Dev Behav Pediatr. 2008 Aug;29(4):303-8. doi: [10.1097/DBP.0b013e3181739b9d](https://doi.org/10.1097/DBP.0b013e3181739b9d). PMID: 18552703.
26. K. Courtenay. **Treating ADHD in People with Intellectual Disabilities.** European Psychiatry, vol 33, supplement, 2016 March, page s538. doi: <https://doi.org/10.1016/j.eurpsy.2016.01.1989>
27. Tsujii N, Usami M, Naya N, Tsuji T, Mishima H, Horie J, Fujiwara M, Iida J. **Efficacy and Safety of Medication for Attention-Deficit Hyperactivity Disorder in Children and Adolescents with Common Comorbidities: A Systematic Review.** Neurol Ther. 2021 Dec;10(2):499-522. doi: [10.1007/s40120-021-00249-0](https://doi.org/10.1007/s40120-021-00249-0). Epub 2021 Jun 4. PMID: 34089145; PMCID: PMC8571469.
28. Sikirica V, Findling RL, Signorovitch J, Erder MH, Dammerman R, Hodgkins P, Lu M, Xie J, Wu EQ. **Comparative efficacy of guanfacine extended release versus atomoxetine for the treatment of attention-deficit/hyperactivity disorder in children and adolescents: applying matching-adjusted indirect comparison methodology.** CNS Drugs. 2013 Nov;27(11):943-53. doi: [10.1007/s40263-013-0102-x](https://doi.org/10.1007/s40263-013-0102-x). PMID: 23975660; PMCID: PMC3824845.

29. Joseph A, Ayyagari R, Xie M, Cai S, Xie J, Huss M, Sikirica V. **Comparative efficacy and safety of attention-deficit/hyperactivity disorder pharmacotherapies, including guanfacine extended release: a mixed treatment comparison.** Eur Child Adolesc Psychiatry. 2017 Aug;26(8):875-897. doi: [10.1007/s00787-017-0962-6](https://doi.org/10.1007/s00787-017-0962-6). Epub 2017 Mar 3. PMID: 28258319; PMCID: PMC5532417.
30. Aman MG, Smith T, Arnold LE, Corbett-Dick P, Tumuluru R, Hollway JA, Hyman SL, Mendoza-Burcham M, Pan X, Mruzek DW, Lecavalier L, Levato L, Silverman LB, Handen B. **A review of atomoxetine effects in young people with developmental disabilities.** Res Dev Disabil. 2014 Jun;35(6):1412-24. doi: [10.1016/j.ridd.2014.03.006](https://doi.org/10.1016/j.ridd.2014.03.006). Epub 2014 Apr 16. PMID: 24732041; PMCID: PMC4532325.
31. Eric Christianson. **Clonidine Versus Guanfacine: ADHD Management.** Med Ed 101.com, 2023 Dec. www.meded101.com/clonidine-versus-guanfacine-adhd-management
32. Seedat YK. **Clonidine and guanfacine--comparison of their effects on haemodynamics in hypertension.** S Afr Med J. 1985 Apr 6;67(14):557-9. PMID: 3887593.
<https://pubmed.ncbi.nlm.nih.gov/3887593/>
33. Wilson MF, Haring O, Lewin A, Bedsole G, Stepansky W, Fillingim J, Hall D, Roginsky M, McMahon FG, Jagger P, et al. **Comparison of guanfacine versus clonidine for efficacy, safety and occurrence of withdrawal syndrome in step-2 treatment of mild to moderate essential hypertension.** Am J Cardiol. 1986 Mar 28;57(9):43E-49E. doi: [10.1016/0002-9149\(86\)90723-x](https://doi.org/10.1016/0002-9149(86)90723-x). PMID: 3513530.
34. Dr Sanil Rege MBBS, MRCPsych, FRANZCP. **Psychopharmacology and Clinical Application of Guanfacine and Clonidine for ADHD – What’s the Difference?** Psych Scene Hub 2022 March, updated 2026 June. www.psychscenehub.com/psychinsights/guanfacine-and-clonidine-for-adhd
35. Singh D, Silver M, Jacob T. **A Randomized Double-Blind Placebo-Controlled Trial of Guanfacine Extended Release for Aggression and Self-Injurious Behavior Associated With Prader-Willi Syndrome.** Am J Med Genet B Neuropsychiatr Genet. 2025 Sep;198(6):62-70. doi: [10.1002/ajmg.b.33032](https://doi.org/10.1002/ajmg.b.33032). Epub 2025 May 21. PMID: 40395104.
36. Parikh, P., Alphonse, A. A., Suthar, H. J., Singh, S. K., Singh, A., & Oza, M. **Integrated psychiatric management of Prader-Willi syndrome: a case report of disruptive mood dysregulation and ADHD.** International Journal Of Community Medicine And Public Health, 2025, 12(7), 3360–3363. doi: [10.18203/2394-6040.ijcmph20252144](https://doi.org/10.18203/2394-6040.ijcmph20252144)
37. Singh D, Wakimoto Y, Filangieri C, Pinkhasov A, Angulo M. **Guanfacine Extended Release for the Reduction of Aggression, Attention-Deficit/Hyperactivity Disorder Symptoms, and Self-Injurious Behavior in Prader-Willi Syndrome-A Retrospective Cohort Study.** J Child Adolesc Psychopharmacol. 2019 May;29(4):313-317. doi: [10.1089/cap.2018.0102](https://doi.org/10.1089/cap.2018.0102). Epub 2019 Feb 6. PMID: 30724590.