Journal of the Endocrine Society, 2026, 10, bvag099
https://doi.org/10.1210/jendso/bvag099
Published: 30 April 2026
Mini-Review

Diazoxide choline extended-release (DCCR) use in Prader–Willi syndrome: patient selection, dosing, and management

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Abstract

Prader–Willi syndrome (PWS) is a rare genetic disorder marked by metabolic, endocrine, and behavioral challenges, with hyperphagia as a central feature contributing to significant health risks. Diazoxide choline extended-release (DCCR; VYKAT™ XR) is a once-daily adenosine triphosphate (ATP)-sensitive potassium channel activator recently approved for the treatment of hyperphagia in individuals with genetically confirmed PWS aged 4 years and older. As this novel therapy enters clinical practice, clinicians require practical guidance on appropriate use. This manuscript provides actionable recommendations for patient selection, baseline assessments, and strategies for optimizing comorbid conditions prior to initiation. Structured, weight-based dosing and titration protocols are outlined, along with recommendations for monitoring glycemia and edema and managing common adverse events (AEs), including hyperglycemia, peripheral edema, and rash. Special considerations are discussed for patients with diabetes, cardiopulmonary risk factors, and those on concomitant medications with potential drug–drug interactions. The guidance is informed by data from the phase 3 DESTINY-PWS program, long-term extension studies, and real-world clinical experience. Emphasis is placed on early identification and management of AEs and the importance of a multidisciplinary approach to care. These recommendations aim to support clinicians in safely and effectively incorporating DCCR into the management of PWS, improving outcomes for affected individuals. Ongoing research and real-world evidence will continue to refine best practices and address remaining gaps in knowledge.

Key Words Prader–Willi syndrome, hyperphagia, diazoxide choline extended-release, patient selection

Prader–Willi syndrome (PWS) is a rare genetic disorder characterized by a complex combination of metabolic, endocrine, and behavioral abnormalities [1-3]. Hyperphagia manifesting as persistent hunger, food obsession, and aggressive food-seeking behaviors is a hallmark and encompassing feature of PWS starting in childhood, creating a lifelong source of life-threatening health risks [4-9]. Together, these features contribute to a significant clinical and psychosocial burden for patients and their families.

Until recently, there were no approved treatments for hyperphagia in PWS. Diazoxide choline extended-release (DCCR) represents a targeted therapeutic approach. DCCR is a potent activator of the adenosine triphosphate (ATP)-sensitive potassium (KATP) channel, a regulator of neuronal excitability that crosses the blood–brain barrier [10]. Its extended-release formulation allows once-daily dosing with stable intraday plasma concentrations [11]. In hypothalamic neurons, activation of the KATP channel reduces secretion of orexigenic neuropeptides and neurotransmitters, including neuropeptide Y, agouti-related peptide, and gamma-aminobutyric acid, potentially attenuating hyperphagia [12].

The clinical evaluation of DCCR has been extensive. The phase 3 DESTINY-PWS trial was a 13-week, randomized, double-blind, placebo-controlled study conducted in 127 participants at 29 sites across the United States and the United Kingdom [13]. While the trial showed a numerical trend toward improvement in hyperphagia questionnaire for clinical trials (HQ-CT) total scores at week 13, the difference vs placebo did not reach statistical significance [13]. In contrast, objective endpoints that were not meaningfully impacted by pandemic-related disruptions (eg, metabolic markers and DXA-based measures) showed statistically significant improvements with DCCR vs placebo, which

Received: January 11, 2026. **Accepted:** April 17, 2026. **Corrected and Typeset:** May 6, 2026

supported continuation of the program. Longer-term data have been more compelling. In the 52-week open-label extension of DESTINY-PWS, patients treated with DCCR demonstrated significant improvements in hyperphagia and several other behavioral and metabolic endpoints compared with baseline, and compared with a nonintervention external control group [11]. More recently, a 16-week randomized withdrawal study confirmed that continued DCCR maintained reductions in hyperphagia, whereas participants switched to placebo experienced worsening, reinforcing the durability of therapeutic benefit (under publication).

The observed safety profile aligns with diazoxide pharmacology. The most frequent adverse reactions (≥10% and at least 2% more common than placebo) include hypertrichosis, edema, hyperglycemia, and rash, with rashes presenting in several forms such as maculopapular eruptions and urticaria [14]. Among these, edema (27% vs 12%) and hyperglycemia (17% vs 5%) were the most clinically relevant events observed in the DESTINY-PWS (C601) trial. Comprehensive incidence data for all treatment-emergent adverse events (AEs) are summarized in Section "AE Management," to support clinical monitoring and risk management. Hyperglycemia and fluid overload have been specifically highlighted as key risks requiring careful monitoring, and they are reflected in the prescribing information as warnings and precautions [14].

On March 26, 2025, the FDA approved DCCR for the treatment of hyperphagia in individuals aged 4 years and older with PWS [10-14]. Given its introduction into clinical practice, expert guidance is needed to support safe, effective, and responsible use. The objective of this expert guidance review paper is to summarize evidence-based dosing and monitoring, and structured approaches to adverse-event mitigation and management based on evidence and clinical experience.

Patient selection

Patient selection for DCCR should target those patients with clinically meaningful hyperphagia and genetically confirmed PWS. Consideration of the safety profile observed in the clinical program is recommended, with particular attention to risks of hyperglycemia and edema/hypervolemia, which included general, localized, peripheral, and pulmonary edema. The goal is to treat genetically confirmed PWS with hyperphagia while anticipating AEs through baseline assessment and structured early monitoring.

Hyperphagia assessment

Patient selection should consider the degree of hyperphagia, since this is the primary therapeutic target of DCCR. In clinical trials, hyperphagia was evaluated using the HQ-CT, a validated 9-question instrument, though it is not routinely used in practice.

In clinical practice, assessment of hyperphagia often relies on caregiver reports of observable behavioral changes rather than formal questionnaire scores. Common clinical indicators suggesting progression into hyperphagic phases include a noticeable increase in food-seeking behaviors (eg, searching for or hoarding food, frequent requests for food outside of meals), heightened anxiety or irritability related to food access, preoccupation with meal timing or menu planning, and increased difficulty redirecting attention away from food topics. Additional cues may include earlier morning awakenings to seek food, loss of control around accessible food, and family disruption caused by persistent food-related behaviors. Incorporating caregiver observations alongside clinical assessment provides a practical means to standardize evaluation and monitor response to DCCR over time, recognizing that no formal tool currently exists for clinical assessment of hyperphagia in routine practice.

Clinical recommendations indicate that treatment should begin once patients have clearly progressed to nutritional phase 2b (increasing appetite and growing food interest), or phase 3 (persistent hyperphagia). Initiating DCCR before these stages, such as during phase 2a when weight gain may reflect reduced energy expenditure rather than food drive, risks making treatment response difficult to evaluate.

Hyperglycemia

Individuals with PWS are at increased risk of prediabetes and type 2 diabetes [15]. The phase 3 cohort began therapy with near-normal glycemia: mean HbA1c of 5.55% (SD = 0.41) and mean fasting glucose of 90 mg/dL (SD = 11.45). Approximately 60% of participants had evidence of prediabetes/type 2 diabetes, based on elevated HbA1c or fasting glucose at baseline, documented history of diabetes or prediabetes, or use of glucose-lowering medications (~8.8%). Only ~2.4% entered the study with HbA1c ≥ 6.5%, limiting direct trial experience at higher baseline HbA1c [16]. Across the program, hyperglycemia AEs occurred in ~33.6%, largely within the first 6 months, and were typically managed with DCCR dose modification, slower titration, and/or standard antidiabetic therapy; discontinuation (1.6%) was uncommon [16].

Individual-level HbA1c trajectories from the phase 3 program show that participants starting with higher baseline HbA1c tended to have greater variability and upward excursions vs those starting in the normoglycemic range (Fig. 1).

For individuals with HbA1c ≥ 6.5% or fasting plasma glucose (FPG) > 110 mg/dL, initiation should be approached with added caution, with preference for starting when glycemia is stable or improving on the current regimen and with intensified early home glucose monitoring [16]. Expert opinion is to avoid initiation if HbA1c > 7% unless glycemia is stable or improving on current therapy and close monitoring is ensured.

DCCR has not been studied in individuals treated with insulin for type 1 or 2 diabetes or in those with recent diabetic ketoacidosis/hyperosmolar hyperglycemic state (DKA/HHS). In insulin-treated patients, initiation should be approached with caution; in patients with recent DKA/HHS, initiation should be deferred and, if considered later, undertaken with extreme caution given the absence of trial data [14].

Practical guidance—hyperglycemia

- Baseline: Obtain HbA1c and FPG; optimize glycemia before starting DCCR.
- When to initiate: Use added caution at HbA1c ≥ 6.5% or FPG > 110 mg/dL; defer if HbA1c ≥ 7% until stable or improving.

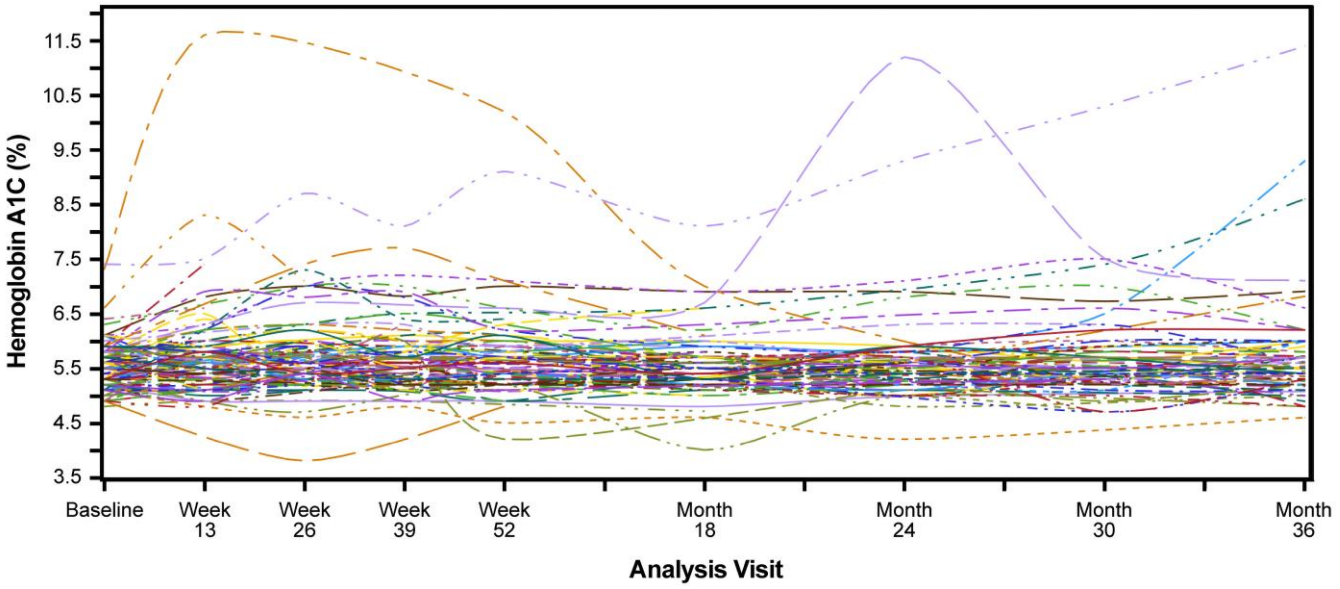

Figure 1 Individual HbA1c (%) trajectories in the DESTINY-PWS and DESTINY-PWS-RWP safety population.

For HbA1c ≥ 8%, initiation is generally deferred due to limited trial data.

- Not studied: Individuals treated with insulin for type 1 or 2 diabetes. If clinicians elect to proceed in select cases, do so only when glycemia is stable and under intensified monitoring.
- Avoid: Recent DKA/HHS. Initiation should be deferred following DKA/HHS.
- Monitoring cadence: FPG weekly for the first 2 weeks, then at least every 4 weeks (more frequently if at-risk or if values rise); HbA1c every 3 months.
- If elevations occur: Confirm that patient was truly fasting as nighttime food seeking can cause unexpected hyperglycemia. Pause titration, reduce dose or temporarily interrupt, and add/adjust antidiabetic therapy as needed; resume once values return toward baseline and are stable.
- Concomitant GH: Not a contraindication. If used with DCCR, ensure routine metabolic surveillance (HbA1c/FPG per schedule) and monitor for edema/weight-related changes during titration.

Peripheral edema

Lower-extremity edema is common in adults with PWS and may reflect multifactorial influences, with obesity and lymphatic dysfunction being the most prominent contributors, compounded by reduced mobility and, in some cases, cardiovascular or venous disease; peripheral edema may also occur during DCCR therapy. The mechanism is presumed to involve DCCR-related sodium retention or peripheral vasodilation, though these effects are typically dose-dependent and reversible. Pitting can be minimal even when edema is clinically meaningful [17]. In the DCCR program, baseline peripheral edema was present in 15.2%; at entry, most participants had no pitting, and higher pitting grades were infrequent over as long as 156 weeks. Participants with ≥ grade 3 edema at baseline were excluded from trial participation.

During treatment, peripheral-edema AEs occurred in 36.8% over a median ∼3.0 years exposure (max 4.5 years), with ≈96% grade 1-2 and few grade 3; no grade 4-5 events were reported in the completed phase 3 trials. In the 13-week randomized study (DESTINY-PWS), the prescribing-information "edema" grouping was 27% (DCCR) vs 12% (placebo). Management favored dose reduction/temporary interruption and slower titration; new loop-diuretic initiation was infrequent (1.6%) and brief (mean:∼46 days) [14].

Practical guidance—peripheral edema

Assessment and management of peripheral edema

Objective evaluation of peripheral edema should combine physical examination findings with reproducible measurements over time. Clinicians are encouraged to document:

- Pitting edema grade (1+ to 5+) using standardized thumb pressure over the pretibial area or ankle.
- Ankle or mid-calf circumference measured at fixed anatomical landmarks (eg, 5 cm above the medial malleolus), ideally at the same time of day and under similar conditions.
- Weight trend relative to baseline, with ≥1-2 kg gain over 1 week warranting review for fluid retention.
- Photographic documentation (if permitted) or descriptive notation (eg, "indentation persists 10 seconds") to enhance reproducibility between visits.
- Functional impact, such as difficulty fitting shoes, reduced walking tolerance, or increased fatigue, as reported by caregivers or the patient.

When feasible, assessments should be performed at each visit during the titration phase and periodically thereafter. Combining objective measures with caregiver observations provides a consistent framework for monitoring edema progression and treatment response.

Pulmonary edema/hypertension

Immediate-release diazoxide in neonates has been linked to reversible pulmonary hypertension and heart failure, likely due to direct cardiopulmonary toxicity and sodium/fluid retention; case series suggest a 2.4-4.8% prevalence in that neonatal context, prompting an FDA warning. There is no FDA warning specific to pulmonary hypertension with DCCR, and pulmonary hypertension was not reported in the DCCR trials; pulmonary edema did occur (including during intercurrent pneumonia in 1 participant), and severe fluid-overload reactions appear in warnings/precautions [14]. The enrolled population ranged 4-44 years, with mean BMI 27.56 ± 9.62 kg/m^2 (z-score 1.53 ± 1.07); weight >135 kg was excluded. Controlled obstructive sleep apnea (OSA) was allowed; uncontrolled moderate–severe OSA remains a cardiopulmonary risk in PWS [16]. In this setting, screening for symptoms (dyspnea, cough, and worsening fatigue) and targeted imaging is prudent at baseline and during dose escalation.

The FDA adverse event reporting system (FAERS) includes 3 hospitalizations reported during postmarketing use through September 2, 2025 (one each: pulmonary edema, pneumonia, and pulmonary hypertension). In these postmarketing cases, potential contributing risk factors included class III obesity, recent pulmonary infections, and poorly controlled/untreated OSA, reinforcing the need for careful cardiopulmonary assessment and optimization before and during DCCR titration.

Practical guidance—pulmonary edema/hypertension

- Screen: In severe obesity or suspected/known OSA, assess control (eg, continuous positive airway pressure or bilevel positive airway pressure [CPAP/BiPAP] adherence) before initiation; evaluate symptoms that could signal pulmonary congestion.
- Baseline testing in at-risk: Consider obtaining C-reactive protein (CRP) and B-type natriuretic peptide (BNP). Consider chest X-ray and transthoracic (surface) echocardiogram; defer initiation if clinical concern for pulmonary hypertension persists. If unsure, obtain input from cardiopulmonary medical provider.

Patients with congestive heart failure/compromised cardiac reserve

- Use DCCR with caution (per labeling). Optimize volume status and heart-failure regimen before initiation. Obtain cardiology input for clearance and monitoring. Start at the low end of the weight-based range, extend titration intervals, and consider a lower maintenance target. Do not initiate during decompensated heart failure.

Patients with chronic lung disease or recent pulmonary infection

- In chronic obstructive pulmonary disease (COPD), interstitial lung disease, or poorly controlled OSA, optimize pulmonary status first and confirm adherence to supportive therapies (eg, CPAP/BiPAP when indicated).
- Because pulmonary edema in the trial occurred during intercurrent pneumonia, and FAERS includes a pneumonia hospitalization, defer initiation during/soon after significant respiratory infections until fully resolved and baseline function is re-established. Use slower titration and closer early follow-up.
- On-treatment red flags: Rapid weight gain, dyspnea, orthopnea, persistent cough, reduced exercise tolerance→interrupt DCCR and evaluate; manage fluid overload per labeling. If decision made for treatment reinitiation, proceed with caution and only after complete resolution of symptoms with consideration of ongoing diuretic therapy.

Medication adherence

DCCR is formulated as an extended-release tablet, and its pharmacokinetics rely on swallowing the intact tablet whole. Crushing, cutting, or chewing alters the release profile, potentially leading to higher peak concentrations and increased risk of dose-dependent adverse effects. For this reason, clinicians must ensure that patients and caregivers understand the importance of correct administration and reinforce adherence behaviors at each follow-up. Young children and individuals without experience swallowing tablets or capsules present a particular challenge, and in such cases, caution is advised before initiating therapy. Patient and caregiver education should emphasize that improper administration can compromise both safety and efficacy.

Practical guidance: medication adherence and patient preparation

Before the first dose (one visit)

- Confirm eligibility (genetically confirmed PWS, age ≥4 year, and weight ≥20 kg). Train on swallowing tablets whole; do not split, crush, or chew (Fig. 2).
- Baseline labs and review: comprehensive metabolic panel (CMP), HbA1c, FPG; reconcile concomitant meds (hyperglycemia/edema-promoting or drug–drug interactions [DDIs]). Consider CRP and/or BNP in patients with risk factors for developing fluid overload.
- Home skills: teach glucometer use; document who records values and how results will be reported.

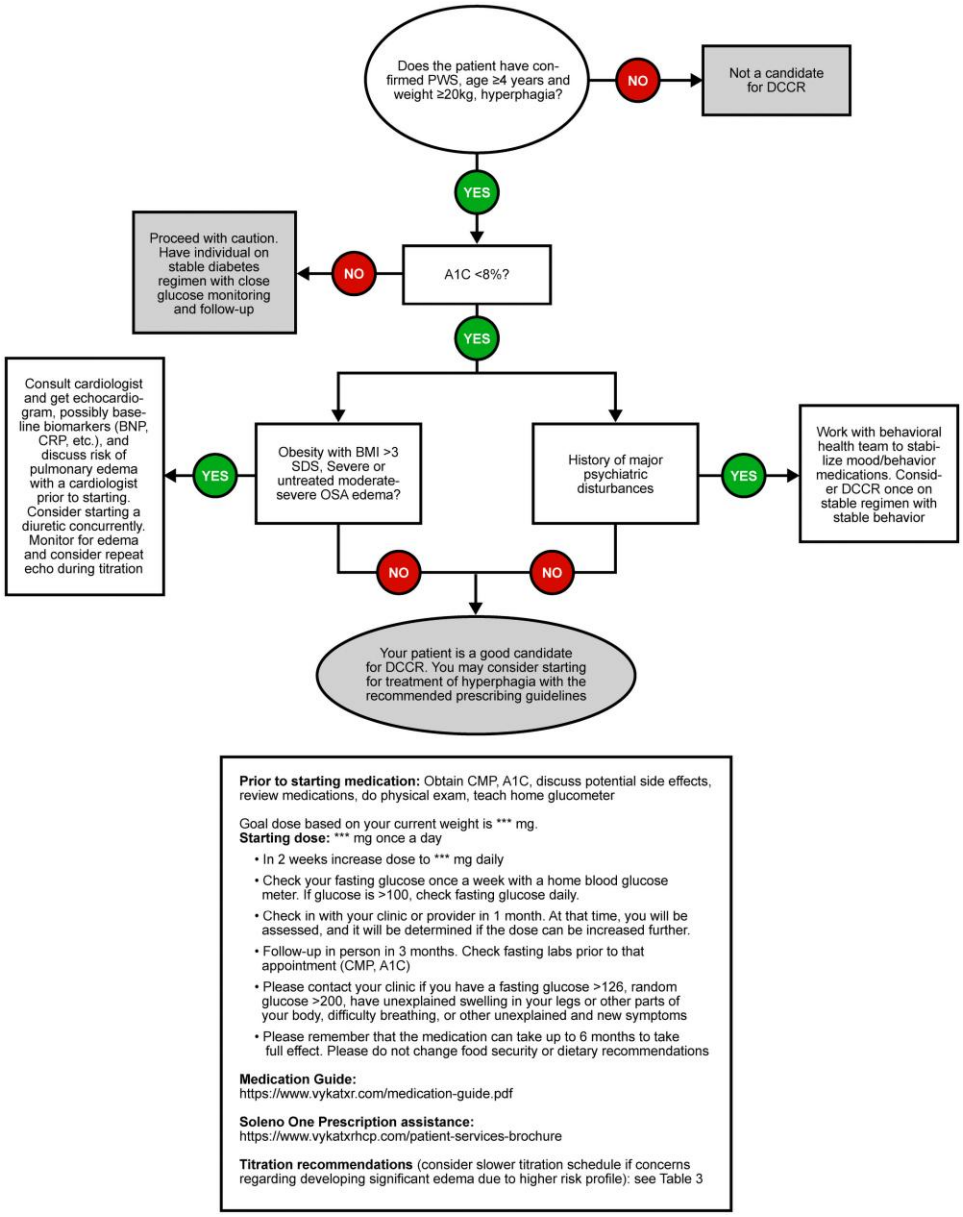

Figure 2 Clinical decision pathway for patient preparation and initiation of DCCR.

At initiation

- Start once daily per weight band; swallow whole with or without food.
- Fasting glucose checks weekly × 2 (more often if baseline risk).
- Provide a 24-hour contact for urgent issues. Schedule 2-week and 1-month check-ins for tolerability and dose decisions.

Follow-up cadence during titration

- Fasting glucose at least every 4 weeks (more frequently if values rise); HbA1c every 3 months.
- In-person at 3 months with labs (CMP in patients with obesity or clinical risk factors, FPG, and HbA1c).
- Reinforce tablet-swallowing and adherence behaviors at every visit.

What to tell families (red-flag symptoms)

- Call immediately for: FPG >126 mg/dL or random >200 mg/dL; new/worsening swelling; unexplained rapid weight gain; dyspnea or shortness of breath; persistent cough; orthopnea or difficulty breathing while supine; concerning systemic symptoms.
- Expected time to clinical benefit may be up to ~6 months; do not relax food security during titration.

Drug–drug interactions

When considering DCCR therapy, it is important to conduct a thorough review of the patient's medication history, as several clinically relevant DDIs have been identified in the prescribing information and trial experience. These interactions are particularly relevant for agents metabolized by CYP pathways, highly protein-bound medications, and diuretics that may exacerbate DCCR-related adverse effects.

CYP1A2 and CYP3A4 interactions

DCCR is both a substrate and an inhibitor of CYP1A2. Coadministration with strong CYP1A2 inhibitors increases diazoxide exposure, which may heighten the risk of AEs. In such cases, clinicians should apply the prescribing information's modified titration schema, which includes targeting a lower maintenance dose and extending titration intervals to every 4 weeks in patients with cardiopulmonary or metabolic risk [14] (Table 1). Because DCCR inhibits CYP1A2, concurrent use of CYP1A2 substrates can increase substrate exposure and toxicity risk. These combinations should be avoided whenever possible or monitored carefully if unavoidable. Strong CYP3A4 inhibitors may further increase diazoxide exposure and require dose reduction and closer surveillance. In contrast, strong CYP3A4 or moderate CYP1A2 inducers reduce exposure, potentially diminishing efficacy, and should generally be avoided.

Highly protein-bound drugs

Because diazoxide is highly protein bound, displacement interactions are possible when used with other agents particularly warfarin and phenytoin. In such situations, clinicians should monitor international normalized ratio values or serum phenytoin concentrations and adjust the concomitant drug doses accordingly.

Diuretics

Both diazoxide and thiazide diuretics are associated with hyperglycemia and hyperuricemia. DCCR can promote sodium and fluid retention via renal tubular effects; thiazide diuretics inhibit Na–Cl reabsorption in the distal tubule and may be used to counteract fluid retention when clinically indicated, with close monitoring of electrolytes and glucose. Chronic/maintenance diuretic therapy is generally discouraged; if needed, favor short courses, and avoid routine long-term loop diuretics. In DESTINY-PWS, the incidence of edema was 27% among patients receiving DCCR compared with 12% in the placebo arm. In long-term follow-up, the preferred management strategy was dose reduction, temporary interruption, or slower titration, while new loop-diuretic initiation was rare (1.6%; mean: 46 days). Concomitant use of DCCR with loop or thiazide diuretics has been observed in postmarketing clinical practice and is not contraindicated; when diuretics are clinically indicated, they may be coadministered with careful monitoring. When diuretics are necessary, clinicians should coordinate therapy with regular glucose testing and interval edema assessments and consider slower titration or temporary DCCR dose reduction if edema or dysglycemia emerges.

When interactions are unavoidable

When interacting drugs cannot be avoided, clinicians should follow the U.S. prescribing information (USPI) recommendations for monitoring and dose modification [14]. If therapy is interrupted because of DDIs or AEs, treatment may be resumed at the prior dose if the interruption is ≥7 days. For longer interruptions (≥7 days), retitration should follow the USPI dosing tables. These measures ensure safe continuation of therapy while minimizing pharmacokinetic interaction risks (Table 2).

Optimization of pretreatment comorbidities

Before starting DCCR, optimize management of comorbidities that intersect with the known safety profile, primarily glycemic control and fluid status, so that titration can proceed safely. Common PWS comorbidities include endocrinopathies, obesity, hyperglycemia, edema/fluid retention, sleep apnea/obesity-hypoventilation, and psychiatric/behavioral disorders. Systematic preinitiation evaluation and targeted management of these issues improves tolerability and treatment continuity.

Hyperglycemia

People with PWS are predisposed to dysglycemia due to obesity; early symptoms often include polydipsia, polyuria, fatigue, headaches, and blurred vision [16]. In PWS, recognition can be atypical: "polydipsia" may reflect baseline high intake behaviors; "polyuria" may be absent due to large, low-tone bladders; and irritability or confusion from hyperglycemia can be hard to distinguish from baseline mood/behavioral features. Because food-seeking complicates fasting labs, HbA1c may be a more practical marker to follow. DCCR can elevate glucose by inhibiting pancreatic insulin release; hyperglycemia, including rare severe events (DKA), is a labeled risk [14]. In DESTINY-PWS, hyperglycemia events clustered early and were usually grade 1-2 and manageable with dose/titration changes and standard antihyperglycemic; discontinuation was uncommon (≈1.6%). However as noted, those individuals in the trial with higher baseline HbA1c had more significant increases in their HbA1c.

Management in PWS should include lifestyle measures (structured diet/food security; activity as tolerated) and pharmacotherapy when indicated (eg, metformin, GLP-1 receptor agonists, and insulin). For appropriate patients, DCCR can help address hyperphagia alongside standard diabetes care. Close follow-up with endocrinology and nutrition is recommended.

Pretreatment

Document HbA1c and FPG; adjust concomitant hyperglycemic agents where possible (eg, systemic corticosteroids, thiazides,

Table 1 DCCR dosing for DDI with CYP1A2

Weight	Recommended once-daily dosage			
	Starting dosage Weeks 1 and 2	Titration dosage Weeks 3 and 4	Titration dosage Weeks 5 and 6	Target maintenance dosage
20 kg to <30 kg	25 mg	25 mg	50 mg	75 mg
30 kg to <40 kg	50 mg	100 mg	100 mg	100 mg
40 kg to <65 kg	50 mg	100 mg	150 mg	150 mg
65 kg to <100 kg	100 mg	150 mg	200 mg	250 mg
100 kg to <135 kg	100 mg	200 mg	250 mg	300 mg
≥135 kg	100 mg	200 mg	300 mg	325 mg

One caveat is that the maintenance dose be subtherapeutic based on weight for those that are not on a concomitant CYP1A2 inhibitor.

Table 2 Practical guidance for DDIs with DCCR

Category	Prevention/management	Mechanism and notes
Strong CYP1A2 inhibitors	Reduce DCCR dose. Use modified titration schema (lower maintenance dose; slower titration every 4 weeks in at-risk patients).	DCCR is a CYP1A2 substrate. Inhibitors ↑ exposure, ↑ adverse reactions.
CYP1A2 substrates	Use caution with concomitant use. Review necessity and consider dose reduction of the CYP1A2 substrate; monitor closely for toxicity.	DCCR inhibits CYP1A2 → ↑ substrate exposure, ↑ adverse effects.
Strong CYP3A4 inhibitors	Monitor AEs, consider dose reduction of DCCR.	Inhibitors ↑ diazoxide exposure, ↑ toxicity risk.
Dual strong CYP3A4/ moderate CYP1A2 inducers	Avoid concomitant use.	Inducers ↓ DCCR exposure → ↓ efficacy.
Highly protein-bound drugs	Monitor international normalized ratio (INR) for coumarins; monitor serum levels of diphenylhydantoin. Adjust doses if needed.	Diazoxide displaces protein-bound drugs. Clinical relevance greatest for narrow therapeutic index drugs.
Thiazide or other diuretics	Monitor for hyperglycemia. Adjust DCCR/diuretic dose. Coordinate with glucose monitoring.	Both DCCR and diuretics cause hyperglycemia, hyperuricemia. Trials: edema managed by dose adjustment, new loop-diuretic use rare.

If interruptions occur due to DDIs or AEs, resume prior dose if <7 days. If ≥7 days, retitrate per USPI tables. When interacting drugs are unavoidable, follow USPI Sections 2.3 and 5.2.

and growth hormone) and bring values to a stable trajectory before the first dose. Use the monitoring cadence in Section "Initiation, monitoring, and titration" during titration [14].

Peripheral edema

Baseline lower-extremity edema is common in adults with PWS and can reflect venous/lymphatic insufficiency and obesity-hypoventilation; in those with severe obesity, edema may present as turgor/swelling of adipose tissue rather than classic pitting, and pitting may be minimal even with clinically meaningful edema. In a Dutch study, 31% of adults with PWS were reported to have leg edema [18]. In the DCCR program, 15.2% had peripheral edema at baseline (mostly grade 0-1), and on-treatment edema was predominantly grade 1-2 and manageable [16]. Management in trials favored dose modification or slower titration; new loop-diuretic initiation was rare (1.6%; mean: 46 days).

Early signs/symptoms to watch include decreased exercise tolerance and rapid weight gain; late complications can include chronic skin changes, ulcers, thrombosis, and cellulitis.

Management options include direct-pressure strategies (compression stockings), rehabilitation/increased physical activity, diuretics when clinically indicated (noting glycemia/uric acid considerations with thiazide diuretics), and oxygen where cardiopulmonary disease is present. Comanagement with a cardiopulmonary specialist should be considered, especially if edema, poorly controlled OSA and obesity are present at baseline.

Clinical pearls

Imaging (chest X-ray/echocardiogram) changes are typically late in cardiopulmonary compromise; end-stage obesity-hypoventilation can progress to heart failure; cellulitis may present with blunted inflammatory markers and delayed fevers—oral antibiotics, sometimes with an antifungal (eg, fluconazole), are often effective.

Pretreatment

Examine and grade edema; correct reversible contributors (deconditioning, edema-promoting medications). If baseline edema is present, consider pretreatment with a diuretic before DCCR initiation (note: only loop diuretics were permitted in the phase 3 program). Do not start if baseline edema is ≥ grade 3 or refractory to oral diuretics. Align early follow-up within the first 3-6 months when risk is highest. Refer to a cardiopulmonary specialist for consultation regarding evaluation, treatment, and follow-up.

Pulmonary edema/pulmonary hypertension context

Neonatal experience with immediate-release diazoxide links fluid retention and reversible pulmonary hypertension; this has prompted vigilance for cardiopulmonary signals in vulnerable populations. In adults with PWS, obesity-hypoventilation and sleep-disordered breathing can mask early decompensation; declining exercise tolerance, rapid weight gain often precede late radiograph/echocardiogram changes. Pretreatment optimization therefore includes screening for uncontrolled sleep apnea/obesity-hypoventilation and ensuring that respiratory support (eg, CPAP/BiPAP) is established when indicated before DCCR titration [17].

Practical guidance–pretreatment

1. Measure and stabilize HbA1c and FPG before the first dose; plan early glucose checks. Where fasting labs are unreliable, trend HbA1c and reinforce food security to support consistent monitoring.
2. Grade edema at baseline; correct contributors and do not initiate if edema is ≥ grade 3 or refractory to oral diuretics. If baseline edema is present, consider pretreatment with a diuretic prior to initiating DCCR as well as concomitant treatment with a diuretic for high-risk individuals. Consider addition of additional measures for baseline and follow-up evaluation such as echo, BNP, or CRP.
3. Address OSA/obesity-hypoventilation and consider baseline imaging in high-risk adults; defer if pulmonary hypertension is suspected
4. Consult with a cardiopulmonary specialist if significant baseline edema is present, especially in those with moderate to severe OSA and suspected obesity-hypoventilation
5. Adjust concomitant medications that raise glucose or promote fluid retention and apply the USPI-based modified titration when interacting drugs are unavoidable
6. Set expectations with families: early months carry the highest risk for glycemia and edema events; reinforce reporting of red flags and keep food security unchanged during titration. Educate caregivers that behavioral changes may obscure classic hyperglycemia symptoms; encourage low-threshold communication and objective home data (FPG/HbA1c).

Initiation, monitoring, and titration

Once a candidate meets selection criteria and pretreatment comorbidities are optimized, initiation should follow a standardized, weight-based approach with early, structured monitoring for glycemia, and fluid status. Glycemic and edema events clustered early, were predominantly grade 1-2, and were typically managed by dose adjustment, brief interruption, slower titration, and/or standard concomitant medications without discontinuation [16].

Preinitiation checklist (complete at or immediately before first dose)

- Indication: DCCR is indicated for adults and pediatric patients ≥4 years with genetically confirmed PWS who experience clinically significant hyperphagia
- Contraindications: Known hypersensitivity to diazoxide, formulation components, or thiazides.
- Medication review/DDI screen: Reconcile prescribed/OTC/nutraceuticals/supplements; screen for strong CYP1A2 inhibitors, CYP1A2 substrates, strong CYP3A4 inhibitors, and dual strong CYP3A4/moderate CYP1A2 inducers; see DDI for management.
- Comorbidities (confirm optimization): Impaired fasting glucose/impaired glucose tolerance/prediabetes/type 2 diabetes, insulin resistance, concomitant GH or glucocorticoids, peripheral or pulmonary edema, pulmonary hypertension, moderate–severe sleep apnea, severe obesity, cardiopulmonary disease, uncontrolled hypertension, and venous thromboembolism history.
- Physical exam baseline: Document edema grade and any signs suggestive of dysglycemia (with or without hyperosmolar symptoms) to serve as reference during titration. Consider baseline echocardiography and laboratory measures (eg, BNP to assess cardiac function if clinically indicated or in high-risk adults).
- Conditions to generally avoid initiation: Untreated or uncontrolled moderate–severe OSA, moderate–severe peripheral edema (≥grade 3) or edema refractory to oral diuretics, uncontrolled diabetes (eg, HbA1c > 7% unless trends are stable/improving with reliable home monitoring and close follow-up), extreme obesity with high-risk comorbidities, or inability to assure caregiver/clinic monitoring.
- Edema management considerations: If diuretics are used during titration, note that loop and thiazide agents may potentiate diazoxide-related hyperglycemia and hyperuricemia; arrange serial glucose (and uric acid if clinically indicated).
- Cardiovascular/pulmonary risk stratification (selected patients): Consider echocardiography, chest x-ray, polysomnography verification of CPAP/BiPAP adherence, and optional serial BNP or NT-proBNP in high-risk adults to help detect early fluid overload; rising natriuretic peptides or worsening edema should prompt dose hold and reassessment.

Table 3 Recommended starting dose and standard titration by body weight

Weight	Starting dosage Weeks 1 and 2	Titration dosage Weeks 3 and 4	Titration dosage Weeks 5 and 6	Target maintenance dosage
20 kg to <30 kg	25 mg	50 mg	75 mg	100 mg
30 kg to <40 kg	75 mg	150 mg	150 mg	150 mg
40 kg to <65 kg	75 mg	150 mg	225 mg	225 mg
65 kg to <100 kg	150 mg	225 mg	300 mg	375 mg
100 kg to <135 kg	150 mg	300 mg	375 mg	450 mg
≥135 kg	150 mg	300 mg	450 mg	525 mg

- Glycemic optimization: Ensure HbA1c/FPG are on a stable or improving trajectory if elevated; plan early home FPG checks.
- Formulation note: Do not substitute diazoxide oral suspension; extended-release delivery is required for once-daily pharmacokinetics.

Starting dose and administration (per label)

DCCR should not be substituted with diazoxide oral suspension, as the pharmacokinetic profiles are different and extended-release delivery is critical to maintaining stable plasma concentrations. The maximum recommended dose is 5.8 mg/kg/day or 525 mg/day. Doses above this threshold have not been studied in patients with PWS. The recommended starting and titration schedule is weight-based (Table 3).

Laboratory testing prior to DCCR initiation

Obtain HbA1c and FPG prior to initiation and ensure glycemia is on a stable/improving trajectory if elevated. Reconcile concomitant medications that can worsen hyperglycemia (eg, systemic corticosteroids and thiazides) or fluid retention and adjust when feasible. Provide brief education on home fasting glucose checks and recognition of early dysglycemia symptoms.

Monitoring during titration and dose escalation

Use a structured titration and monitoring plan. In higher-risk patients (eg, baseline edema/fluid overload, OSA/COPD, obesity with elevated FPG/HbA1c, and interacting drugs), apply a conservative schema (lower starting dose/target and longer steps, eg, every 4 weeks). In pooled safety analyses, most hyperglycemia occurred within the first 6 months (all grade 1-2 in DESTINY-PWS), and most edema events first appeared within ~3-6 months, largely grade 1-2; 6-month event-free survival was ~78% for hyperglycemia and 68% for peripheral edema [16]. This timing justifies closer early surveillance and slower up-titration in higher-risk patients. In high-risk patients, titration may be stopped at any lower step if clinically appropriate (Table 4).

Monitoring schedule and action thresholds

The recommended monitoring schedule and dose-modification triggers are summarized in Table 5.

Monitoring and dosage modifications due to adverse reactions

Hyperglycemia

If FPG or HbA1c rises meaningfully, pause titration, reduce or temporarily interrupt, and add/adjust antidiabetic therapy. In the program, discontinuation for hyperglycemia was uncommon (~1.6%); cohort mean HbA1c remained ~5.5-5.7% long-term after an early rise, and fasting glucose stabilized near baseline.

Fluid overload: surveillance and response

Monitor for ankle/foot/leg/facial swelling or generalized swelling, dyspnea/shortness of breath, and unexpected weight gain (≥5 lb or ≥5% of body weight, whichever is less). If edema develops, slow or reverse titration, reduce or interrupt the dose, and re-assess clinically. Consider short diuretic courses case-by-case; new loop-diuretic initiation in trials was infrequent (1.6%) and brief (mean: ~46 days). Stop DCCR for clinically significant fluid overload; when resolved, retitrate only to the last well-tolerated dose with consideration of ongoing concomitant loop or thiazide diuretic.

Modified titration schema after adverse reactions

For patients who experience glycemic elevations or edema, a more conservative, extended titration may be used, with increments every 2-4+ weeks and lower final targets (Table 6).

Dosage modifications for concomitant strong CYP1A2 inhibitors

If strong CYP1A2 inhibitors are required, apply the USPI's reduced target-dose schema and consider longer step intervals (eg, every 4 weeks), especially in patients with cardiovascular, pulmonary, or metabolic risks or other interacting drugs.

Table 4 Modified titration schema for patients with risk factors

Step Duration	Starting dose 2 to 4+ weeks	Step 2 2 to 4+ weeks	Step 3 2 to 4+ weeks	Step 4 2 to 4+ weeks	Step 5 2 to 4+ weeks	Step 6 2 to 4+ weeks	Target Maintenance therapy
20 to <30 kg	25 mg	50 mg	75 mg	100 mg	100 mg	100 mg	100 mg
30 to <40 kg	75 mg	150 mg	150 mg	150 mg	150 mg	150 mg	150 mg
40 to <65 kg	75 mg	150 mg	225 mg	225 mg	225 mg	225 mg	225 mg
65 to <100 kg	75 mg	150 mg	225 mg	300 mg	375 mg	375 mg	375 mg
100 to <135 kg	75 mg	150 mg	225 mg	300 mg	375 mg	450 mg	450 mg
≥135 kg	75 mg	150 mg	225 mg	300 mg	375 mg	450 mg	525 mg

Smaller dose adjustments may be made using the 25-mg tablet to change doses in 25-mg increments, while remaining within USPI-recommended target and maximum doses.

Table 5 Monitoring schedule and dose-modification triggers [14]

Parameter	Monitoring frequency	Action if abnormal
Fasting glucose	Weekly × first 2 weeks; then every 4 weeks	If ≥110 mg/dL sustained → increase monitoring; if ≥126 mg/dL or HbA1c ≥ 6.5% → reduce dose, hold, or add antidiabetic therapy
HbA1c	Every 3 months	If ≥6.5% sustained → interrupt or down-titrate, optimize antidiabetic therapy
Weight	Each visit; inquire about gain ≥5 lbs or ≥5% BW	If above threshold → assess for fluid overload
Clinical exam (edema)	Every visit; targeted if symptomatic	Grade ≥2 pitting edema → hold or reduce dose; Grade ≥3 → discontinue
Dyspnea/respiratory symptoms	At each visit	If concerning, interrupt dose; evaluate with echo/chest x-ray as indicated
Missed/interrupted dose	Continuous	Resume prior dose if <7 days missed; retitrate if ≥7 days per USPI schema

Table 6 Modified titration schema for patients who experience adverse reactions [14]

Step Duration	Starting dose 2 to 4+ weeks	Step 2 2 to 4+ weeks	Step 3 2 to 4+ weeks	Step 4 2 to 4+ weeks	Step 5 2 to 4+ weeks	Step 6 2 to 4+ weeks	Target Maintenance therapy
Body weight:							
20 to <30 kg	25 mg	50 mg	75 mg	100 mg	100 mg	100 mg	100 mg
30 to <40 kg	75 mg	150 mg	150 mg	150 mg	150 mg	150 mg	150 mg
40 to <65 kg	75 mg	150 mg	225 mg	225 mg	225 mg	225 mg	225 mg
65 to <100 kg	75 mg	150 mg	225 mg	300 mg	375 mg	375 mg	375 mg
100 to <135 kg	75 mg	150 mg	225 mg	300 mg	375 mg	450 mg	450 mg
≥135 kg	75 mg	150 mg	225 mg	300 mg	375 mg	450 mg	525 mg

The same framework may be applied reactively if AEs emerge during titration (see DDI and Table 5) [14].

Dosage interruption, missed dose, and discontinuation

If a dose is interrupted or missed for <7 days, resume at the previous dose. If the interruption is ≥7 days, retitrate per the appropriate schema (standard or CYP1A2-modified). Tapering is not required when discontinuing DCCR.

AE management

AE monitoring and management are central to the safe and effective use of DCCR in PWS. Across the clinical development program, DCCR has been administered to 125 patients aged 4 years and older, at dosages up to 5.8 mg/kg/day (maximum: 525 mg/day) for as long as 4.9 years (median: 3.0 years). The safety profile has been generally consistent with the parent molecule diazoxide. The most common AEs were hypertrichosis, edema, and hyperglycemia, with rash and behavioral symptoms observed less frequently.

Table 7 Common AEs in DCCR clinical development (DESTINY-PWS study)

AE	DCCR (%)	Placebo (%)	Typical onset	Severity	Course/duration
Hypertrichosis	36	14	Weeks–months	Mild–Mod	Reversible with stop
Edema	27	12	Early in titration	Mostly Grade 1-2	Improves with adjustment
Hyperglycemia	17	5	First 4-8 weeks	Variable	Requires monitoring
Rash	12	2	Variable	Mild	Transient
Affect lability	5.3	<2	Variable	Mild	Self-limited
Hirsutism	5.3	<2	Months	Mild	Reversible
Abnormal behavior	5.3	5.1		Mild–Mod	Comparable to placebo

Pooled AE terms are defined as in the DESTINY-PWS (C601/C602) clinical database: "Edema" includes peripheral, localized, generalized, and periorbital edema and swelling-related events; "Hyperglycemia" includes hyperglycemia, blood glucose increased, and diabetes-related events; "Rash" includes maculopapular/papular rashes, dermatitis, erythema multiforme, and urticaria.

Common AEs

In the randomized controlled study (DESTINY-PWS), AEs occurring in ≥10% of patients and ≥2% above placebo included hypertrichosis (36% vs 14%), edema (27% vs 12%), hyperglycemia (17% vs 5%), and rash (12% vs 2%) [16]. Hypertrichosis was dose-dependent, typically presented within the first few months, and reversible upon discontinuation. Edema usually emerged early in titration, was predominantly grade 1-2, and improved with dose adjustment or short courses of diuretic therapy. Hyperglycemia was more frequent in patients with baseline risk factors (prediabetes, obesity, or concomitant growth hormone therapy). Rash was generally mild and transient.

In the DESTINY-PWS-RWP (C602-RWP), overall AE rates were similar between DCCR and placebo (73.7% vs 74.4%; Table 7). Most events reflected common complications of PWS rather than treatment-related toxicities. Notably, affect lability (5.3%) and hirsutism (5.3%) were slightly more frequent in DCCR-treated patients, while abnormal behavior occurred at comparable rates (5.1% placebo vs 5.3% DCCR). Serious AEs were uncommon; the only SAE reported was in the placebo arm and unrelated to study drug.

Serious or dose-limiting AEs

Dose-limiting events were primarily metabolic (hyperglycemia/DKA) or fluid-related (peripheral/pulmonary edema). Severe pulmonary edema was reported in one case in DESTINY-PWS, precipitated by a concurrent respiratory infection. No dose-limiting cardiovascular, hepatic, or renal toxicities were identified, though caution is warranted in patients with underlying risk factors. Expert opinion supports immediate dose interruption or discontinuation for grade ≥3 fluid overload or uncontrolled hyperglycemia despite appropriate therapy.

Management principles and dose modification

AE management requires anticipatory monitoring, early intervention, and dose flexibility. Label-based guidance recommends interrupting or reducing DCCR for significant glycemic excursions or edema, then resuming at the last tolerated dose. In high-risk patients, slower titration (intervals every 4 weeks) is appropriate (Table 8).

Hyperglycemia: special considerations

Hyperglycemia occurred in 17% of DCCR-treated patients in DESTINY-PWS, and 34% across long-term exposure. Risk was greatest in those with baseline diabetes/prediabetes, obesity, or concomitant growth hormone or corticosteroids [16]. Rare cases of DKA were observed.

Recommendations

- Screen for baseline diabetes, impaired fasting glucose, and family history.
- Optimize glycemic control before initiation.
- Weekly fasting glucose for the first 2 weeks, then every 4 weeks; HbA1c every 3 months.
- Educate families on hyperglycemia and DKA symptoms.
- If elevations occur: interrupt or reduce dose, adjust titration, and initiate antidiabetic therapy.

Edema and fluid retention

Peripheral edema occurred in 27% of DCCR vs 12% placebo in DESTINY-PWS. Most were grade 1-2, but rare severe fluid overload and pulmonary edema occurred. Pretreatment evaluation should include cardiac/pulmonary history, baseline weight, and review of fluid-retaining medications.

Clinical recommendations

- Interrupt or reduce dose for moderate/severe edema.
- Discontinue in pulmonary edema.
- Diuretics may be used selectively, but underlying causes (eg, infection) should also be addressed.

Other notable AEs

Rash, generally mild and self-limiting, occurred in 12% of DCCR vs 2% placebo. Behavioral events (affect lability, irritability)

Table 8 AE management strategies and dose-modification triggers

AE	Monitoring/triggers	Recommended actions
Hyperglycemia	FPG weekly ×2, then q4w; HbA1c q3mo. Triggers: sustained FPG >150-180 mg/dL, HbA1c rise >1%.	Pause titration; reduce/interrupt dose; initiate or adjust antidiabetic therapy; resume after control.
Diabetic ketoacidosis risk	Symptoms: abdominal pain, tachypnea, confusion.	Stop DCCR immediately; manage as medical emergency.
Edema	Assess weight gain ≥5 lbs or ≥5% BW; ankle/leg swelling, dyspnea.	Dose reduction or temporary interruption; add diuretic if indicated; discontinue if pulmonary edema.
Rash/ hypersensitivity	Dermatologic exam if rash develops.	Usually self-limited; discontinue if severe or systemic.
Behavioral AEs	Monitor for new or worsening affect lability, irritability.	Supportive management; assess for DDIs.

were infrequent and comparable to background rates in PWS, suggesting they may reflect disease-related variability rather than drug toxicity. Gastrointestinal and neurologic symptoms were rare. Hypersensitivity events were mild; no anaphylaxis was reported.

Conclusion

Hyperphagia in PWS is a lifelong driver of morbidity, mortality, and caregiver burden, and until recently clinicians had no approved pharmacologic option specifically targeting this symptom. DCCR provides a mechanistically rational therapy that can meaningfully reduce hyperphagia and improve related metabolic and behavioral outcomes when used thoughtfully in a structured clinical framework. The experience from the DESTINY program and subsequent open-label and real-world data shows that benefit is achievable across a broad age and weight range, if treatment is anchored in careful patient selection and systematic monitoring.

The guidance presented in this article is intended to translate trial evidence into practical decision pathways that fit the complexity of everyday PWS care. By emphasizing when to initiate therapy, how to optimize glycemic control, edema, and cardiopulmonary status beforehand, and how to apply weight-based titration with predefined monitoring thresholds, these recommendations aim to help clinicians use DCCR in a way that maximizes therapeutic gain while limiting preventable AEs. Treating hyperglycemia and fluid overload as predictable and manageable risks, instead of unforeseen complications, helps healthcare providers identify issues sooner, adjust doses promptly, and maintain therapy for many patients who benefit clinically. Implementation of this guidance also underscores the importance of multidisciplinary care.

Finally, these recommendations should be viewed as a foundation rather than a fixed endpoint. Ongoing postmarketing experience, registry data, and future studies will clarify the role of DCCR in younger patients, in those with more advanced metabolic disease, and in combination with other emerging therapies. Regular reassessment will be needed as new evidence accumulates. In addition, DCCR is now under review in a number of regulatory agencies in countries outside of the United States and so updates may be needed in the future to account for differences among the countries. For now, this expert opinion provides a structured, clinically grounded approach to integrating DCCR into comprehensive PWS care, with the goal of improving both health outcomes and day-to-day quality of life for individuals living with this complex disorder.

Acknowledgments

The authors would like to thank Drs Julie Perry, Michael Huang, Neil Cowen, and Mitch Nagao of Soleno Therapeutics for providing responses to product questions for this review. The authors also thank the support for the initial need for this review from the PWS patient advocacy groups Prader–Willi Syndrome Association (Stacy Ward) and Foundation for Prader–Willi Research (Carline Vrana-Diaz and Theresa Strong). The authors also acknowledge Bhavadharini Balaji, PhD (Wunderbar Medical & Scientific Writing) and J.D. Cox, PhD (Mayville Medical Communications) for editorial support, which was funded by Soleno Therapeutics, in accordance with Good Publication Practice 2022 ethical guidelines.

Funding

Editorial support was funded by Soleno Therapeutics.

Disclosures

J.L.M. reports receiving research funding from Soleno Therapeutics, Rhythm Pharmaceuticals, Aardvark Therapeutics, and Harmony Biosciences. A.H.S. reports receiving research funding from Rhythm Pharmaceuticals, Aardvark Therapeutics, and Eli Lilly, as well as consulting fees from Rhythm Pharmaceuticals and an honorarium from Soleno Therapeutics. P.S. reports receiving research funding from Acadia Therapeutics, Eli Lilly, and the Foundation for Prader–Willi Research, consulting fees from Soleno Therapeutics, and honoraria from Medscape. J.M.-C. reports receiving research funding from Aardvark Therapeutics, Soleno Therapeutics, and the Foundation for Prader–Willi Research, as well as consulting fees from Soleno Therapeutics.

Data availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

References

1. Lionti T, Reid SM, White SM, Rowell MM. A population-based profile of 160 Australians with Prader-Willi syndrome: trends in diagnosis, birth prevalence and birth characteristics. *Am J Med Genet A*. 2015;167A(2):371-378.
2. Gillentine MA, Lupo PJ, Stankiewicz P, Schaaf CP. An estimation of the prevalence of genomic disorders using chromosomal microarray data. *J Hum Genet*. 2018;63(7):795-801.
3. Miller JL, Lynn CH, Driscoll DC, *et al.* Nutritional phases in Prader-Willi syndrome. *Am J Med Genet A*. 2011;155A(5):1040-1049.
4. Butler MG, Manzardo AM, Heinemann J, Loker C, Loker J. Causes of death in Prader-Willi syndrome: Prader-Willi Syndrome Association (USA) 40-year mortality survey. *Genet Med*. 2016;19(6):635-642.
5. Stevenson DA, Heinemann J, Angulo M, *et al.* Deaths due to choking in Prader-Willli syndrome. *Am J Med Genet A*. 2007;143(5):484-487.
6. McCandless SE; Committee on Genetics. Clinical report-health supervision for children with Prader-Willi syndrome. *Pediatrics*. 2011;127(1):195-204.
7. Bellis SA, Kuhn I, Adams S, Mullarkey L, Holland A. The consequences of hyperphagia in people with Prader-Willi syndrome: a systematic review of studies of morbidity and mortality. *Eur J Med Genet*. 2022;65(1):104379.
8. Kayadjanian N, Vrana-Diaz C, Bohonowych J, *et al.* Characteristics and relationship between hyperphagia, anxiety, behavioral challenges and caregiver burden in Prader-Willi syndrome. *PLoS One*. 2021;16(3):e0248739.
9. 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;69(5):417-427.
10. Kishore P, Boucai L, Zhang K, *et al.* Activation of K(ATP) channels suppresses glucose production in humans. *J Clin Invest*. 2011;121(12):4916-4920.
11. Miller JL, Gevers E, Bridges N, *et al.* Diazoxide choline extended-release tablet in people with Prader-Willi syndrome: results from long-term open-label study. *Obesity (Silver Spring, Md)*. 2023;32(2):252-261.
12. Cowen N, Bhatnagar A. The potential role of activating the ATP-sensitive potassium channel in the treatment of hyperphagic obesity—PubMed. *Genes (Basel)*. 2020;11(4):450.
13. Miller JL, Gevers E, Bridges N, *et al.* Diazoxide choline extended-release tablet in people with Prader-Willi syndrome: a double-blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2023;108(7):1676-1685.
14. VYKATTM XR (diazoxide choline) extended-release tablets. Package insert. Soleno Therapeutics 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/216665s000lbl.pdf. Accessed April 29 2026.
15. Crinò A, Grugni G. Update on diabetes mellitus and glucose metabolism alterations in Prader-Willi syndrome. *Curr Diab Rep*. 2020;20(2):7.
16. Shoemaker AH, Yanovski JA, Gevers EF, *et al.* OR35-07 the glycemic outcomes of diazoxide choline extended-release (DCCR) tablets for administered for hyperphagia in individuals with Prader-Willi syndrome over 4 years. *J Endocr Soc*. 2025;9(Suppl 1):bvaf149-087.
17. Gourash LM. Oedema (Fluid retention) in Prader-Willi Syndrome 2007. https://pittsburghpartnership.com/handouts/Oedema%20in%20PWS_Linda%20Gourash%20revised.pdf. Accessed April 29 2026.
18. Pellikaan K, van Weijen PMH, Rosenberg AGW, *et al.* What endocrinologists can do to prevent cardiovascular complications in adults with Prader-Willi syndrome: lessons from a case series. *Front Endocrinol (Lausanne)*. 2023;14:1145066.