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New Drug Evaluation: diazoxide choline, oral

Date of Review: August 2025
Generic Name: diazoxide choline

End Date of Literature Search: 05/21/2025
Brand Name (Manufacturer): Vykat XR (Soleno Therapeutics, Inc.)

Dossier Received: No

Plain Language Summary:

- Prader-Willi Syndrome is a rare genetic condition that affects the body's metabolism and affects childhood development and behavior.
- Vykate XR (diazoxide choline extended-release) are tablets taken by mouth to treat a condition called hyperphagia, which is an unusually strong feeling of hunger that can lead to overeating in people with Prader-Willi syndrome.
- One study compared diazoxide choline to placebo pills and found that caregivers did not notice a difference in overeating with people who got the medicine. A second study was conducted that did seem to show a small difference with the medicine, with less food-seeking behaviors compared to people who got placebo.
- Side effects seen with diazoxide choline included high blood sugar, fluid in the legs or ankles, increased hair growth, nausea, vomiting, and rash.
- Prescribers of diazoxide choline for a patient on the Oregon Health Plan will need to receive prior authorization from the Oregon Health Authority before it will be covered. This process is meant to ensure appropriate prescribing of the medicine.

Research Questions:

1. What is the evidence for the efficacy of diazoxide choline extended-release tablets in managing hyperphagia in people with Prader-Willi syndrome (PWS)?
2. What are the harms of diazoxide choline extended-release tablets in people with PWS?
3. Are there specific subpopulations for which diazoxide choline is better tolerated, more effective, or safer when used for hyperphagia in people with PWS?

Conclusions:

- VYKAT XR (diazoxide choline) extended-release tablets are Food and Drug Administration (FDA)-approved for the treatment of hyperphagia in adults and pediatric patients aged 4 years and older with PWS.[1] The safety and efficacy of diazoxide choline was studied in a phase 3, randomized controlled trial (RCT) and an extension trial with different methods and varying results.
- The phase 3 RCT was conducted in 124 patients aged 4 years and older with hyperphagia and PWS (DESTINY PWS).[2] The primary endpoint was the change in the Hyperphagia Questionnaire for Clinical Trials (HQ-CT) from baseline to Week 13.[2] A change from baseline of 7 points was considered clinically significant.[2] At 13 weeks there was no difference in the HQ-CT score between diazoxide and placebo (least-square mean [LSM] −5.94 vs −4.27; mean difference [MD], -1.67; 95% confidence interval [CI] -4.24 to 0.89; P=0.193; low-quality evidence).[2]

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- In an open-label extension trial, all patients initially received diazoxide choline. At the end of the open-label period, 77 patients were randomized 1:1 to continue receiving diazoxide or switch to placebo. At 16 weeks, the LSM change from baseline in HQ-CT score was worse in the placebo-treated patients than those who continued diazoxide choline (7.6 vs. 2.6; LSM difference -5.0; 95% CI -8.1 to -1.8; very low-quality evidence).[1] Although this change was considered statistically significant, it did not meet the clinical significance of a 7-point change identified in the DESTINY PWS RCT. The results of this phase of the trial have not been published and they are only reported in the manufacturer's prescribing information.
- The most common adverse events reported with diazoxide in clinical trials included hypertrichosis, edema, hyperglycemia, and rash.[1] Adverse events leading to discontinuation in diazoxide-treated patients included aggression, diabetes mellitus, fluid retention, hirsutism, hyperglycemia, lower respiratory tract infection, peripheral edema, pulmonary edema, and papular rash.[1]
- Hyperglycemia, including severe adverse events associated with diabetic ketoacidosis, occurred in diazoxide-treated patients.[1] Fasting glucose should be monitored more frequently for the first few weeks of treatment in patients with risk factors for hyperglycemia, such as obesity, elevated fasting plasma glucose (FPG), hemoglobin A1c (HbA1c) at the upper limit of normal or above, concomitant use of growth hormone, or concomitant use of systemic corticosteroids.[1]
- Severe adverse events associated with fluid overload, including pulmonary edema, were reported in diazoxide-treated patients during clinical trials.[1] Diazoxide has not been studied in patients with compromised cardiac reserve and should be used with caution in these patients.[1] Patients should be monitored for signs or symptoms of edema or fluid overload, and if clinically significant, the diazoxide dose should be reduced or the drug discontinued.[1]

Recommendations:

- Designate diazoxide choline extended-release tablets as non-preferred on the Preferred Drug List (PDL) with prior authorization (PA) criteria to ensure appropriate utilization in patients with hyperphagia due to PWS.

Background:

Prader-Willi syndrome is a rare neurodevelopmental condition due to errors in genomic imprinting involving chromosome 15.[3] This leads to the loss of expression of paternally derived genes caused by paternal deletion, maternal disomy, or an imprinting center defect.[3] Prader-Willi syndrome is associated with intellectual disability, low muscle mass, neuroendocrine abnormalities including growth hormone and gonadotropin deficiency, behavioral problems including aggression, anxiety and compulsivity, and hyperphagia resulting in severe obesity if not controlled.[4] It is the most common genetic cause of life-threatening obesity in humans.[3] The estimated prevalence of PWS is 1 in 10,000 to 20,000 individuals with a reported range of 1 in 8,000 to 1 in 30,000.[3] The number of individuals worldwide with PWS is estimated at 400,000 and about 20,000 individuals in the United States.[3] All ethnic groups are represented, but PWS is reported disproportionately more in White people with a 1:1 gender ratio.[3] Approximately 89 people enrolled in the Oregon Health Plan (OHP) have a diagnosis of PWS, with about 20 people enrolled in fee-for-service (FFS).

The clinical presentation of PWS has historically been divided into 2 distinct clinical stages with failure-to-thrive and feeding problems representing the first stage and onset of obesity representing the second stage.[3] Hypotonia and poor feeding in infancy almost always requires some type of assisted feeding for a period of time.[5] Hyperphagia, which occurs at a median age of 8 years, presents as food obsession, aggressive food seeking, and lack of satiety, with progression to severe obesity if energy intake is not restricted.[4] The etiology of the switch from the stage of poor feeding/failure-to-thrive to obesity/hyperphagia stage has yet to be determined, but is thought to be associated with abnormalities in the hypothalamic circuitry or peripheral satiety signals.[5] Individuals with PWS have differences in various gut hormones, including high levels of obestatin (an appetite suppressant hormone) in infancy, with markedly elevated levels of ghrelin (an appetite stimulant hormone) in childhood and adulthood.[5] These shifts in gut hormones may possibly correspond to the change between the poor feeding and

failure to thrive stage and the hyperphagia and obesity stage of PWS.[5] Individuals with PWS have also been shown to have structural brain abnormalities which may contribute to appetite aberrations.[5]

In PWS, weight control and diet restriction are key management issues.[3] Caloric restrictions of 6–8 calories/cm of height will usually allow for weight loss and 10–12 calories/cm of height may be required to maintain weight in PWS subjects.[3] This calorie requirement to maintain weight is about 60% of normal.[3] Medications to suppress appetite have met with little success in PWS individuals.[3] Growth hormone therapy helps to increase stature and muscle mass in patients with PWS but is not effective in managing hyperphagia.[3]

The primary endpoint in the placebo-controlled diazoxide choline trials was improvement in the HQ-CT score. The HQ-CT is a care-giver reported questionnaire that focuses on food-seeking behaviors in people with PWS during the previous 2 weeks.[6] It consists of 9 questions with responses ranging from 0-4 units each (possible total score range: 0-36).[1] A score of 0 indicates an absence of behaviors and a score of 4 indicating the most frequent or severe behaviors.[1] Higher scores indicate greater overall severity of hyperphagic and food-related behaviors.[1] There is no established threshold for hyperphagia severity based on the HQ-CT score and a minimal clinically effective difference (MCID) has not been developed for this assessment.

VYKAT XR (diazoxide choline) extended-release tablets are FDA-approved for the treatment of hyperphagia in adults and pediatric patients aged 4 years and older with PWS.[1] The exact mechanism of action of diazoxide in the treatment of hyperphagia is unknown.[1] Diazoxide is a potent activator of the adenosine triphosphate (ATP)-sensitive potassium (K_{ATP}) channel that is capable of crossing the blood-brain barrier.[7] Activation of the K_{ATP} channel in neuropeptide Y (NPY)/Agouti related-protein (AgRP) neurons has the potential to reduce secretion of NPY and AgRP, potent endogenous appetite stimulatory neuropeptides, which may contribute to a reduction in hyperphagia.[7] This medication is designated as an orphan drug by FDA.[1] Dosing is weight-based and maintenance dosing ranges from 225 mg once daily (40 to 64 kg) to 525 mg once daily (≥ 135 kg) after the initial titration over 6 weeks.[1] Diazoxide choline is available in 25 mg, 75 mg, and 150 mg tablets.

PROGLYCEM (diazoxide) oral suspension received initial FDA approval in 1976 for treatment of adults with hyperinsulinemia and hypoglycemia associated with inoperable islet cell adenoma or extra pancreatic malignancy.[8] In pediatric patients, diazoxide oral suspension is indicated for management of hypoglycemia due to hyperinsulinism associated with leucine sensitivity, islet cell hyperplasia, nesidioblastosis, extrapancreatic malignancy, islet cell adenoma, or adenomatosis.[8] If other specific medical therapy or surgical management has either been unsuccessful or is not feasible, treatment with diazoxide should be considered.[8]

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and Pharmacokinetic Properties are listed in **Appendix 2**.

Clinical Efficacy:
The efficacy of diazoxide choline in patients with hyperphagia due to PWS was first evaluated in a 13-week, multicenter, double-blind, phase 3 RCT (DESTINY PWS).[2] The study enrolled males and females with genetically confirmed PWS, aged 4 years and older with moderate to severe hyperphagia (defined by the investigators as an HQ-CT score ≥ 13), weighing between 20 and 135 kg.[2] The enrolled participants who continued to meet the inclusion criteria at the end of a 2-week single-blind, placebo run-in were randomly assigned 2:1 to treatment with diazoxide choline or matching placebo stratified by growth hormone treatment (currently treated, not currently treated) and baseline HQ-CT score (scores from 13-19 and from 20-36).[2] A total of 181 people with PWS were screened for the study, 158 of whom were enrolled; among these, 31 were not eligible for randomization because of failure to continue to meet inclusion criteria after the

placebo run-in, and 127 were randomly assigned.[2] Patients were titrated to target dose of diazoxide choline 3.3 to 5.8 mg/kg within 6 weeks.[2] The daily dose ranged from 100 to 450 mg.[2] The primary endpoint was decreased hyperphagia based upon changes in the HQ-CT score from baseline to week 13.[2] A decrease of 7 points from baseline represented clinical improvement.[2] The mean age of patients in the study was 13.5 years, most of the patients were White (85%) and 56% were female.[2] The median baseline HC-QT score was 22.6 points and 84% of enrolled patients were being treated with growth hormone.[2] Additional study details that contribute to the efficacy data for this indication are described and evaluated below in **Table 2**.

At 13 weeks there was no statistically significant difference in the LSM HQ-CT score between diazoxide choline and placebo (−5.94 vs −4.27; MD = -1.67; 95% CI -4.24 to 0.89; P=0.198).[2] However, in a prespecified analysis focused on patients with severe hyperphagia with a baseline HQ-CT score 22 points or higher (40 patients received diazoxide and 19 patients received placebo), diazoxide choline-treated patients had a LSM improvement of -9.67 compared to the -4.26 change seen in placebo-treated patients (95% CI not reported [NR]; p=0.012).[2] Secondary endpoints included Clinical Global Impression of Improvement (CGI-I), Caregiver Global Impression of Change (CGI-C) and body fat measured using dual energy x-ray absorptiometry (DEXA).[2] If the primary end point was statistically significant, then each of the secondary end points was tested in order, with each subsequent analysis reported as significant only if the preceding analysis was significant.[2] Two of 3 secondary end points were improved when diazoxide was compared to placebo (CGI-I: 3.7 vs. 4.0; 95% CI NR; p=0.029 and Fat Mass: -0.80 kg vs. 0.25 kg 95% CI NR; p=0.023).[2]

Eligible patients were subsequently enrolled in 52-week open-label study in which all patients received diazoxide choline. After completion of the open-label extension study, 77 patients participated in a 16-week randomized medication withdrawal phase.[1] This group of patients was randomized 1:1 to continue their current weight-based diazoxide choline regimen or switch to placebo.[1] The mean baseline HC-QT score at the beginning of the withdrawal period was 9.0 points for diazoxide choline-treated patients and 8.1 points for placebo-treated patients. At 16 weeks, the LSM change from baseline in HQ-CT score was less in the placebo-treated patients than those who continued diazoxide choline (7.6 vs. 2.6; LSM difference -5; 95% CI -8.1 to -1.8).[1] Although this was considered statistically significant, it did not reach the clinical endpoint of a 7-point change in the HC-QT score that was used in DESTINY PWS. The results of this phase of the trial have not been published and are only reported in the manufacturer's prescribing information.

Clinical Safety: Adverse events leading to discontinuation in diazoxide choline-treated patients in clinical trials included aggression, diabetes mellitus, fluid retention, hirsutism, hyperglycemia, lower respiratory tract infection, peripheral edema, pulmonary edema, and papular rash.[1] The most common adverse events were hypertrichosis, edema, hyperglycemia, and rash.[1] **Table 1** presents adverse reactions that occurred in at least 5% of patients in the DESTINY PWS trial who received diazoxide choline compared with placebo.

Table 1. Adverse Reactions Reported with Diazoxide and Placebo[1]

Adverse Reaction	**Diazoxide Choline Extended Release N=84**	**Placebo N=42**
Hypertrichosis	36%	14%
Edema	27%	12%
Hyperglycemia	17%	5%
Rash	12%	2%
Pyrexia	6%	0%
Arthralgia	5%	2%

Influenza	5%	2%
Nasopharyngitis	5%	2%

Warnings and Precautions
Diazoxide choline increases blood glucose, due primarily to an inhibition of insulin release from the pancreas.[1] Hyperglycemia, including severe adverse reactions associated with diabetic ketoacidosis, occurred in diazoxide-treated patients during clinical trials.[1] Before initiating diazoxide choline, the manufacturer recommends obtaining an FPG and HbA1c.[1] After initiating treatment with diazoxide choline, FPG and HbA1c should be routinely monitored.[1] Fasting glucose should be monitored more frequently for the first few weeks of treatment in patients with risk factors for hyperglycemia, such as obesity, elevated FPG, HbA1c at the upper limit of normal or above, concomitant use of growth hormone, or concomitant use of systemic corticosteroids.[1]

Severe adverse reactions associated with fluid overload, including pulmonary edema, were reported in diazoxide choline-treated patients during clinical trials.[1] The antidiuretic property of diazoxide may lead to significant fluid retention, which may precipitate congestive heart failure in patients with compromised cardiac reserve.[1] Diazoxide choline has not been studied in patients with compromised cardiac reserve and should be used with caution in these patients.[1] Patients should be monitored for signs or symptoms of edema or fluid overload and if clinically significant should be managed with either diazoxide choline dosage reduction or treatment interruption.[1]

Drug Interactions
Diazoxide choline is a substrate of CYP3A4 and CYP1A2.[1] Concomitant use of diazoxide choline and CYP1A2 substrates (e.g., fluvoxamine) is not recommended.[1] Concomitant use of diazoxide with strong CYP3A4 inhibitors (e.g., itraconazole) increases exposure of diazoxide, which may increase the frequency and/or severity of adverse reactions from diazoxide choline.[1] Concomitant use of diazoxide choline with strong CYP3A4/moderate 1A2 inducers (e.g., rifampin) may decrease exposure of diazoxide and may decrease the efficacy of diazoxide.[1]

Diazoxide choline is highly bound to serum proteins.[1] Diazoxide choline may displace other drugs which are also highly bound to protein resulting in higher or lower blood levels of the concomitantly used drugs.[1] The impact of protein binding displacement is expected to be clinically important for drugs with narrow therapeutic range such as coumadin or phenytoin.[1] Protein binding displacement may result in an increased risk of adverse reactions due to higher blood levels of coumadin or loss of efficacy due to lower exposures of phenytoin.[1]

Look-alike / Sound-alike Error Risk Potential: Diazepam, Dyazide

Comparative Endpoints:

Clinically Meaningful Endpoints:
1) Reduction in the HQ-CT score
2) Improvements in provider assessments (CGI-I and CGI-C)
3) Reduction in body weight and body fat
4) Serious adverse events
5) Study withdrawal due to an adverse event

Primary Study Endpoint:
1) Reduction in the HQ-CT score

Table 2. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/NNT	Safety Outcomes	ARR/NNH	Risk of Bias/ Applicability
1.Miller, et al[2] DESTINY PWS NCT03714373 DB, PC, MC, Phase 3 RCT	1. DCCR 100 to 450 mg (weight-based) po once daily 2. Placebo po once daily	Demographics: -Mean age: 13.4 y -Female: 56% -Hispanic/Latino: 10% White: 85% Black: 5% Asian: 1% Other: 2% -Baseline HQ-CT score: 22.6 -Treated with growth hormone: 84% Key Inclusion Criteria: -Genetically confirmed PWS w/ hyperphagia -Age ≥4 y -Stable care setting for ≥ 6 months -HC-QT score ≥ 13 -Weight 20-135 kg Key Exclusion Criteria: -Pregnancy	ITT: 1. 82 2. 42 PP: 1. 73 2. 40 Attrition: 1. 9 (11%) 2. 2 (5%)	Primary Endpoint: LSM change in HQ-CT from baseline to Week 13 (ITT) 1. -5.94 2. -4.27 MD = -1.67 95% CI -4.24 to 0.89 P=0.198 Secondary Endpoints: LSM CGI-I change from baseline to Week 13 (ITT) 1. 3.7 2. 4.0 MD = 0.3 95% CI NR P=0.029 LSM CGI-C change from baseline to Week 13 (ITT) 1. 3.7 2. 4.0 MD = 0.3 P=0.41 LSM change in body fat mass change from baseline to Week 13 in ITT analysis 1. -0.80 kg 2. 0.25 kg MD = -1.05 95% CI NR P=0.023 LSM change from baseline in HC-QT in a prespecified subgroup analysis of patients with severe hyperphagia (HC-QT ≥22) 1.-9.67 (n=40) 2.-4.26 (n=19) MD = -5.41	NS NA NS NA NA	Hypertrichosis 1. n=30 (36%) 2. n=6 (14%) Edema 1. n=17 (20%) 2. n=4 (10% Hyperglycemia: 1. n=10 (12%) 2. n=0 (0%) Adverse Events 1. n= 70 (83.3%) 2. n=31 (73.8%) Serious Adverse Events: 1. n=6 (7%) 2. n=0 p-value and 95% CI NR	NA for all	**Risk of Bias (low/high/unclear)**: Selection Bias: Low. Randomized 2:1 via a centralized generator, stratified by GH treatment and baseline HQ-CT score. Baseline characteristics balanced between groups. Performance Bias: High. Patients, caregivers, investigators blinded. Placebo tablets were matched to appearance of DCCR tablets. Side effects observed with DCCR may have resulted in unmasking of treatment assignment. Detection Bias: Unclear. Method of blinding not described for outcome assessors. Primary endpoint was a care-giver assessment of changes in hyperphagia. Attrition Bias: High. More discontinuations in treatment arm compared with placebo arm., due to adverse events. Not clear how missing data was handled. Reporting Bias: Unclear. Only p-values were reported for study results. Confidence intervals not reported in the publication – found some results at clinicaltrials.gov Study protocol available on-line. Other Bias: High: Sponsored by manufacturer. Several authors received financial support from the manufacturer. **Applicability**: Patient: Two-week run-in period resulted in exclusion of 17% of potential participants. Reasons for exclusion not clearly explained. Intervention: Dosing determined in Phase 2 RCT. Comparator: Placebo is an appropriate comparator as no other drugs are approved for hyperphagia in PWS. Outcomes: HC-QT questionnaire may be subject to caregiver bias. Exploratory endpoints included parameters of body composition. Setting: 29 sites in the United States (80%) and United Kingdom (20%)

				95% CI NR P=0.012				

Abbreviations: ARR = absolute risk reduction; CGI-I = Clinical Global Impression of Improvement; CI = confidence interval; double-blind; DCCR = diazoxide choline controlled release; GH =growth hormone; HQ-CT = Hyperphagia Questionnaire; kg = kilogram; ITT = intention-to-treat; LSM = least-square mean; MC = multi-center; MD = mean difference: mITT = modified intention to treat; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; NS = not statistically significant; PC = placebo controlled; po = oral route; PP = per protocol; PWS = Prader-Willi Syndrome; RCT = randomized controlled trial; y = years.

References:

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Appendix 1: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VYKAT XR safely and effectively. See full prescribing information for VYKAT XR.

VYKAT™ XR (diazoxide choline) extended-release tablets, for oral use
Initial U.S. Approval: 1973

----------INDICATIONS AND USAGE----------
VYKAT XR is indicated for the treatment of hyperphagia in adults and pediatric patients 4 years of age and older with Prader-Willi syndrome (PWS). (1)

----------DOSAGE AND ADMINISTRATION----------
- Prior to initiation, test fasting plasma glucose and HbA1c; optimize blood glucose in patients who have hyperglycemia. (2.1)
- Do not substitute with diazoxide oral suspension. (2.1)
- Administer orally once daily. (2.2)
- Recommended starting dosage and titration schedule is based on patient's body weight. (2.2)

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

- The maximum recommended dosage is 5.8 mg/kg/day or 525 mg per day. (2.2)
- Interrupt VYKAT XR or reduce dosage for clinically significant elevations in fasting glucose or HbA1c; consider dosage reduction or interruption for clinically significant fluid overload. (2.3)
- See full prescribing information for VYKAT XR dosage modifications due to drug interactions (2.4)
- Following dosage interruption or a missed dose of 7 days or more, re-titrate according to Table 1 or Table 2. (2.5)

----------DOSAGE FORMS AND STRENGTHS----------
Extended-release tablets: 25 mg, 75 mg, and 150 mg of diazoxide choline. (3)

----------CONTRAINDICATIONS----------
Known hypersensitivity to diazoxide, other components of VYKAT XR, or to thiazides. (4)

----------WARNINGS AND PRECAUTIONS----------
- *Hyperglycemia*: Hyperglycemia, including diabetic ketoacidosis, has been reported. During treatment, monitor fasting glucose and HbA1c. Monitor fasting glucose more frequently during first few weeks of treatment in patients with risk factors for hyperglycemia. (2.3, 5.1)
- *Risk of Fluid Overload*: Edema, including severe reactions associated with fluid overload, has been reported. Monitor for signs or symptoms of edema or fluid overload. (2.3, 5.2)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence ≥10% and at least 2% greater than in placebo) are hypertrichosis, edema, hyperglycemia, and rash. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Soleno Therapeutics, Inc. at 1-833-765-3661 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- *Strong CYP1A2 Inhibitors*: Reduce VYKAT XR dosage. (2.4, 7)
- *CYP1A2 Substrates*: Concomitant use with VYKAT XR is not recommended. (7)
- See full prescribing information for additional clinically significant drug interactions. (7)

----------USE IN SPECIFIC POPULATIONS----------
- *Renal Impairment or Hepatic Impairment*: Use is not recommended. (8.6, 8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2025

Appendix 2. Pharmacology and Pharmacokinetic Properties.

Table 1. Diazoxide Choline Extended-Release Tablets[1,9]

Parameter	
Mechanism of Action	Exact mechanism in treatment of hyperphagia in PWS in unknown.
Oral Bioavailability	Peak concentrations occurs after 16 hours. Steady state is reached after 7 days.
Distribution and Protein Binding	Volume of distribution = 44.9 L Extensively protein bound: 91% to 93% (primarily albumin)
Elimination	Excreted primarily (85% to 92%) in urine as a free or conjugated compound
Half-Life	Healthy patients: 28.7 to 32.4 hours. Patients with PWS: 106 hours
Metabolism	Metabolized by CYP1A2 (major) and CYP3A4 (minor)

Abbreviations: L = liters; PWS = Prade-Willi Syndrome

Diazoxide Choline Extended-Release Tablets

Goals:

- Ensure appropriate utilization in people with hyperphagia due to Prader-Willi syndrome.
- Allow case-by-case review for members covered under the EPSDT program.

Length of Authorization:

- Up to 12 months

Requires PA:

- Vykat ER (diazoxide choline extended-release tablets)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for continuation of therapy in a patient previously approved by FFS?	**Yes:** Go to Renewal Criteria	**No:** Go to #3
3. Is this an FDA-approved indication?	**Yes**: Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Is the diagnosis funded by OHP?	**Yes:** Go to #6	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP. If eligible for EPSDT review: Go to #5.

Approval Criteria		
5. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.)	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical necessity.
6. Is the medication prescribed by an endocrinologist or in consultation with a provider that specializes in caring for patients with Prader-Willi syndrome?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness.
7. Has extent of baseline hyperphagia behavior been documented using the caregiver Hyperphagia Questionnaire for Clinical Trials (HQ-CT) assessment or a comparable assessment tool?	**Yes:** Approve for 6 months Document baseline HQ-CT score: _____	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. Has hyperphagia behavior decreased since beginning therapy as assessed by improvement in the HQ-CT score or a comparable assessment tool?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny for lack of treatment response.

P&T/DUR Review: 8/25; (DM)
Implementation: TBD