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Subject: Diazoxide Choline (Vykat XR) Tablet

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Diazoxide choline (Vykat XR) extended-release tablet was approved by the U.S. Food and Drug Administration (FDA) in March 2025 for the treatment of hyperphagia in adults and pediatric patients 4 years of age and older with Prader-Willi syndrome (PWS). Vykat XR is the first and only (as of April 2025) FDA-approved treatment to specifically address hyperphagia associated with PWS. The exact mechanism of action of diazoxide choline in the treatment of hyperphagia in patients with PWS is not fully understood but is believed to be related to reducing the synthesis and secretion of the appetite stimulatory neuropeptides Y (NPY) and agouti-related protein (AgRP).

Prader-Willi syndrome is a rare and complex genetic neurodevelopmental disorder caused by an abnormality in the gene expression on chromosome 15 and occurs in approximately 1 in every 15,000 live births. In March 2025, Soleno (the manufacturer of Vykat XR) estimates that there are approximately 10,000 patients in the U.S. who currently qualify for treatment based on the FDA-approved label. PWS is clinically and genetically diverse, but the syndrome is most often characterized by severe hypotonia, poor appetite, and feeding difficulties in early infancy, followed by severe hyperphagia and gradual development of morbid obesity in early childhood. Individuals often exhibit developmental delays, behavioral issues, and cognitive impairment. Hypogonadism is present in both males and females resulting in hypoplasia, incomplete pubertal development, and, often, infertility. Common physical features include short stature due to growth hormone (GH) deficiency, distinct facial characteristics, strabismus, and scoliosis. PWS is initially suspected in patients with hallmark symptoms and is confirmed through genetic testing. A methylation analysis can detect the vast majority of cases and is often follow by more comprehensive evaluation to determine the specific molecular subtype. Most PWS diagnoses are made within the first year of life.

Hyperphagia associated with PWS is present in over 90% of patients and is likely caused by a hypothalamic abnormality that causes a lack of satiety. The onset of weight gain and increased appetite

often begins around 3 years of age and progresses to extreme hyperphagia between 5 and 13 years of age. Food-seeking behaviors may include hoarding, foraging, stealing, and attempting to consume garbage and inedible objects. These behaviors have significant psychosocial impacts on patients and create a substantial burden on caregivers. Caregivers must physically restrict access to food by installing locks on cabinets, refrigerators, and garbage cans and must implement very strict rules around access to food. According to a 2017 mortality study, the mean age of death in a patient with PWS was 29.5 ± 16 years, and the most common causes of death were associated with hyperphagia and/or obesity-related complications. Management of PWS is symptom- and patient-specific and often requires the coordinated efforts of a team of specialists, including clinical geneticists, pediatricians, orthopedists, endocrinologists, speech therapists, psychologists, and dieticians. In June 2000, the FDA approved the use of human GH therapy for the treatment of children with genetically confirmed PWS to address growth failure. Prior to diazoxide choline, there were no effective treatments for hyperphagia.

The safety and efficacy of diazoxide choline leading to the FDA approval for treatment of hyperphagia in adults and pediatric patients ages 4 years and older with PWS was established in a 16-week, double-blind, placebo-controlled, randomized withdrawal study period (Study 2-RWP; NCT03714373) that followed an open-label study period of diazoxide choline. During Study 2-RWP, 77 patients with hyperphagia and PWS were randomized in a 1:1 ratio to continue their current oral dosage using a weight-based dosage regimen of diazoxide choline or placebo. Prior to participating in Study 2-RWP, patients received double-blind and/or open-label diazoxide choline for a mean duration of 3.3 years (range 2.5 to 4.5 years; Study 1 and Study 2-OLE).

Demographic and baseline disease characteristics were similar for the diazoxide choline and placebo groups. The mean age was 14.9 years of age (range 7 to 29 years of age). Most of the participants were White (86%), 7% were Black or African American, and 8% were of multiple races. The majority of participants were non-Hispanic (91%) and female (56%).

The primary efficacy endpoint was the Change from Baseline in the Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Total Score at Week 16. The HQ-CT is a 9-item, observer-reported outcome measure that assesses a range of hyperphagic and food-related behaviors during the prior 2 weeks. An item score of 0 indicates an absence of behaviors, with a score of 4 indicating the most frequent or severe behaviors. The HQ-CT Total Score may range from 0 to 36, with higher scores indicating greater overall severity of hyperphagic and food-related behaviors.

At the end of the 16-week randomized withdrawal study period, there was statistically significant worsening of hyperphagia in the placebo group relative to the diazoxide choline group, as assessed by the HQ-CT Total Score (see Table below).

Table 1: Study 2-RWP HQ-CT Total Score, Least Square Mean Change from Baseline to the End of the Randomized Withdrawal Period (Week 16) in Patients with Hyperphagia and PWS

Treatment Group	Number of Patients	Mean Baseline Score (SD)	LS Mean Change from Baseline (SE)	LS Mean Difference* (95% CI)
Diazoxide choline	38	9.0 (6.3)	2.6 (1.1)	-5.0 (-8.1, -1.8)
Placebo	39	8.1 (5.1)	7.6 (1.1)	

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of diazoxide choline (Vykat XR) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. The member has a diagnosis of Prader-Willi syndrome (PWS) as confirmed by genetic testing showing a deletion, maternal disomy, or an imprinting defect on chromosome 15q11.2q13 – the genetic testing results must be submitted
2. The member has moderate to severe hyperphagia as determined by frequent (more than once per week) food-related aggression or manipulation and food preoccupation that interferes with normal daily activities – chart notes documenting the baseline frequency and severity of these behaviors (as assessed within the past 3 months) must be submitted
3. The member's caregiver has implemented, and will continue, strategies to establish a food-secure environment [e.g., locked food storage (refrigerator, cabinets) and garbage cans]
4. Diazoxide choline is prescribed by an endocrinologist, neurologist, or psychiatrist with experience in the management of PWS
5. The member is 4 years of age or older, **OR** the member's age is within the FDA labeling for the requested indication
6. The maintenance dosage of diazoxide choline does not exceed the following based on the member's body weight – documentation of the member's baseline body weight (measured within the past 30 days) must be submitted:
    - Less than 30 kg (66 lbs) - 100 mg once daily
    - 30 to less than 40 kg (88 lbs) - 150 mg once daily
    - 40 to less than 65 kg (143 lbs) - 225 mg once daily
    - 65 to less than 100 kg (220 lbs) - 375 mg once daily
    - 100 kg to less than 135 kg (298 lbs) - 450 mg once daily
    - 135 kg or greater - 525 mg once daily

Approval duration: 6 months

Continuation of diazoxide choline (Vykat XR) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "7"):

1. An authorization or reauthorization for diazoxide choline (Vykat XR) has been previously approved by Florida Blue in the past year for the treatment of hyperphagia due to Prader-Willi syndrome, **OR** the member meets **ALL** indication-specific criteria (with the exception of criteria #2).

2. The member has had a beneficial response to diazoxide choline as demonstrated by an improvement in hyperphagic symptoms, such as a decrease in food-related aggression or manipulation and lessened food preoccupation that interferes with normal daily activities – chart notes documenting an improvement must be submitted
3. The member's caregiver will continue strategies to establish a food-secure environment [e.g., locked food storage (refrigerator, cabinets) and garbage cans].
4. Diazoxide choline is prescribed by, or in consultation with, an endocrinologist, neurologist, or psychiatrist with experience in the management of PWS
5. For adult members (18 years of age and older) only - the prescriber has determined that the member is likely to still benefit from therapy (i.e., member has not entered the phase of symptom improvement sometimes observed in adulthood)
6. The member is 4 years of age or older, **OR** the member's age is within the FDA labeling for the requested indication
7. The maintenance dosage of diazoxide choline does not exceed the following based on the member's body weight – documentation of a recent weight (measured within the past 30 days) must be submitted:
    - Less than 30 kg (66 lbs) - 100 mg once daily
    - 30 to less than 40 kg (88 lbs) - 150 mg once daily
    - 40 to less than 65 kg (143 lbs) – 225 mg once daily
    - 65 to less than 100 kg (220 lbs) - 375 mg once daily
    - 100 kg to less than 135 kg (298 lbs) - 450 mg once daily
    - 135 kg or greater - 525 mg once daily

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Indicated for the treatment of hyperphagia in adults and pediatric patients 4 years of age and older with Prader-Willi syndrome (PWS).
- The recommended oral dosage of diazoxide choline is based on body weight. Prior to initiating treatment with diazoxide choline, test fasting plasma glucose (FPG) and HbA1c and optimize blood glucose in patients who have hyperglycemia.

Weight	Recommended Once Daily Dosage			
	Starting Dosage	Titration Dosage	Titration Dosage	Target

	Weeks 1 and 2	Weeks 3 and 4	Weeks 5 and 6	Maintenance Dose
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

- The maximum recommended dosage is 5.8 mg/kg/day or 525 mg per day. Dosages above 5.8 mg/kg/day or 525 mg per day have not been evaluated in patients with PWS. Do not substitute Vykat XR with diazoxide oral suspension because the pharmacokinetic profiles are different. Administer orally with or without food once daily. Swallow tablets whole. Do not split, crush, or chew the extended-release tablets because doing so may compromise the extended-release characteristics, efficacy, or safety.
- After initiating treatment with diazoxide choline monitor: (1) fasting glucose (FPG or fasting blood glucose) at least once every week for the first 2 weeks, then at least once every 4 weeks, and as clinically indicated, and (2) HbA1c every 3 months and as clinically indicated. Monitor fasting glucose more frequently during the first few weeks of treatment in patients with risk factors for hyperglycemia.

Dose Adjustments

- Adverse Reactions:
    - Elevations in Fasting Glucose or HbA1c: If clinically significant elevations in fasting glucose or HbA1c occur during treatment, temporarily interrupt diazoxide choline or reduce the dosage until glycemic parameters are appropriately managed. Consider initiation or adjustment of standard antidiabetic therapy(ies). Refer the FDA-approved product labeling for the recommended titration dosage after resolution of the elevated fasting glucose or HbA1c. If clinically significant glucose elevations are noted during titration, titrate over a longer duration and/or to a lower dosage
    - Fluid Overload: Monitor for signs or symptoms of edema or fluid overload. Consider dosage reduction or temporary dosage interruption in the event of clinically significant fluid overload. Refer the FDA-approved product labeling for the recommended titration dosage after resolution of fluid overload. If clinically significant fluid overload is noted during titration, titrate over a longer duration and/or to a lower dosage.
- Concomitant Use with Strong CYP1A2 Inhibitors: Dosage reduction is required. Refer the FDA-approved product labeling for the recommended dosage based on the member's body weight.
- Hepatic impairment: Diazoxide choline has not been studied in patients with renal impairment and is not recommended in patients with renal impairment.

- Renal impairment: Diazoxide choline has not been studied in patients with hepatic impairment and is not recommended in patients with hepatic impairment.

Drug Availability

- 25, 75, and 150 mg tablets packaged in 30-count bottles.
- Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15° and 30°C (59° and 86°F). Keep in tightly closed container. Protect from humidity. Do not remove desiccant.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Known hypersensitivity to diazoxide, other components of Vykat XR, or to thiazides. Erythema multiforme has been reported with diazoxide choline.

Precautions/Warnings

- **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.
- **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.

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non chemotherapeutic, NOS

ICD-10 Diagnosis Codes That Support Medical Necessity

Q87.1	Prader-Willi syndrome

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

07/01/25	New Medical Coverage Guideline.