diazoxide choline (Vykat XR™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO328

Description

Diazoxide choline (Vykat XR ™) is an adenosine triphosphate (ATP)-dependent potassium channel agonist, that increases blood glucose, due to inhibition of insulin release from the pancreas.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
diazoxide choline (Vykat XR)	Treatment of hyperphagia in patients with Prader-Willi syndrome (PWS)	25mg XR Tablets	120 tablets/30 days
		75mg XR Tablets	210 tablets/30 days
		150 mg XR Tablets	120 tablets/30 days

Initial Evaluation

I. **Diazoxide choline (Vykat XR)** may be considered medically necessary when the following criteria are met:
   A. Member is 4 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with an endocrinologist, geneticist, pediatrician, or neurologist; **AND**
   C. Member's weight is documented within the last 3 months; **AND**
   D. A diagnosis of **Prader-Willi syndrome** when the following are met:
      1. Diagnosis is confirmed by documentation of genetic analysis with identification of abnormal DNA methylation of chromosome 15q11.2-q13; **AND**
      2. Documentation the member has moderate to severe hyperphagia, defined as frequent (more than once per week) food-related aggression or manipulation and food preoccupation that interferes with normal daily activities; **AND**
      3. Documentation of caregiver having implemented and intends to continue strategies to establish a food-secure environment (e.g., locked food storage, behavior modifications, therapy, etc.)

II. Diazoxide choline (Vykat XR) is considered <u>not medically necessary</u> when criteria above are not met and/or when used for:
   A. Prader Willi Syndrome *without* hyperphagia

III. Diazoxide choline (Vykat XR) is considered investigational when used for all other conditions, including but not limited to:
   A. Hyperinsulinemic hypoglycemia

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member's weight has been documented in the last 3 months; **AND**
IV. Chart note documentation member has exhibited an improvement or decrease in hyperphagic and food-related behaviors [e.g., food related preoccupations, food-seeking behaviors]

Supporting Evidence

I. Diazoxide choline (Vykat XR) is a long-acting salt formulation of diazoxide (also known as DCCR), for the treatment of hyperphagia in adults and children four years of age and older with Prader-Willi syndrome (PWS). The proposed mechanism of action (MOA) for diazoxide is as a potassium channel opener; however, the exact MOA is unknown. Diazoxide suspension (brand name Proglycem) has been available for the treatment of hyperinsulinemic hypoglycemia in pediatric and adult patients when other specific medical therapy or surgical management for hypoglycemia is unsuccessful or is not feasible.
II. Prader-Willi syndrome (PWS) is characterized by early failure to thrive, hypotonia in infants (i.e. low muscle tone/floppy infant syndrome), followed by the onset of hyperphagia sometime in early childhood, leading to obesity. Hyperphagia, a persistent sensation of hunger, is a key manifestation of PWS. Some patients may experience periods without hyperphagia, and the severity of symptoms varies. Individuals with PWS have shown high rates of choking, accidents, and gastrointestinal perforation that is presumably related to uncontrolled hyperphagia, and a study found that food-seeking behavior contributed to about one-third of all reported deaths among patients with PWS and about one-half of deaths among patients with PWS under 18 years of age. European guidelines on Prader-Willi syndrome (2024) state that hyperphagia and food-seeking behaviors begin in early childhood and persist throughout the patient's life. Food security practices can include physical interventions, such as locks on refrigerators or cupboards.
III. Hyperphagia is managed by supervising meal preparation and food intake, implementing food security measures (e.g., locks on cabinets and refrigerators), and supervision of the person with PWS. These interventions may impact activities of daily living, and may prevent

full participation in school, employment, social life, and independent living, all of which are burdensome and impact quality of life for patients, families, and caregivers.

IV. A diagnosis of PWS is completed through the presence of characteristic clinical features and confirmed by genetic testing. Prader-Willi syndrome arises due to absent paternal expression on chromosome 15q11.2-q13, which is verified via genetic testing. Due to the specialized skills required for evaluation and diagnosis of this condition as well as the monitoring required in conjunction with diazoxide choline (Vykat XR) treatment coverage requires treatment to be prescribed by or in consultation with a physician who specializes in PWS, such as an endocrinologist, geneticist, pediatrician, or neurologist.

V. Treatment of PWS consists of management of an individual patient's symptoms. In 2000, the FDA approved the use of human growth hormone (hGH) therapy to normalize growth and improve body composition in patients with PWS. Prior to the approval of diazoxide choline (Vykat XR), there were no treatment options for PWS that addressed hyperphagia. The current standard of care for the management of hyperphagia in PWS includes food restriction methods and behavioral interventions. Guidelines additionally mention dietary strategies and exercise programs to prevent weight gain. Diazoxide choline (Vykat XR) is the first treatment indicated for hyperphagia in adults and children four years of age and older with PWS. Guidelines have not been updated since the approval of diazoxide choline (Vykat XR). Additionally, there are no consensus guidelines on the use of anti-obesity medications (e.g., topiramate, metformin, liraglutide, semaglutide, tirzepatide, etc.) in PWS.

VI. The safety and efficacy of diazoxide choline (Vykat XR) were evaluated in two trials. The DESTINY-PWS (C601) trial was a 13-week, randomized double-blind, placebo-controlled study in 126 patients. The primary endpoint was the change in hyperphagia from baseline through week 13 measured using the Hyperphagia Questionnaire for Clinical Trials (HQ-CT), a 9-item, validated questionnaire that assessed food-related behaviors associated with hyperphagia. The HQ-CT total score ranges from 0 to 36 (higher scores indicate greater severity of hyperphagia and food-related behaviors). Treatment with diazoxide choline did not demonstrate a statistically significant reduction from baseline HQ-CT compared to placebo. Although diazoxide choline did not significantly improve the primary endpoint of hyperphagia overall, it did improve this endpoint in participants with severe hyperphagia.

VII. Upon completion of DESTINY-PWS, patients (N=115) entered Study C602-OLE, which was a long-term, open-label, maintenance trial. Patients who successfully completed this phase entered a 16-week double-blind placebo-controlled randomized withdrawal treatment phase (N=77). Patients that continued diazoxide choline treatment saw a 2.6-point increase in HQ-CT scores, while those on placebo saw a 7.6-point increase — a 5-point difference that was statistically significant. The manufacturer notes that at least 31% of patients (N=38) who had at least 1 post-baseline assessment of HQ-CT (N=124) experienced interrupted visits, possibly due to COVID-19 as a contributing factor to missing data in C601.

VIII. Although patients who switched from diazoxide choline to placebo demonstrated a statistically significant worsening in hyperphagia compared to those who remained on treatment, a significant clinical benefit (e.g., a reduction in food-seeking behaviors) of diazoxide choline (Vykat XR) has not been established. While the HQ-CT has been developed and validated for use in the assessment of hyperphagia related behaviors in clinical studies in PWS, the quality of the evidence is poor given one RCT trial (DESTINY-PWS) with higher degree of design/execution, but did not show statistically significant results and the OLE trial with lower (acceptable) degree of design/execution, but did result in statistically significant change in HQ-CT. Although this change was considered statistically significant, it did not meet the clinical significance of a 7-point change. There is a general positive trend seen when diazoxide is used long term for potentially addressing behavioral problems in PWS based on two RCTs. Additional applicability concerns include, the HC-QT questionnaire being subject to caregiver bias, potential Attrition Bias (more discontinuations in treatment arm compared with placebo arm, due to adverse events).

IX. The primary clinical outcome assessment for hyperphagia-associated behaviors in PWS is the HQ-CT, a caregiver-reported assessment of hyperphagic behaviors during the past 2 weeks including food seeking behaviors, tendency toward being upset or distressed when denied food or asked to stop talking about food and the extent to which these behaviors interfere with daily life, which has been shown to be sensitive to change in the setting of clinical trials for drugs targeting hyperphagia in the PWS population. However, this questionnaire has not been fully characterized in real-word setting in a large PWS population, nor in typically developing individuals. The HQ-CT consists of nine items with responses ranging from 0-4 (best to worst). Scores from 9 items are summed for a possible total score range of 0-36, where higher scores indicate more severe hyperphagia symptoms. A reduction in score from baseline indicates improvement in symptoms.

X. The most common adverse reactions reported in clinical trials (incidence ≥10% and at least 2% greater than placebo) were hypertrichosis, edema, hyperglycemia, and trash. Diazoxide choline (Vykat XR) has warnings for hyperglycemia and risk of fluid overload. Per the diazoxide choline (Vykat XR) prescribing information, it is recommended prior to initiating treatment to test fasting plasma glucose (FPG) and HbA1c and optimize blood glucose in patients who have hyperglycemia. Fasting glucose and HbA1c monitoring is also recommended during treatment and for dosage modifications based on results, as it is recommended to interrupt treatment or reduce dosage for clinically significant elevations in fasting glucose or HbA1c, as well as considerations for dosage reduction or interruption for clinically significant fluid overload.

XI. Requirements for coverage include ensuring the member has the ability to swallow, as the diazoxide choline (Vykat XR) tablets must be taken whole, and not split, crushed, or chewed, due to compromising the extended-release characteristics of treatment. Swallowing and behavioral concerns are common in the PWS population and confirming that the member

can swallow tablets prior to approval is medically necessary to ensure the integrity of treatment and reduce drug waste.

Investigational or Not Medically Necessary Uses

I. Diazoxide choline (Vykat XR) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Prader Willi Syndrome without hyperphagia
      i. Diazoxide choline (Vykat XR) is only indicated for the treatment of hyperphagia in patients with Prader-Willi syndrome. No data is available on the treatment of hyperphagia in patients without documented Prader-Willi syndrome, and is therefore considered not medically necessary.
   B. Hyperinsulinemic hypoglycemia
      i. Diazoxide choline (Vykat XR) tablets are not FDA-approved for use in hyperinsulinemic hypoglycemia. Diazoxide suspension (generic and brand Proglycem) is FDA-approved for hyperinsulinemic hypoglycemia and available for use when other specific medical therapy or surgical management for hypoglycemia is unsuccessful or is not feasible. Per diazoxide choline (Vykat XR) prescribing information, these agents should not be substituted based on differences in their pharmacokinetic profiles.

Appendix

I. Diazoxide choline (Vykat XR) is administered orally once daily with the starting dosage and titration schedule based on body weight. The maximum recommended dosage is 5.8 mg/kg/day or 525 mg per day.

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

References

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3. Shaikh MG, Barrett TB, Bridges N, et al. Prader-Willi syndrome: guidance for children and transition into adulthood. Endocr Connect. 2024; 13(8):e240091
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8. Matesevac L, et al. Analysis of Hyperphagia Questionnaire for Clinical Trials (HQ-CT) scores in typically developing individuals and those with Prader-Willi syndrome. *Sci Rep*. 2023;13(1):20573. doi:10.1038/s41598-023-48024-5
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Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
Human Growth Hormone Policy	Short stature associated with Prader-Willi Syndrome
EOCCO: setmelanotide (Imcivree®) Policy	Chronic weight management in monogenic or syndromic obesity due to POMC, PCSK1, or LEPR deficiency, variants interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS)
	Chronic weight management in monogenic or syndromic obesity due to Bardet-Biedl syndrome (BBS)*

Policy Implementation/Update

Action and Summary of Changes	Date
Policy created	10/2025