COBENFY™ – OR Medicaid Written Testimony

Summary

Thank you for your unsolicited request regarding written testimony for COBENFY™ (xanomeline and trospium chloride) to review at the upcoming Oregon Medicaid P&T Committee meeting.

As requested, please find the following attached:

- **Oregon Medicaid Written Testimony**
- **Conflict of Interest Form**

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

COBENFY is contraindicated in patients with:

- urinary retention
- moderate (Child-Pugh Class B) or severe (Child-Pugh Class C) hepatic impairment
- gastric retention
- history of hypersensitivity to COBENFY or trospium chloride. Angioedema has been reported with COBENFY and trospium chloride.
- untreated narrow-angle glaucoma

WARNINGS AND PRECAUTIONS

Risk of Urinary Retention: COBENFY can cause urinary retention. Geriatric patients and patients with clinically significant bladder outlet obstruction and incomplete bladder emptying (e.g., patients with benign prostatic hyperplasia (BPH), diabetic cystopathy) may be at increased risk of urinary retention.

COBENFY is contraindicated in patients with pre-existing urinary retention and is not recommended in patients with moderate or severe renal impairment.

In patients taking COBENFY, monitor for symptoms of urinary retention, including urinary hesitancy, weak stream, incomplete bladder emptying, and dysuria. Instruct patients to be aware of the risk and promptly report symptoms of urinary retention to their healthcare provider. Urinary retention is a known risk factor for urinary tract infections. In patients with symptoms of urinary retention, consider reducing the dose of

COBENFY, discontinuing COBENFY, or referring patients for urologic evaluation as clinically indicated.

Risk of Use in Patients with Hepatic Impairment: Patients with hepatic impairment have higher systemic exposures of xanomeline, a component of COBENFY, compared to patients with normal hepatic function, which may result in increased incidence of COBENFY-related adverse reactions.

COBENFY is contraindicated in patients with moderate or severe hepatic impairment. COBENFY is not recommended in patients with mild hepatic impairment.

Assess liver enzymes prior to initiating COBENFY and as clinically indicated during treatment.

Risk of Use in Patients with Biliary Disease: In clinical studies with COBENFY, transient increases in liver enzymes with rapid decline occurred, consistent with transient biliary obstruction due to biliary contraction and possible gallstone passage.

COBENFY is not recommended for patients with active biliary disease such as symptomatic gallstones. Assess liver enzymes and bilirubin prior to initiating COBENFY and as clinically indicated during treatment. The occurrence of symptoms such as dyspepsia, nausea, vomiting, or upper abdominal pain should prompt assessment for gallbladder disorders, biliary disorders, and pancreatitis, as clinically indicated.

Discontinue COBENFY in the presence of signs or symptoms of substantial liver injury such as jaundice, pruritus, or alanine aminotransferase levels more than five times the upper limit of normal or five times baseline values.

Decreased Gastrointestinal Motility: COBENFY contains trospium chloride. Trospium chloride, like other antimuscarinic agents, may decrease gastrointestinal motility. Administer COBENFY with caution in patients with gastrointestinal obstructive disorders because of the risk of gastric retention. Use COBENFY with caution in patients with conditions such as ulcerative colitis, intestinal atony, and myasthenia gravis.

Risk of Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with COBENFY and trospium chloride, a component of COBENFY. In one case, angioedema occurred after the first dose of trospium chloride. Angioedema associated with upper airway swelling may be life-threatening. If involvement of the tongue, hypopharynx, or larynx occurs, discontinue COBENFY and initiate appropriate therapy and/or measures necessary to ensure a patent airway. COBENFY is contraindicated in patients with a history of hypersensitivity to trospium chloride.

Risk of Use in Patients with Narrow-angle Glaucoma: Pupillary dilation may occur due to the

anticholinergic effects of COBENFY. This may trigger an acute angle closure attack in patients with anatomically narrow angles. In patients known to have anatomically narrow angles, COBENFY should only be used if the potential benefits outweigh the risks and with careful monitoring.

Increases in Heart Rate: COBENFY can increase heart rate. Assess heart rate at baseline and as clinically indicated during treatment with COBENFY.

Anticholinergic Adverse Reactions in Patients with Renal Impairment: Trospium chloride, a component of COBENFY, is substantially excreted by the kidney. COBENFY is not recommended in patients with moderate or severe renal impairment (estimated glomerular filtration rate (eGFR) <60 mL/min). Systemic exposure of trospium chloride is higher in patients with moderate and severe renal impairment. Therefore, anticholinergic adverse reactions (including dry mouth, constipation, dyspepsia, urinary tract infection, and urinary retention) are expected to be greater in patients with moderate and severe renal impairment.

Central Nervous System Effects: Trospium chloride, a component of COBENFY, is associated with anticholinergic central nervous system (CNS) effects. A variety of CNS anticholinergic effects have been reported with trospium chloride, including dizziness, confusion, hallucinations, and somnolence. Monitor patients for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing the dose. Advise patients not to drive or operate heavy machinery until they know how COBENFY affects them. If a patient experiences anticholinergic CNS effects, consider dose reduction or drug discontinuation.

Most Common Adverse Reactions (≥5% and at least twice placebo): nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness, and gastroesophageal reflux disease.

Use in Specific Populations:

- Moderate or Severe Renal Impairment: Not recommended
- Mild Hepatic Impairment: Not recommended

COBENFY (xanomeline and trospium chloride) is available in 50mg/20mg, 100mg/20mg, and 125mg/30mg capsules.

Please see U.S. Full Prescribing Information, including Patient Information.

Greetings DMAP Team,

Please find the information below in response to public comments regarding your August new drug review of VYKAT™ XR (diazoxide choline) extended release tablets.

Measurement of Hyperphagia in Prader-Willi Syndrome:

What is Hyperphagia in Prader-Willi Syndrome (PWS):

PWS is a genomic imprinting disorder caused by the deletion or lack of expression of one or more paternally inherited genes in the chromosome 15q11.2-q13 region resulting in a heterogeneous, multi-systemic, progressive neurobehavioral-metabolic disorder[1]. Hyperphagia in PWS is a chronic, often life-threatening condition characterized by feelings of intense, persistent hunger, food pre-occupation, and an extreme drive to seek and consume food and non-food items, all of which can gravely impact individuals with PWS and their families[2]. Complications stemming from uncontrolled hyperphagia in this complex genetic and neurocognitive impairing condition account for approximately 1/2 of deaths in childhood and 1/3 adult deaths in PWS[3]. Addressing hyperphagia was ranked as the highest priority unmet medical need in PWS to be addressed in the development of new therapeutics according to a recent survey of 457 caregivers[4].

What is HQ-CT and How is it Used to Measure Hyperphagia in Clinical Trials:

Given the challenges of self-reporting in the PWS population, caregivers and healthcare providers are often used as surrogates in reporting treatment impacts since they are typically involved in the decision-process and treatment approaches for their patients. The FDA acknowledges the role of patient partners, i.e., caregivers, in reporting on patient experiences[5].

The Hyperphagia Questionnaire for Clinical Trials (HQ-CT) is a 9-item, caregiver-completed questionnaire intended to assess a range of hyperphagia-related behaviors in PWS. The HQ-CT was designed, developed, and validated for use in the highly structured clinical trial environment in patients with PWS, and can be licensed from the Foundation for Prader-Willi Research for such use[5]. To ensure that consistent and reliable data is obtained from the HQ-CT, clinical trial investigators, study personnel and caregivers need extensive training in its proper use and administration, and stringent procedures need to be employed to minimize the potential for bias in the assessment.

As of March 2025, more than a dozen studies have relied upon the HQ-CT as a validated tool for assessing hyperphagia in clinical trial subjects[6]. The HQ-CT is considered standard protocol for measuring hyperphagia by PWS-specialized clinicians in clinical trials[7] and is recognized by regulatory experts as the appropriate tool to measure hyperphagia, the endpoint for which substantial evidence of effectiveness needs to be demonstrated for FDA approval.

Why HQ-CT is Not Used in Clinical/Community Practice:

The HQ-CT is not used in or validated for use in routine clinical practice and was developed specifically for caregiver input. Additionally, its use in daily clinical practice is not advocated by the expert community. Most physicians treating patients with PWS have not been exposed to HQ-CT because it is only used in the clinical trial setting. Neither the physician, nor their staff would have administered or have been trained in administering this instrument—and it is not structured or calibrated for use outside of clinical trials. Further, the duration of recall (2 weeks) required for HQ-CT in clinical trials is not aligned with clinical practice where the patient may be seen only every 3 or 6 months. This likely means that critical aspects of hyperphagia measurement may be excluded from the assessment. Finally, this instrument should not be used without permission and licensing from the Foundation for Prader-Willi Research (FPWR).

Current Practice and Recommendations on Measuring Hyperphagia in PWS:

A standard questionnaire for assessing and quantifying the impacts of hyperphagia in the real-world setting (outside of clinical trials) has not been established, and physicians vary in which techniques they use clinically for evaluating the many serious behavioral impacts of this disorder on the patient and his/her caregivers. It is not uncommon for a rare disease with a small population to have no

standard for reporting clinical improvement or worsening beyond HCP attestation, which can effectively encapsulate and summarize both patient and caregiver testimony[5].

Following confirmation of PWS by a genetic technique such as identification of abnormal DNA methylation of chromosome 15, clinical diagnosis and documented symptoms of hyperphagia, treatment initiation and symptom improvement should be assessed by or in consultation with an endocrinologist or other providers who are experienced in the condition being treated. These health care providers are best equipped to document symptoms and determine response to treatment.

Letter of Information: Measurement of Hyperphagia and HQ-CT (**H**yperphagia **Q**uestionnaire – for **C**linical **T**rials)
Additional information is available by contacting Soleno Therapeutics Medical Information at 1-650-213-8444 or emailing MedInfo@Soleno.life.

REFERENCES:

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Michelle Bice
Director, National Accounts
Soleno Therapeutics, Inc. | 100 Marine Parkway, Suite 400 | Redwood City, CA 94065

From: Emily Wilson
Sent: Tuesday, July 15, 2025
To: Pharmacy Drug Information
Subject: Vykat XR Coverage for PWS

Our daughter, 33 years, continues to struggle daily with food intake and the interference of life due to the 24 hour food demand her body tells her she needs.

This medication could change the course for Emily. Access to this medication may allow Emily to spend time pursuing life goals that do not include food intake, the pursuit of food, stealing food and asking for food. Emily would enjoy life with more normalcy and this would include a job.

Please continue to obtain Medicare/Medicaid coverage for this all important drug that could help so many.

Sincerely,
Emily Wilson

Hello members of the Pharmacy and Therapeutics Committee,

My name is Brandon Lawrence, and along with my wife Melissa Lawrence, our daughter Kelsey and son Kyle, we would like to submit written testimony regarding VYKAT XR. We live in Tigard. Our 2.5 year old daughter, Kelsey, lives with Prader-Willi Syndrome (PWS) and receives Medicaid in the state of Oregon. First, we would like to thank the committee for everything you do. This is hugely impactful work, and we are grateful for the time and effort you put into this.

When we were given Kelsey's diagnosis in the NICU, our life changed. We learned that our daughter would face many challenges such as low muscle tone, excessive daytime sleepiness, developmental delays, and behavioral challenges. We would do everything we could to help her overcome these challenges and live life to her fullest potential. But there was one item in the long list of symptoms that kept up us at night – hyperphagia. Hyperphagia is an insatiable hunger which leads to obesity, obsessive behaviors like skin picking, outbursts, and other severe behavioral issues.

Even though Kelsey doesn't have hyperphagia yet, we live in constant fear of its onset and do everything we can to delay it. We follow a strict diet, constantly monitor the food she has access to, and how much she's allowed to eat. Food is EVERYWHERE and we are on high alert at story time, the playground, and at playdates. Access to food even played a role in our recent selection of preschools. As a toddler, it's fairly simple to keep her safe, but what happens when she gets older and goes to school, or is invited to a birthday party or a sleepover, or wants to get her driver's license? How do we keep her safe outside of our home and allow her independence? We have friends with older children living with PWS who need to lock their fridges/pantries and decline social engagements (like parties or picnics), because it's too difficult to stop their children from food seeking and eating anything and everything they can get their hands on. This is why we were overjoyed at the recent FDA approval of VYKAT XR.

VYKAT XR is the first FDA approved treatment for hyperphagia. Knowing that there is a treatment for hyperphagia gives us so much hope for the future. If this drug is covered by Medicaid, we have confidence that out daughter will not suffer the extreme effects of hyperphagia. Instead, she can be mainstreamed in public school, attend college, get a job, and live independently. It would change her life to have access to VYKAT XR, and we encourage the Committee to consider this. Thank you again for the vital work you do, and please let us know if you have any questions.

Sincerely,
Brandon, Melissa, Kelsey, and Kyle Lawrence

My name is Tracy Chin. I live in Portland, OR. My child living with Prader-willi syndrome is 3.5 years old and receives secondary Medicaid in the state of Oregon. Thank you to the members of the committee for all the work you do and continue to do for Oregonians. It is very much appreciated.

PWS is a very medically and behaviorally complex disease. My husband and I are registered nurses and had never heard of it when my daughter was in the hospital and we got the diagnosis. Because of its complexity, it has required numerous medical appts and therapies for our daughter each week. It has required her to get a growth hormone injection every night. It has required us to change the way we socialize with others given the fixation on food that starts at an early age. It has required her to get surgery for a feeding tube when she was 5 months old, which she thankfully no longer needs. It has required us to pay out of pocket for therapies that are not covered by insurance. It has taken a toll on our mental and physical health as her parents and caregivers.

In terms of unmet needs of PWS, there are too many to name. The most important one is that there is currently no cure. And until Vykat XR, there was no effective treatment for hyperphagia–the classic symptom of PWS that results in insatiable hunger. Our daughter isn't able to participate in social gatherings the way other neurotypical kids do because of her fixation on food. We are nervous about sending her to kindergarten when the time comes given the lack of funding in our public school system. We fear she will not have the necessary support she requires for her hyperphagia, speech, and mobility difficulties.

She currently does not meet the criteria to start Vykat XR right now given her age and mild hyperhphagia; however we are so unbelievably thankful that there is a drug that exists now to treat hyperphagia. That symptom dictates how our children live their lives, as food is everywhere. Experiencing hyperphagia is akin to having an addiction. It also puts them at risk for obesity and other life-threatening conditions.That's why Vykat XR is literally life changing and will give our daughter and others like her a better quality of life.

My hope for the approval of drugs to treat hyperphagia in PWS is that Vykat XR is just the beginning. I hope more research and drug trials are conducted so our daughter and the rest of the PWS community can lead a more "normal" life. I'm proud to live in a state that is leading the way for the rest of our country. I hope others will follow suit and Vykat XR can be more accessible and available to everyone who needs it.

To whom it may concern:

Almost 19 years ago I had my first and only child, Sequoia. When she was born the doctors knew right away something was wrong, or what like to say, “not typical”. She had extremely low muscle tone which affected her ability to eat and cry. Sequoia was urgently transported to a children’s hospital where she spent 16 days until she had a feeding tube surgically placed so I could take her home. At that time no one knew why she was failing to survive. I wanted answers but was just so grateful she survived and was home with me starting our new life together.

After 3 months of blood tests, MRIs, and cat scans she was finally diagnosed with Prader Willi Syndrome (PWS). The geneticist gave me a biology lesson about chromosomes and listed all the challenges my new favorite person could have. The most relevant characteristic he explained was regarding the insatiable hunger, which could cause her to be obese and have very challenging behaviors. I thought to myself, how could he possibly know and limit my daughter’s future, she was just a baby! He said this to prepare me, but all I could focus on was my perfect baby. Turns out 19 years later, he nailed it - That 15th chromosome would have been a good one for Sequoia to have.

People have asked me her entire life, “Isn’t there a cure, medication or surgery to fix her?” The answer has always been no. I explain there are medications and treatments to lessen some of the characteristics such as physical and occupational therapy, CPAP machines, growth hormone injections, surgery for scoliosis, and medications for diabetes, mental health diagnosis, and other medical disadvantages. There has never been any medication to make her less hungry, UNTIL NOW. (hooray!)

I want to explain the level of hunger Sequoia experiences. Often people joke thinking it’s funny (it’s not) they must have this syndrome. When I hear this, I want to ask them if they can stop eating. I want to ask if they would eat someone else’s old food out of trash cans? I want to ask them if seeing food, they cannot eat can trigger them into fight or flight mode? This is the case for Sequoia. The near sight of food in her learning environment at school was proven to be the reason she did not receive a free and appropriate education. This led to a huge legal battle against her school district regarding the impact food has on her ability to learn. It cost the school district $600,000 in legal fees. You can look up her journey at *teamsequoia.org*.

You can see a video where she advocates about her hunger and the news clips surrounding the legal case.

Her hunger and obsession with food has caused countless pseudo seizures with ambulance rides to the hospital. She has been admitted into two mental health hospitals and has been in the ER for suicidal ideation five times. All these scenarios were connected to food exposures and hunger as the cause. Imagine living in a world that celebrates what can genetically kill you or make you want to kill yourself?

Sequoia knows she is different. She has cried and begged me saying, "Mommy, can you please take the Prader Willi out of me? I don't want to be hungry like this. I just want to play and not worry about food." Since I could not take PWS away I did the next best thing. I secured her placement at a school that specializes in Prader Willi Syndrome. They have created an environment with controlled access to food, no food rewards, portion regulations, and what is known in our community as *Total Food Security*. People with PWS want this level of structure and security because it makes them feel safe.

If I could have one wish for my child… It would be that she could live a life without feeling constant insatiable hunger. It is truly a miracle there is now a medication that could reduce her hunger and reduce her anxiety. With access to this medication the quality and longevity of her life could completely change, opening so many possibilities for her. Could she live independently? Could she attend social gatherings where there is food? Could she live as the rest of us do? Sequoia's anxiety caused by hunger is the most deliberating characteristic of her disability. I ask and beg for Oregon to secure the coverage of Vykat XR for Sequoia and all others with Prader Willi Syndrome. This is life changing for the individuals who suffer from hunger AND their loved ones.

Thank you for your time to read and consideration of this medication. If you have any questions or would like more information, please feel free to contact me. I am open to any discussion to support Vykat XR approval through Medicare, Medicaid, and private insurance.
Sincerely,

Kelly Gutierrez

Clinical Summary:

Secuado (asenapine) Transdermal system 3.8 mg/24 hours, 5.7 mg/24 hours, 7.6 mg/24 hours

Background

- Schizophrenia is a severe, chronic psychiatric disorder that affects more than 21 million people worldwide. It has been estimated that 1.5% to 3.0% of total U.S. national healthcare expenditures are directed towards this patient population.
- Schizophrenia has a profound impact on affected individuals, their families, and society. Patients experience multiple limitations to independent living, healthy social relationships, and successful employment, and most require caregiver support.
- Many patients with schizophrenia also suffer from other comorbid psychiatric conditions, such as major depression, drug and alcohol abuse or dependency, and anxiety disorder.
- Adult patients with schizophrenia also have a dramatically increased risk of premature mortality, commonly caused by cardiovascular disease, cancer, and accidents.
- Patients with schizophrenia are also at an increased risk of suicide.
- Adherence to antipsychotic medication use is consistently low in patients with schizophrenia.
- Pivotal drivers of patient non-adherence are the side effects and clinical limitations of existing drugs.
- Based on the limitations of existing treatments, and the high cost burden of schizophrenia, a recent critical appraisal concluded that different modes of antipsychotic medication administration are needed.
- The development of a transdermal antipsychotic option helps to address the need for different modes of administration and offers schizophrenia patients a route of administration that may contribute to improved adherence.

Secuado Safety and Efficacy

- Secuado® (asenapine) transdermal (patch) system (HP-3070) is a U.S. Food and Drug Administration (FDA)-approved atypical antipsychotic that differs from the originally approved formulation of asenapine (sublingual [SL] asenapine; Saphris®) in dosage form and approved indications. Secuado is indicated for the treatment of adults with schizophrenia.
- Available Secuado dosage strengths are: 3.8 mg/24 hours (9.0 mg asenapine Maleate per patch), 5.7 mg/24 hours (13.5 mg asenapine Maleate per patch) and 7.6 mg/24 hours (18.0 mg asenapiine Maleate per patch).
- The primary evidence supporting the efficacy of Secuado for the treatment of adults with schizophrenia was obtained from three Phase 1 trials and one Phase 3 clinical trial
- Patients treated with Secuado 9.0 mg or 18.0 mg transdermal patches for 6 weeks demonstrated significant improvements in the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression – Severity (CGI-S) scale compared to patients treated with placebo.
- With repeat application of the Secuado patch containing 4.5, 9.0, 13.5, and 18.0 mg asenapine maleate in patients with schizophrenia, plasma concentrations of asenapine reached steady-state in 48 to 72 hours, with minimal peak-trough concentration fluctuations.
- In the Phase 3 clinical trial, Secuado was well-tolerated; adverse events were generally mild to moderate in severity.
- The most common adverse reactions were extrapyramidal disorder, application site reaction, and weight gain.
- Observed skin irritations such as erythema, pruritus, papules, discomfort, pain edema or irritation were reported. Discontinuations due to application site reactions were infrequent (≤0.5% per treatment group).
- The comparative effectiveness of Secuado relative to other antipsychotic drugs has not been studied.

Conclusion

- Secuado (asenapine) transdermal patch is a new SGA approved by the U.S. FDA for the treatment of adult patients with schizophrenia. Secuado has a demonstrated safety, efficacy, and tolerability profile that is supported by evidence from Phase 1 and Phase 3 clinical trials, and it is the first antipsychotic therapy available as an alternative formulation in the U.S.
- Medication non-adherence poses an undue societal and economic burden for this patient population.
- Secuado represents a treatment option to address an unmet need for a more reliable mode of antipsychotic medication administration.
- Secuado transdermal asenapine provides a valuable addition to currently available atypical antipsychotic treatment options, and exhibits the potential to improve clinical, economic, and societal outcomes.

Written Public Comments on Final NDE of diazoxide choline extended-release (DCCR), oral tablets

July 17, 2025

Pharmacy & Therapeutics Committee
Oregon State University, Drug Use Research & Management
500 Summer Street NE, E3
Salem, Oregon 97301-1079

Dear Pharmacy & Therapeutics Committee:

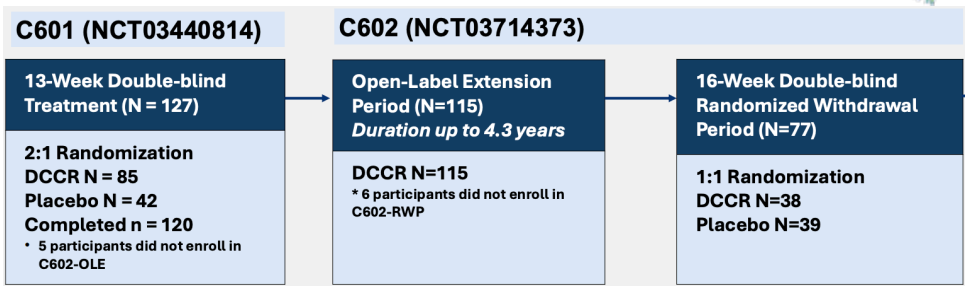
Thank you for opening to additional written public comments on the Final New Drug Evaluation (NDE) of VYKAT™ XR (diazoxide choline) extended-release tablets. Based on our review of the Final NDE, we offer the following comments and recommended changes for your consideration:

- VYKAT™ XR (**diazoxide choline** extended-release) is commonly referred to as "**DCCR**" in primary and secondary scientific literature for brevity.
    - **VYKAT XR Prescribing Information** (Section 2.1) states: "Do not substitute VYKAT XR with diazoxide oral suspension because the pharmacokinetic profiles are different."[1]
    - "diazoxide" is an inaccurate abbreviation for diazoxide choline extended-release tablets
    - In the Final NDE the term "diazoxide" is inaccurately used to abbreviate "diazoxide choline extended release" in 70+ instances. **Please update to "diazoxide choline", "DCCR", or "VYKAT XR"**
    - Additionally, PROGLYCEM (diazoxide) does not have an FDA-approved indication in PWS, or hyperphagia in PWS.[2] The inclusion of PROGLYCEM information is not pertinent to the VYKAT XR NDE, nor to hyperphagia in PWS. Please delete this paragraph OR include bullet 1 from the FDA USPI above.

- Coverage Criteria
    - **Please remove: "Documentation of baseline HQ-CT score"** – See Public Comment in Final NDE.
        - HQ-CT is not validated for use in community practice settings; it is inaccessible outside of clinical trial settings as it requires licensure from the Foundation for Prader-Willi Research (FPWR).
        - **Physician attestation of a diagnosis of Hyperphagia is a crucial moment in PWS treatment.**

- Study C602-RWP was the primary efficacy study. Please update the statement from the conclusion of Study C602-RWP from the Final NDE: "*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"* as it is inaccurate and not applicable to the RWP study design.
    - The study design/statistical analysis plans were different for C601/DESTINY PWS versus the C602-RWP study design/statistical analysis plan and drawing the conclusion that is currently drafted is not applicable to the study results for C602-RWP.
        - To present the conclusion accurately, **please delete "Although" and "it did not meet the clinical significance of a 7-point change identified in the DESTINY PWS RCT"**
    - After Study C601 (DESTINY-PWS[3]; NCT03440814), eligible patients transitioned to open-label extension (Study C602-OLE; NCT03714373)). During C602-OLE, LS mean HQ-CT reductions of [SE] of -8.8 [0.72] at 26 weeks and -9.9 [0.77] at 52-weeks (prior to C602-RWP randomization) were observed.[4] A maintenance of these improvements up to 156 weeks were observed for patients on diazoxide choline extended-release (DCCR).[5] Next, these treatment-experienced patients from C602-OLE were randomized into the primary efficacy trial Study C602-RWP (NCT03714373) to receive placebo (withdrawn from DCCR treatment), or to continue to receive DCCR. The patients who were randomized to placebo (withdrawn from DCCR treatment) experienced statistically significant worsening of their hyperphagia. **Additionally, the patients on placebo worsened to the point that they would meet the inclusion criteria to enter into the DCCR Phase 3 clinical program for hyperphagia in PWS.** Whereas, the patients who were randomized to continue on DCCR would no longer be eligible to enter the Phase 3 clinical program for hyperphagia as the treatment continued to provide efficacy, even after a median of 3-years of continued exposure to DCCR treatment prior to randomization into the RWP study.

DCCR Phase 3 Clinical Trials[6]



- Sections “Comparative Endpoints” and “Clinically Meaningful Endpoints”
    - None of the phase 3 trials mentioned in the USPI had study designs to evaluate "Weight Loss" or "Weight Reduction". The VYKAT XR USPI has no mentions of weight loss/gain, change in BMI, nor maintenance of long-term weight reduction.[1] Furthermore, a patient’s weight was not a prespecified endpoint in the phase 3 clinical program. The primary endpoints of the placebo-controlled phase 3 clinical trials evaluated change in hyperphagia (independent of weight) from baseline versus end of study.
    - There are no mentions of “Improvements in provider assessments” in the VYKAT XR USPI.[1]
        - Note that HQ-CT is a *caregiver*-reported assessment
    - Please note that the “Primary Study Endpoint” is currently incomplete and potentially misrepresented:
        - Please update to: Change in HQ-CT total score from baseline to week 16.

- For the **plain language summary of hyperphagia in PWS**, please consider the medication guide in the USPI.
    - “VYKAT XR is a prescription medicine used to treat extreme hunger, constant thoughts about food, and constant urge to eat that cannot be satisfied with food (hyperphagia)”[1]

Diazoxide choline (VYKAT™ XR) extended-release tablets is indicated for the treatment of hyperphagia in adults and pediatric patients 4 years of age and older with Prader-Willi syndrome (PWS).[1] Please refer to the enclosed package insert (link here) for Full Prescribing Information with Medication Guide for approved indication, dosing, efficacy, and safety information regarding VYKAT XR.

Please note that the enclosed materials may contain references to, or information regarding uses of VYKAT XR (diazoxide choline) extended-release tablets that have not been approved by the U.S. Food and Drug Administration (FDA). Furthermore, this information should not be construed as recommendation for use of, or intent to promote VYKAT XR for unapproved uses. *Soleno Therapeutics recommends that VYKAT XR be used consistent with the approved product labeling.*

Soleno Therapeutics monitors the safety of its products. To report SUSPECTED ADVERSE REACTIONS, contact Soleno Safety at 1-833-765-3661 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

If you have any further questions, please contact me directly.

Sincerely,
Mae Kwong, PharmD, Medical Managed Markets, Soleno Therapeutics, Inc.
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REFERENCES

1) VYKAT™ XR (diazoxide choline) extended-release tablets. Package insert. Soleno Therapeutics; 2025 [Link]
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6) Obrynba K, Yanovski J, Felner E, et al. Resuming Diazoxide Choline Extended-Release (DCCR) after 16-week Randomized Withdrawal is Associated with Significant Improvements in Hyperphagia and Behavioral Symptoms in PWS (Study C614). *Pediatric Endocrine Society (PES).* May 2025.