CLINICIAN STATEMENT

VYKAT XR™ (diazoxide choline): Safety Considerations for People with Prader-Willi Syndrome

Important information for healthcare professionals prescribing or considering VYKAT XR for patients with PWS

The intent of this statement is to increase awareness of:

- **Reports of serious adverse events** associated with diazoxide choline/VYKAT XR™ use in patients with Prader-Willi syndrome (PWS)
- **Conditions that may put patients with PWS at high risk** of serious adverse events, especially those related to fluid overload, when starting diazoxide choline/VYKAT XR
- **The availability of a recent publication** (PMICD: PMC13148164) authored by physicians with expertise in treating patients with PWS. This publication provides practical guidance for the use of diazoxide choline/VYKAT XR in PWS, including patient selection, risk factor optimization and monitoring of high-risk patients.
- **Additional resources** such as experienced providers who are available for consultation to help with the management of high-risk patients

Hyperphagia, or the intense sensation of hunger accompanied by food-seeking behaviors, is the main underlying cause of morbidity and mortality in Prader-Willi syndrome (PWS). Diazoxide choline, (DCCR, or VYKAT XR™) was approved by the FDA in the spring of 2025 for the indication of treatment of hyperphagia in adults and children 4 years of age and older with PWS. The prescribing information (package insert) “warnings and precautions” include the risk of fluid overload, based on an increased incidence of edema during clinical studies of VYKAT XR in patients with PWS.

Clinical trials in rare diseases are necessarily relatively small, highly controlled, and often do not include the most severely affected patients for safety reasons, so it is not unexpected that since the drug became widely available, additional reports of edema and associated complications have been made through the FDA’s Adverse Event Monitoring System (AEMS). **These reports (as of July 31, 2026) include seven reports of death and more than 100 additional reports of serious adverse events, most of which were related to edema, respiratory and cardiac complications.** Cases resulting in death or other serious outcomes were characterized by complex medical issues, use of multiple medications, and for many, pre-existing obesity.

These reports do not determine which, if any, of the medicines the individual was using may have contributed to the adverse event or death. It is important to note that many medical complications are common in people with PWS, especially when weight and obstructive sleep apnea are not well controlled. Compared to the general population, mortality is higher at all ages in people with PWS, and published data suggest that each year 1-3% of people with PWS die in all age groups. It cannot be determined from these adverse event reports whether these deaths and complications are directly related to VYKAT XR treatment or if they are part of the underlying challenges of PWS. However, these particular complications do not appear to be common among individuals providing medical information to the caregiver-reported outcomes in the Global PWS Registry, recognizing that the Global PWS Registry population may differ from the VYKAT XR-treated cohort with respect to disease severity or clinical management

The intention of this statement is to increase awareness of the risks for people with PWS when starting diazoxide choline/VYKAT XR**. Issues that appear to be associated with increased risk that deserve further study include:**

- **obesity, particularly severe obesity**
- **underlying heart problems**
- **pre-existing edema or fluid retention**
- **severe breathing issues, including obesity-related and central hypoventilation**
- **untreated or inadequately treated obstructive sleep apnea**
- **history of severe respiratory infections or pneumonia**

There may be other risk factors of which we are not yet aware.

If prescriptions for diazoxide choline/VYKAT XR are being made or considered, it would be prudent to ensure that the physician is familiar with the complications and challenges of managing PWS, including the fact that individuals with PWS often do not complain of pain or discomfort. Beyond the published guidelines in the labelling information for the drug (package insert), ordering providers should also be aware of the need for **individualized patient assessment, close monitoring, potentially slowing the titration process,** and additional safety testing (such as an echocardiogram or specific assessment of fluid retention) before and during drug use (especially during dose increases) in individuals with risk factors, as well as the types of symptoms that should raise concern during drug initiation, titration, and maintenance (e.g., worsened edema, orthopnea, dyspnea, or unexpected weight gain).

If the prescriber is not highly experienced in caring for individuals with PWS, they may wish to consult with a more experienced provider prior to starting therapy (all 3 major patient

support groups can assist with these consultations). Finally, a recent publication from several experienced physicians who care for individuals with PWS offers helpful guidelines for use of diazoxide choline/VYKAT XR (PMID: 42100354; PMCID: PMC13148164).

The PWS community is grateful for the continued partnership with pharmaceutical companies in developing and testing new drugs for the complex medical and behavioral features of PWS. We welcome long-term follow-up clinical studies focused on safety and efficacy of all licensed and potential treatments, including post licensing surveillance, to improve the quality of life for individuals with PWS and their families.

PWS Patient Organizations:

Foundation for Prader-Willi Research	https://www.fpwr.org/
International Prader-Willi Syndrome Organization	https://ipwso.org/
Prader-Willi Syndrome USA	https://www.pwsausa.org/

The following PWS clinicians contributed to this statement:

Elisabeth Dykens [2]

Nick Finer [4]

Tony Goldstone [1,2,3,4]

Tony Holland [4]

Shawn E. McCandless [1,2,3,4]

Elizabeth Roof [2]

Diane Stafford [1,2,3,4]

[1] Investigator in one or more DCCR studies; [2] has provided consulting to Soleno or Neurocrine in the past; [3] has received an honorarium to provide educational programing about PWS and use of VYKAT-XR; [4] has provided consulting, been an Investigator, or received speaker honorarium for other pharmaceutical companies developing treatments for PWS