

Positive Quality Intervention: Netupitant/Fosnetupitant and Palonosetron (Akynzeo®) for Chemotherapy-Induced Nausea and Vomiting

Description: This PQI serves to review the use of the combination product Akynzeo® for patients with acute and delayed chemotherapy-induced nausea and vomiting (CINV).

Background:¹⁻⁵ Nausea and vomiting from chemotherapy can occur acutely (within 24 hours) or have a more delayed onset (>24 hours up to several days after therapy). CINV is an avoidable toxicity that often leads to increased acute care visits, re-evaluation of the chemotherapeutic regimen (such as dose reductions or delays to chemotherapy), increased healthcare costs, and ultimately a significant reduction in a patient's quality of life. Akynzeo® is a combination product containing a 5-HT₃ receptor antagonist and a neurokinin-1 (NK-1) receptor antagonist that is available in both oral (netupitant-palonosetron) and injectable (fosnetupitant-palonosetron) formulations. Palonosetron is a highly selective 5-HT₃ receptor antagonist that prevents nausea and vomiting during the *acute* phase. Netupitant is a selective substance-P/NK-1 receptor antagonist that prevents nausea and vomiting during both the *acute and delayed* phase after chemotherapy; fosnetupitant is a prodrug of netupitant. Administered as a single-dose, Akynzeo® simultaneously targets two critical antiemetic pathways, providing simplified efficient dosing and preventing CINV for up to 5 days. In a clinical study involving 135 patients who were taking cisplatin-based chemotherapy, patients given an oral dose of Akynzeo® with dexamethasone were compared against patients given an oral dose of palonosetron, a different antiemetic treatment, with dexamethasone:

- 90% of patients who received Akynzeo® had no vomiting up to 5 days post chemo.
- 99% of patients who received Akynzeo® had no vomiting within 24 hours of chemo.

Akynzeo® is used with dexamethasone for the prevention of acute and delayed CINV associated with initial and repeat courses of chemotherapy, including, but not limited to, highly emetogenic chemotherapy. The capsules and injection have been studied in patients receiving platinum-based chemotherapy; however, only the oral formulation has been studied in patients receiving anthracycline and cyclophosphamide-based chemotherapy. NCCN guidelines list both Akynzeo® capsules and injection as a category 1 antiemetic agent for highly and moderately emetogenic chemotherapy regimens.

PQI Process:

- Determine which formulation is most appropriate for each patient:
 - Consider using the oral regimen when the patient's prescription insurance covers the medication
 - Consider the IV formulation in patients who have difficulty swallowing or have poor adherence to oral medications
 - Akynzeo® injection contains no polysorbate 80 which may be useful for patients with egg allergies. In contrast, fosaprepitant injection contains polysorbates and aprepitant injection contains soy²
 - It requires no reconstitution or refrigeration, providing operational efficiency
- Dosing and administration:¹⁻²
 - Oral: Take one capsule (netupitant 300 mg; palonosetron 0.5 mg) PO as a single dose approximately 60 minutes prior to chemotherapy
 - IV: Administer 1 vial (fosnetupitant 235 mg; palonosetron 0.25 mg) IV over 30 minutes, given as a single dose approximately 30 minutes prior to chemotherapy

Important Notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. Updated 3.21.22

- Withdraw contents from the vial and dilute into an IV bag containing NS or D5W
- Akynzeo® is compatible with dexamethasone IV solution and may be mixed in the same bag or infused simultaneously
- At the end of the infusion, flush the infusion line with the same carrier solution to ensure complete drug administration
- Drug interactions:¹⁻²
 - Netupitant is extensively metabolized primarily by CYP3A4 so the pharmacist must carefully screen for potential drug interactions
 - There is a potential drug-drug interaction with concomitant use of Akynzeo® and dexamethasone. The package insert recommends limiting the dexamethasone dose to 12 mg on day 1, and 8 mg on days 2-4 (if needed)
 - Risk of serotonin syndrome is increased with concomitant use of serotonergic drugs
- Special populations:¹
 - Avoid use of Akynzeo® in pregnancy, severe hepatic impairment, severe renal impairment, and end-stage renal disease

Patient Centered Activities:

- Patient counseling:¹⁻²
 - Advise the patient to bring the dose to the appointment if possible, and to take the dose once administration of chemotherapy is confirmed (to avoid wasting a dose)
 - Oral capsules may be taken with or without food
 - Side effects are generally mild but may include headache, asthenia, dyspepsia, fatigue, constipation, and erythema
- Patient Assistance: [NCODA Financial Assistance Tool](#)

References:

1. [Akynzeo® \[package insert\]](#).
2. Akynzeo®. Clinical Pharmacology powered by ClinicalKey. Elsevier. July 21, 2021. <http://www.clinicalkey.com>.
3. Rapoport BL. Delayed Chemotherapy-Induced Nausea and Vomiting: Pathogenesis, Incidence, and Current Management. *Front Pharmacol.* 2017;8:19. doi:10.3389/fphar.2017.00019.
4. Navari RM, Binder G, Bonizzoni E, Clark-Snow R, Olivari S, Roeland EJ. Single-dose netupitant/palonosetron versus 3-day aprepitant for preventing chemotherapy-induced nausea and vomiting: a pooled analysis [published online ahead of print, 2021 Apr 21]. *Future Oncol.* 2021. doi:10.2217/fon-2021-0023.
5. National Comprehensive Cancer Network. Antiemesis.