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Building quality cancer care together

Helsinn Group announces the FDA approval of the IV formulation of AKYNZEO® (fosnetupitant/palonosetron) in the United States

Lugano, Switzerland April 20, 2018 – Helsinn, a Swiss pharmaceutical group focused on building quality cancer care products, today announces that the U.S. Food and Drug Administration (FDA) has approved the intravenous formulation of AKYNZEO® (NEPA, a fixed antiemetic combination of fosnetupitant, 235mg, and palonosetron, 0.25mg) as an alternative treatment option for patients experiencing CINV.

The FDA has approved AKYNZEO® IV in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy. AKYNZEO® for injection has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

Oral AKYNZEO® was previously approved by the FDA as a fixed combination oral agent in 2014 for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. AKYNZEO® is an oral fixed combination of palonosetron and netupitant: palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

The bioequivalence of the IV with the oral formulation of netupitant was demonstrated and the safety of IV NEPA was established through a repeated dose safety study in cancer patients to potentially uncover adverse drug reactions that may appear during subsequent clinical practice. No anaphylactic and injection site reactions related to IV NEPA were reported in this study.

Currently a repeated dose safety study is ongoing in patients receiving anthracycline plus cyclophosphamide to further establish the safety profile in this setting.

The prevention of CINV has been refined in treatment guidelines over the past several decades. Currently the combination treatment of antiemetic medicines with different mechanisms of actions are recommended for the prevention of CINV.

The approval of AKYNZEO® in IV formulation will offer to US patients and healthcare providers an alternative route of administration of the only fixed antiemetic combination targeting two distinct CINV pathways in a single dose.

Riccardo Braglia, Helsinn Group Vice Chairman and CEO, commented: "The approval of the intravenous formulation of AKYNZEO® paves the way to bring this important therapeutic option to more patients in a new formulation, and we are delighted that we are now able to push ahead with launching this product in the United States in May 2018"

Helsinn plans to launch AKYNZEO® in IV formulation in the US in May 2018.

About Akynzeo®

INDICATION

AKYNZEO® (netupitant 300mg/palonosetron 0.5mg) capsules was approved in October 2014 in the United States and is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

AKYNZEO® (fosnetupitant 235mg/palonosetron 0.25) for injection was approved in April 2018 in the United States and is indicated in combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.

Limitations of Use

AKYNZEO for injection has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

AKYNZEO is a combination of palonosetron, a serotonin-3 ($5\text{-}HT_3$) receptor antagonist, and netupitant or fosnetupitant, substance P/neurokinin-1 (NK-1) receptor antagonists: palonosetron prevents nausea and vomiting during the acute phase and netupitant/fosnetupitant prevents

nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Hypersensitivity reactions, including anaphylaxis, have been reported in patients receiving palonosetron, one of the components of AKYNZEO, with or without known hypersensitivity to other 5-HT_3 receptor antagonists.

- Serotonin syndrome has been reported with 5-HT_3 receptor antagonists alone but particularly with concomitant use of serotonergic drugs. Serotonin syndrome can be life threatening. Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes, autonomic instability, neuromuscular symptoms, seizures, and gastrointestinal symptoms. Patients should be monitored for the emergence of serotonin syndrome, and if symptoms occur, discontinue AKYNZEO and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if AKYNZEO is used concomitantly with other serotonergic drugs.

Adverse Reactions

- Most common adverse reactions for AKYNZEO capsules and injection: headache, asthenia, dyspepsia, fatigue, constipation and erythema

Drug Interactions

- Use with caution in patients receiving concomitant medications primarily metabolized by CYP3A4. The plasma concentrations of CYP3A4 substrates can increase when co-administered with AKYNZEO. The inhibitory effect on CYP3A4 can last for multiple days

    - Dexamethasone doses should be reduced when given with AKYNZEO. A more than two-fold increase in the systemic exposure of dexamethasone was observed 4 days after a single dose of netupitant or a single infusion of fosnetupitant

  - Consider the potential effects of increased plasma concentrations of midazolam or other benzodiazepines metabolized via CYP3A4 (alprazolam, triazolam) when administering with AKYNZEO. When administered with netupitant, the systemic exposure to midazolam was significantly increased

- Avoid concomitant use of AKYNZEO in patients on chronic use of a strong CYP3A4 inducer such as rifampin as this may decrease the efficacy of AKYNZEO

Use in Specific Populations

- Avoid use of AKYNZEO in patients with severe hepatic impairment, severe renal impairment, or end-stage renal disease
- Avoid use in pregnancy, limited data is available, may cause fetal harm.

For more information about AKYNZEO please see the full Prescribing Information

About the Helsinn Group

Helsinn is a privately owned pharmaceutical group with an extensive portfolio of marketed cancer care products and a robust drug development pipeline. Since 1976, Helsinn has been improving the everyday lives of patients, guided by core family values of respect, integrity and quality. The Group works across pharmaceuticals, biotechnology, medical devices and nutritional supplements and has expertise in research, development, manufacture and the commercialization of therapeutic and supportive care products for cancer, pain and inflammation and gastroenterology. In 2016, Helsinn created the Helsinn Investment Fund to support early-stage investment opportunities in areas of unmet patient need. The company is headquartered in Lugano, Switzerland, with operating subsidiaries in Switzerland, Ireland, the U.S., Monaco and China, as well as a product presence in approximately 190 countries globally.

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