Helsinn Group announces FDA approval of a new liquid formulation of AKYNZEO® (fosnetupitant/palonosetron) injection in the United States

Lugano, Switzerland, June 2, 2020 – Helsinn, a Swiss pharmaceutical group focused on building quality cancer care and rare disease products, today announces that the U.S. Food and Drug Administration (FDA) has approved the ready-to-dilute liquid formulation of AKYNZEO® (fosnetupitant/palonosetron) injection. This new liquid solution provides several improvements to storage and handling:

- AKYNZEO® injection does not require refrigeration at any stage of distribution, preparation or storage
- AKYNZEO® injection eliminates the need for reconstitution prior to dilution, reducing the preparation process for intravenous administration of AKYNZEO to one step before use.
- AKYNZEO® injection may now be stored for up to 24 hours at room temperature after dilution, allowing more flexibility in preparation for busy clinicians

AKYNZEO® injection is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy in adults, when given with dexamethasone. It has not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy. AKYNZEO® injection does not contain polysorbate 80 or allergenic excipients such as soy or egg lecithin.

Riccardo Braglia, Helsinn Group Vice Chairman and CEO, commented: "We are pleased to announce FDA's approval of the liquid formulation of AKYNZEO®. This new formulation will reduce the steps in administering this CINV treatment, improving the efficiency in preparation. Extended storage time following dilution provides more flexibility to clinics and hospitals to prepare AKYNZEO® for use throughout the day. AKYNZEO® is the only medication to target two distinct CINV pathways in a single dose and can help clinicians prevent CINV in appropriate patients. We are targeting launch of the liquid formulation in the second half of this year and look forward to updating the market in due course."

Paul Rittman, CEO, Helsinn Therapeutics (U.S.), Inc, said: "I am pleased that we can now

offer this improved form of AKYNZEO® to clinicians across the US. We hope that the elimination of refrigerated storage, the increase in room-temperature storage time once diluted, and the reduction in preparation steps, will all be of assistance to those administering the treatment, allowing for greater efficiency as they help prevent CINV in patients undergoing chemotherapy."

About AKYNZEO®

AKYNZEO® is the first and only 5-HT_3 and NK_1 receptor combination approved for the prevention of chemotherapy induced acute and delayed nausea and vomiting. A single dose of AKYNZEO® given with dexamethasone has been shown to prevent chemotherapy induced nausea and vomiting for 5 days.

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 and AKYNZEO® injection was approved in May 2020 in the United States. Each 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 and AKYNZEO® injection have 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-HT3) 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.

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Building quality cancer care together

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 Swiss Pharma Company which, since 1976, has been improving the lives of patients, guided by core family values of respect, integrity and quality. The Group has an extensive portfolio of marketed innovative cancer and rare disease therapies, a robust drug development pipeline and ambitions to further accelerate its growth through in-licensing and acquisition to address unmet medical needs. Helsinn operates a unique integrated licensing business model, achieving success with over 80 long-standing partners in 190 countries, who share our values. The Group's pharmaceutical business (Helsinn Healthcare) is headquartered in Lugano, Switzerland with operating subsidiaries in the U.S. (Helsinn Therapeutics US) and China (Helsinn Pharmaceuticals China) which market the Group's products directly in these countries. The Group has additional operating subsidiaries in Switzerland (Helsinn Advanced Synthesis, an active pharmaceutical ingredient manufacturer) and Ireland (Helsinn Birex Pharmaceuticals, a drug product manufacturer). Helsinn Investment Fund was created to enhance the future of healthcare by providing funding and strategic support to innovative companies.

Helsinn Group plays an active and central role in promoting social transformation in favor of people and the environment. Corporate social responsibility is at the heart of everything we do which is reinforced in the company's strategic plan by a commitment to sustainable growth.

To learn more about Helsinn Group please visit www.helsinn.com

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AKYN-US-0066