Clinical Pharmacology NDA Review-Memorandum

NDA Number (SDN)	NDA 214375/S-1 (SND 73)
Link to EDR	\\CDSESUB1\EVSPROD\nda214375\0072\
Submission Date	July 31, 2024
Submission Type	Efficacy supplement
Brand Name	XENOVIEW
Generic Name	Hyperpolarized 129-Xe
Dosage Form and Strengths	Dose delivery bags: 300 mL, 500 mL, 750 mL and 1000 mL. Each bag should contain 75 mL to 100 mL Dose Equivalent (DE) of hyperpolarized xenon Xe 129 within 5 minutes of administration, in a volume of 250 mL to 750 mL total xenon with additional nitrogen added to reach a total volume of the dose delivery bag.
Route of Administration	Oral Inhalation
Proposed Dose	The recommended target dose of XENOVIEW for adult and pediatric patients aged 6 years and older is 75 mL to 100 mL DE volume of hyperpolarized xenon Xe 129 by oral inhalation of the entire contents of one XENOVIEW dose delivery bag.
Proposed Indications	For use with magnetic resonance imaging (MRI) for evaluation of lung ventilation in adults and pediatric patients aged 6 years and older.
Applicant	Polarean, Inc.
OCP Review Team	Wentao Fu, PhD, Sriram Subramaniam, PhD (TL)
OCP Final Signatory	Brian Booth, PhD

In 2022, XENOVIEW was approved for use with MRI for evaluation of lung ventilation in adults and pediatric patients aged 12 years and older under the original NDA 214375 submission. The recommended dosage of hyperpolarized xenon Xe 129 in adults and pediatric patients 12 years and older is 75 mL to 100 mL Dose Equivalent (DE)[1] by oral inhalation with a 1000 mL dose delivery bag. A delivery bag should contain 75 mL to 100 mL DE of hyperpolarized xenon Xe 129 measured within 5 minutes of administration, in a volume of 250 mL to 750 mL total xenon with nitrogen filled to reach a total volume of 1000 mL. The recommended dose should be administered within 5 minutes of DE measurement.

[1] DE is the volume (mL) of pure 100% hyperpolarized Xe 129 that would produce the equivalent net magnetization as the Xe 129 dose.
DE = (total volume xenon gas) × (fraction of xenon Xe 129 isotopic enrichment in the xenon gas) × (fraction of hyperpolarization)

This NDA supplement for XENOVIEW includes introduction of three new sizes of dose delivery bags (300 mL, 500 mL, and 750 mL). The selection of the dose delivery bags is based on estimates of the patient's Total Lung Capacity (TLC) or Forced Vital Capacity (FVC) (see Table 1) using American Thoracic Society (ATS) plethysmography-based predictive equations for sex and height.

Table 1. Recommended Dose Delivery Bag Volume Based on TLC

TLC (L)	FVC* (L)	Dose Delivery Bag (mL)
<2.0	<1.5	300
2.0 to <3.3	1.5 to <2.5	500
3.3 to <5.0	2.5 to <3.8	750
≥5.0	≥3.8	1,000

*FVC is used when TLC is not available.

The proposed dosage of XENOVIEW in pediatric patients 6 years and older is the same as in adults and pediatrics > 12 years and older, i.e., 75 mL to 100 mL DE by oral inhalation. Each dose delivery bag should contain 75 mL to 100 mL DE of hyperpolarized xenon Xe 129 measured within 5 minutes of administration, in a volume of 250 mL to 750 mL total xenon with nitrogen to fill the remaining volume of the dose delivery bag.

With regards to the proposed DE range for pediatric patients 6 years and older, the pervious FDA review (Reference ID: 4867776) in the original NDA 214375 submission concluded that the available literature data supported the same DE dosage of XENOVIEW in pediatric patients 6 years and older as those in adults and pediatric patients 12 years and older. However, XENOVIEW was not approved under the original NDA 214275 for pediatric patients 6 years and older due to the limit of the 1000 mL delivery bag.

There are no clinical pharmacology studies and no clinical pharmacology summary module in this submission for clinical pharmacology review.

The acceptability of proposed delivery bags and the proposed selection of dose delivery bags in pediatric patients 6 years and old, based on TLC or FVC, are deferred to the Clinical Team and CDRH.

Recommendation:

This sNDA is approvable from a clinical pharmacology perspective, pending acceptability of the selection of dose delivery bags and the Applicant and the Agency come to an agreement regarding the labeling language.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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