Molina Clinical Policy
XENOVIEW (Xenon MRI): Policy No. 667

Last Approval: 6/12/2024
Next Review Due By: June 2025

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Hyperpolarized Xenon 129 is a contrast agent composed of hyperpolarized Xenon Xe 129 gas (HP129Xe) and is the active pharmaceutical ingredient in XENOVIEW. It is chemically identical to non-polarized Xenon Xe 129. Xenon is a clear, colorless, monoatomic, inert, stable, noble gas and naturally abundant in air at a level of 0.087 ppm. Atmospheric Xenon is composed of nine non-radioactive isotopes, of which Xenon Xe 129 comprises 26.4%. The atomic weight of Xenon Xe 129 is 128.9 (FDA 2022).

Xenon 129 is used in diagnostic nuclear magnetic resonance (NMR)-based imaging. Upon inhalation, the HP129Xe is distributed throughout the lungs. Magnetic resonance imaging (MRI), immediately following HP129Xe administration, allows for the visualization of lung structures based on the distribution pattern of the gas. The method may aid in diagnosing specific lung abnormalities. Through hyperpolarization, NMR signals are enhanced and provides imaging for the assessment of lung function (PubChem 2016).

United States Food and Drug Administration (FDA)

Two 510(k) devices were cleared by the FDA related to XENOVIEW:

On December 23, 2022, the FDA issued a 510(k) premarket notification regarding XENOVIEW ventilation defect percent (VDP). It has been approved for use with MRI for evaluation of lung ventilation in adults and pediatric patients aged 12 years and older. XENOVIEW VDP is imaging processing software than can analyze pulmonary HP129Xe MRI and a proton chest MRI to provide visualization and evaluation of lung ventilation in adults and pediatric patients aged 12 years and older. The image analysis platform measures normalized Xenon intensity of a ventilated space using a pulmonary HP129Xe ventilation MRI and accompanying proton chest image. The dose of XENOVIEW is created with the Polarean HPX hyperpolarization system and is administered in a single 10-15 second breath hold MRI procedure. XENOVIEW is the first inhaled MRI hyperpolarized contrast agent for novel visualization of lung ventilation. The method does not expose patients to ionizing radiation and eliminates the associated risks. XENOVIEW provides regional maps of ventilation in the lungs to assist pulmonologists, surgeons, and other respiratory specialists with managing patients and their disease (FDA 2022).

On December 23, 2022, the United States Food and Drug Administration (FDA) issued a 510(k) premarket notification regarding XENOVIEW 3.0T Chest Coil. This is a flexible, single channel, transmit-receive (T/R) RF coil tuned to 129Xe frequency on a 3.0T MRI magnetic field of a compatible MRI scanner. The XENOVIEW 3.0T Chest Coil is designated for use in conjunction with compatible 3.0T MRI scanners and approved HP129Xe for oral inhalation for evaluation of lung ventilation in adults and pediatric patients aged 12 years and older. The Chest Coil is worn by a patient who inhales HP129Xe (XENOVIEW) to obtain an MR image of the regional distribution of hyperpolarized 129Xe in the lungs (FDA 2022).

COVERAGE POLICY

XENOVIEW magnetic resonance imaging (MRI) **may be considered medically necessary** when the following criteria are met:

1. Member has breathing difficulty and has been diagnosed with **ONE** of the following:
   a. Allergic rhinitis
   b. Asthma
   c. Bronchitis
   d. COPD
   e. Cystic fibrosis
   f. Emphysema
   g. Interstitial lung disease
   h. Idiopathic pulmonary fibrosis
   i. Post-transplant lymphoproliferative disorder
   j. Pulmonary fibrosis
   k. Pulmonary mass

2. Member is being considered for lung resection (e.g., segmentectomy, lobectomy, or pneumonectomy) or transplant surgery

3. Member has symptoms which have been unexplained to date with standard pulmonary management
   a. Is experiencing ongoing symptoms from COVID-19
   b. Has received a lung or heart-lung transplant
   c. History of an infectious or parasitic disease
   d. Long term use of steroids (inhaled or systemic)

4. Member is aged 12 years or older
5. Members baseline oxygen saturation on room air or their normal supplementation is ≥90%
6. Member is able to fit in MRI coil
7. Member is not pregnant or breastfeeding
8. Member can tolerate MRI with at most mild sedation

Limitations and Exclusions

1. XENOVIEW has not been evaluated for use with lung perfusion imaging
2. May cause transient hypoxemia and patients should be monitored closely
3. No studies to date have assessed the risk in pregnant or breastfeeding adults

PRESCRIBER REQUIREMENTS: Prescribed by or in conjunction with a pulmonologist

AGE RESTRICTIONS: Age ≥ 12 years

DOSING CONSIDERATIONS: 75 mL to 100 mL Dose Equivalent (DE) of HP129Xe

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Two prospective, multicenter, randomized, open-label, cross-over clinical trials compared XENOVIEW MRI to Xenon Xe 133 scintigraphy in adult patients with pulmonary disorders. Study 1 (NCT03417687) included patients being

evaluated for possible lung resection surgery. Study 2 (NCT03418090) included patients being evaluated for possible lung transplant surgery. The mean XENOVIEW dose used in the trials was 99 mL DE of hyperpolarized Xenon Xe 129 at the time of measurement within 5 minutes of administration. The most common adverse reactions reported in both clinical trials included oropharyngeal pain, headache, and dizziness (NLM 2018).

In Study 1, XENOVIEW and Xenon Xe 133 imaging were compared in patients being evaluated for lung resection surgery with respiratory disorders – pulmonary mass (44%), COPD (35%), cough (15%), sleep apnea syndrome (12%), and asthma (12%). A total of 32 patients who completed both scans and had a mean age of 62 years (range 25 to 77 years); 78% were White and 69% were male. For the XENOVIEW and Xenon Xe 133 scan, the fraction of total signal in the lungs was calculated for six zones (upper, middle, and lower regions in each lung). The values were used to estimate the post-operative percentage of lung ventilation expected to remain after a planned resection of a pre-specified lung area. A total of 31 patients who completed both scans were included in the primary analysis. The mean within-patient difference in the predicted post-operative percentage of remaining lung ventilation between XENOVIEW and Xenon Xe 133 imaging was within a pre-specified equivalence interval with an observed estimate of 1.4% (95% confidence interval: -0.8%, 3.6%). An exploratory analysis standardized the within-patient difference of the predicted remaining lung ventilation between XENOVIEW and Xenon Xe 133 imaging to each patient's Xenon Xe 133 results. The percentage of patients who had standardized differences within ± 10%, ± 15%, and ± 20% were 81% (25/31), 94% (29/31), and 94% (29/31), respectively (NLM 2018).

In Study 2, XENOVIEW and Xenon Xe 133 scintigraphy imaging was compared in 49 patients who were being evaluated for probable lung transplant surgery. This was a multicenter, randomized, open-label, cross-over Phase 3 study. Patients had respiratory disorders that included: interstitial lung disease (49%), idiopathic pulmonary fibrosis (29%), COPD (22%), sleep apnea syndrome (16%), other pulmonary fibrosis (14%), allergic rhinitis (12%), and cough (10%). The mean age of patients was 62 years (range 19 to 77 years), 94% were White, and 69% were male. For both the XENOVIEW and Xenon Xe 133 images, right lung signal and total signal in the lungs were calculated and used to estimate the percentage of overall lung ventilation contributed by the right lung. Primary analysis showed that the mean within-patient difference in the percentage of overall lung ventilation contributed by the right lung between XENOVIEW and Xenon Xe 133 imaging was within a pre-specified equivalence interval with an observed estimate of 1.6% (95% confidence interval: -3.7%, 0.5%). An exploratory analysis standardized the within-patient difference of right lung ventilation between XENOVIEW and Xenon Xe 133 imaging to that of each patient's Xenon Xe 133 results. The percentage of patients who had standardized differences of ± 10%, ± 15%, and ± 20% were 65% (32/49), 80% (39/49), and 96% (47/49), respectively (NLM 2018). Secondary outcome measures were the percentage of lung function contributed by each of the individual 6 lung zones.

Foo et al. (2023) studied functional lung imaging using novel and emerging MRI techniques. To aid in early diagnosis, there is a need for sensitive and non-invasive tools. While CT is known as the gold standard for structural lung imaging, it lacks functional information and exposes the patient to considerable radiation exposure. Lung MRI has presented challenges due to its short T2 and low proton density. Hyperpolarized gas MRI is an emerging technique that can overcome these difficulties to allow for the functional and microstructural evaluation of the lung. The Xe 129 MRI has been routinely used since 2015 in the United Kingdom and was not approved in the United States until December 2022. The authors note that this technology has the potential to aid in analyzing a range of cardiopulmonary disorders through analysis of cardiogenic signal oscillations arising from Xe 129 dissolved in the pulmonary circulation.

Willmering et al. (2022) conducted a prospective study on Xe 129 gas-transfer MRI in children. A total of 77 participants were included (38 males, age = 17.7 ± 15.1 years, range 5-68 years, 16 healthy) and separated into four pediatric disease cohorts. Eighty percent successfully completed Xe 129 gas-transfer MRI. Participants who were bone marrow transplant recipients showed impaired ventilation (90% of reference) and increased dissolved Xe 129 standard deviation (242%). Those with bronchopulmonary dysplasia showed a decreased barrier-uptake (69%). Cystic fibrosis participants showed impaired ventilation (91%) and increased RBC-transfer (146%). Those with childhood interstitial lung disease subjects showed increased ventilation heterogeneity (113%). The authors concluded that use of Xe 129 gas-transfer MRI was sufficiently successful for pediatric patients; gas-transfer metrics correlated with age. Abnormalities were reported in a range of pediatric obstructive and restrictive lung diseases.

CODING & BILLING INFORMATION

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	Description
C9791	Magnetic resonance imaging with inhaled hyperpolarized Xenon-129 contrast agent, chest, including preparation and administration of agent
A9610	Xenon Xe-129 hyperpolarized gas, diagnostic, per study dose

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

06/12/2024 Reviewed policy; no changes to coverage criteria. Updated Summary of Medical Evidence and References.
10/12/2023 Updated coding section.
06/14/2023 New policy. IRO Peer Review on June 2, 2023, by a practicing, board-certified physician with a specialty in Pulmonology.

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