Kepro

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2023 Quarter 1 Newsletter

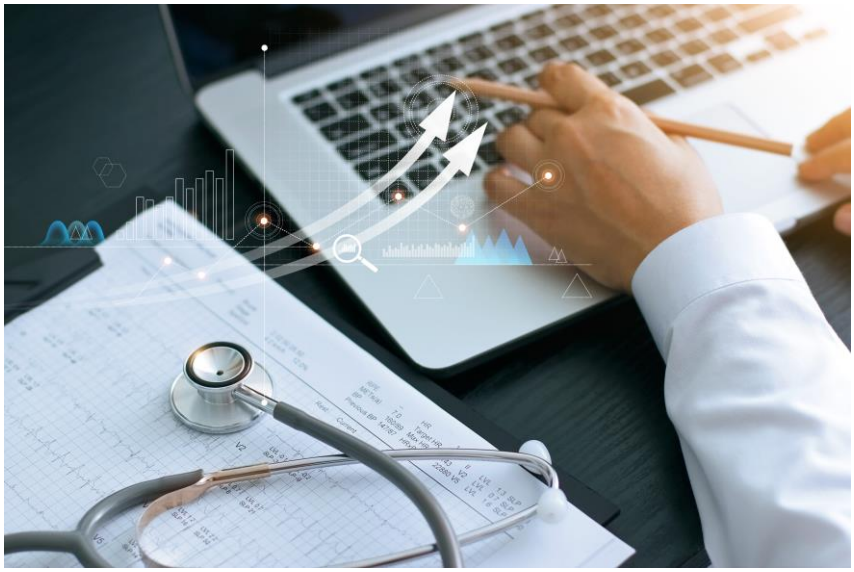
MESSAGE FROM THE VENDOR

Let us introduce ourselves! Our company Keystone Peer Review Organization (Kepro) has a long and fulfilling history of serving federal, state, and local healthcare programs and helping them to provide the highest quality care to their patients and resources to their providers. ***Our mission is to improve lives through healthcare quality and clinical expertise***.

January 01, 2023, marks the beginning of our contract to perform and facilitate retroactive drug utilization review (RDUR) services to the West Virginia Department of Health Services and state Medicaid program. We are honored to serve you to our fullest capacity and look forward to a long-lasting and successful relationship.

References:

- Kepro. About Us, Kepro. Available at: https://www.kepro.com/about (Accessed: March 16, 2023).



FDA-APPROVAL SPOTLIGHT

LEQEMBI™ (lecanemab-irmb) INJECTION FOR INTRAVENOUS USE 100 mg/mL

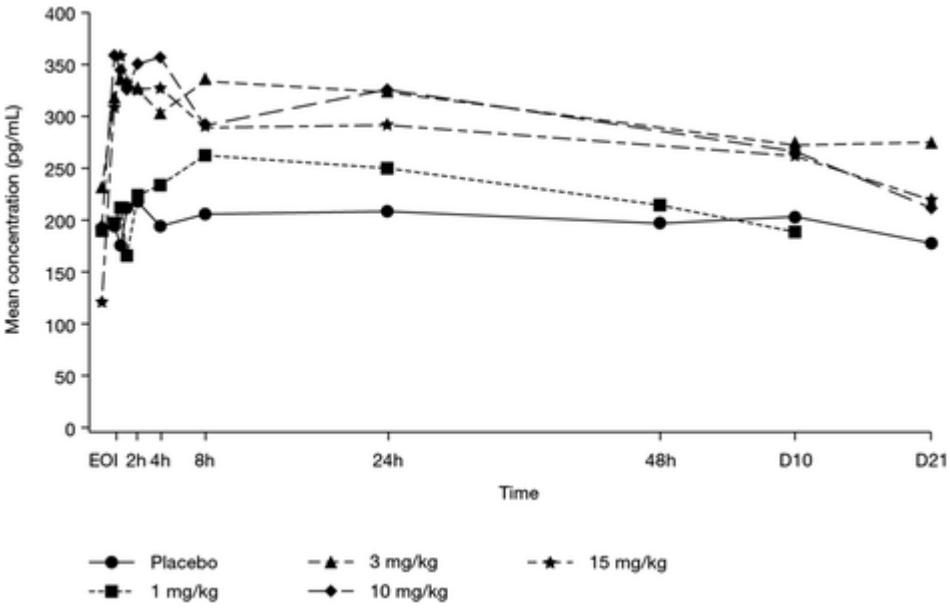
The Food and Drug Administration (FDA) confirmed accelerated approval for Leqembi (lecanemab-irmb) for the treatment of Alzheimer's Disease (AD) on January 06, 2023, with full approval estimated on July 06, 2023. This is the second monoclonal antibody for this indication, and preliminary data is promising. The table below compares the clinical trials. Of note, the patient population for all clinical trials comprised patients of ages 50-90 years old with mild cognitive impairment (MCI) due to AD or mild AD.

Clinical Trial	Trial Type	Treatment Arms	Primary Endpoint	Secondary Endpoint(s)
Phase 1	Randomized Parallel Double-blinded Placebo-controlled	Lecanemab 2.5 mg/kg Lecanemab 5 mg/kg Lecanemab 10 mg/kg Placebo	# of participants w/ ADRs	Pharmacokinetics (Cmax, tmax, AUC, CL, Vss, etc.)
Phase 2	Randomized Parallel Triple-blinded Placebo-controlled	Lecanemab 2.5 mg/kg biweekly Lecanemab 5 mg/kg biweekly Lecanemab 10 mg/kg biweekly Lecanemab 5 mg/kg monthly Lecanemab 10 mg/kg monthly Placebo	Change from baseline in ADCOMS at 12 months	Change in brain amyloid patho-physiology on MRI at 12 and 18 months Change in ADCOMS at 18 months Change in CDR-SB at 12 and 18 months Change in ADAS-cog at 12 and 18 months Change in CSF biomarkers at 12 and 18 months Change in total hippocampal volume on vMRI at 6, 12, and 18 months
Phase 3 (in progress)	Randomized Parallel Quadruple-blinded	Lecanemab 10 mg/kg biweekly Placebo	Change in CDR-S8 at 18 months	Change in amyloid PET at 18 months Change in ADAS-cog14 at 18 months

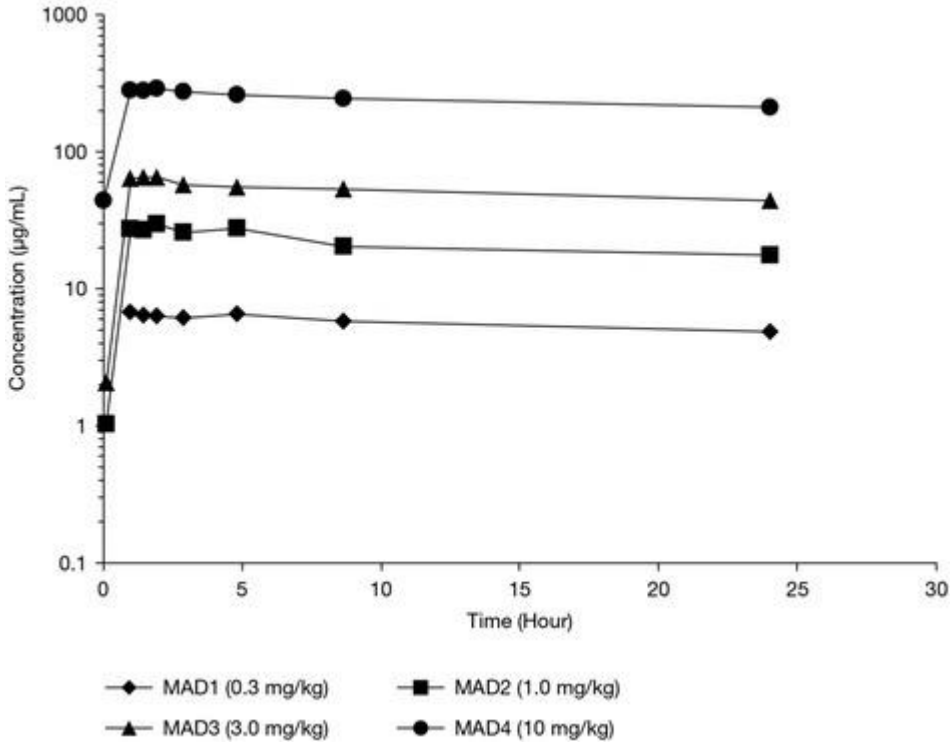
	Placebo-controlled			Change in ADCOMS at 18 months Change in ADCS MCI-ADL at 18 months

Leqembi acts as an amyloid beta-directed, IgG1 monoclonal antibody. Its action against the pathogenic plaques formed by the amyloid beta proteins requires initial and follow-up MRI assessment to rule out amyloid-related imaging abnormalities (ARIA). It is administered as a dosage of 10 mg/kg once every two weeks via intravenous infusion over one hour, but future studies are planned to research the use of subcutaneous injections to increase the accessibility. Of note, the clinical trials initiated Leqembi treatment in patients with only mild cognitive impairment or mild Alzheimer's disease. Notable results from Phase 1 and 2 trials are described in the table and figures below.

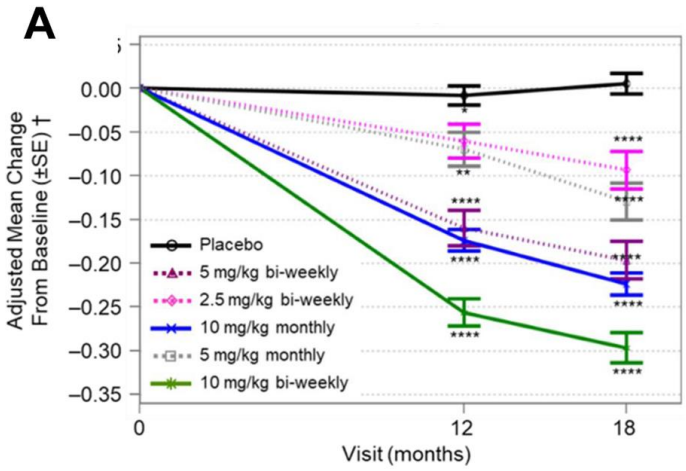
Clinical Trial	Notable Results
Phase 1	ARIAs incidence comparable to placebo Leqembi exposure and PK parameters approximately dose proportional Serum half-life of ~7 days Slight increase of plasma Aβ observed compared to placebo
Phase 2	Significant improvement in ADCOMS in 10 mg/kg biweekly dose at 12 months Significant reduction in brain amyloid levels and ADCOMS in 10 mg/kg biweekly dose at 18 months 9.9% incidence of ARIAs in 10 mg/kg biweekly dose



Phase 1: Mean concentrations of Aβ vs nominal time



Phase1: Mean serum concentrations of Lequembi after last dose



N (PET-SUVr)	0 Months	12 Months	18 Months
Placebo	99	96	88
2.5 mg/kg biweekly	28	27	23
5 mg/kg monthly	28	27	23
5 mg/kg biweekly	27	25	24
10 mg/kg monthly	89	88	82
10 mg/kg biweekly	44	43	37

Phase 2: Change from baseline in amyloid PET SUVr

The most common adverse drug reactions (ADRs) found in the clinical trials were mild infusion-related reactions. A more serious class of ADRs that can occur with Leqembi are ARIAs, which are potentially fatal reactions that include intracranial edema, microhemorrhage, superficial siderosis, and status epilepticus. Below is the incidence of ARIAs found in the clinical trials.

	Leqembi (N=161)	Placebo (N=245)
Symptomatic ARIA	3% (5)	0% (0)
Asymptomatic ARIA	12% (20)	5% (13)
Infusion-related reactions	20% (32)	3% (8)
Decreased lymphocyte count	38% (61)	2% (5)
Increased neutrophil count	22% (35)	1% (2)

Although no comparative studies have been completed with Leqembi, there have been concerns about its place in therapy for Alzheimer's disease based on the efficacy of the other approved anti-amyloid monoclonal antibody Aduhelm (aducanumab). Time and further studies will tell if this is truly the breakthrough therapy that providers and patients alike desire Leqembi to be.

References:

- Leqembi [package insert]. Nutley, NJ: Eisai Inc. https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf?hash=3d7bf1a2-5db2-4990-8388-81086f415676. Jan 06, 2023.
- Logovinsky V, Satlin A, Lai R, Swanson C, Kaplow J, Osswald G, Basun H, Lannfelt L. Safety and tolerability of BAN2401--a clinical study in Alzheimer's disease with a protofibril selective Aβ antibody. Alzheimers Res Ther. 2016 Apr 6;8(1):14. doi: 10.1186/s13195-016-0181-2. PMID: 27048170; PMCID: PMC4822297.
- Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody [published correction appears in Alzheimers Res Ther. 2022 May 21;14(1):70]. Alzheimers Res Ther. 2021;13(1):80. Published 2021 Apr 17. doi:10.1186/s13195-021-00813-8
- van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, Kanekiyo M, Li D, Reyderman L, Cohen S, Froelich L, Katayama S, Sabbagh M, Vellas B, Watson D, Dhadda S, Irizarry M, Kramer LD, Iwatsubo T. Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023 Jan 5;388(1):9-21. doi: 10.1056/NEJMoa2212948. Epub 2022 Nov 29. PMID: 36449413.
- Tolar M, Abushakra S, Hey JA, Porsteinsson A, Sabbagh M. Aducanumab, gantenerumab, BAN2401, and ALZ-801-the first wave of amyloid-targeting drugs for Alzheimer's disease with potential for near term approval. Alzheimers Res Ther. 2020 Aug 12;12(1):95. doi: 10.1186/s13195-020-00663-w. PMID: 32787971; PMCID: PMC7424995.

2023 GUIDELINE UPDATES

As of January 06, 2023, the Global Initiative for Chronic Obstructive Lung Disease has released a 2023 update to the GOLD 2023 report. There are several notable changes in this report. A summary of these updates is given below.

Overall, the report highlights a more aggressive approach to initial therapy in combination with a reorganization of the previous ABCD assessment tool to a consolidated ABE assessment tool. (See Table 1 for more detail). Additionally, new definitions for COPD and a COPD exacerbation were proposed for the purpose of better differential diagnosis. Vaccination recommendations have also been updated to reflect Center for Disease Control (CDC) guidelines with relation to the Covid-19 pandemic.

	GOLD 2017 Update	GOLD 2023 Update
COPD definition	Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases.	Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.
COPD exacerbation definition	Acute worsening of respiratory symptoms that results in additional therapy	Dyspnea and/or cough and sputum that worsens over ≤14 days with possible tachypnea and/or tachycardia caused by airway infection, pollution, or other insult to the airways
Vaccinations	Influenza PCV13 and PPSV23	Influenza SARS-CoV-2 PCV20 or PCV15 x1 dose, then PPSV23 dTaP/dTPa (not vaccinated in adolescence) Zoster (age >50 years old)
Assessment categories	***A*** ≤1 exacerbations not leading to hospitalization	***A*** ≤1 moderate exacerbations +

	+ mMRC ≤1, CAT <10 ***B*** ≤1 exacerbations not leading to hospitalization + mMRC >1, CAT ≥10 ***C*** >1 moderate exacerbation OR any exacerbation leading to hospitalization + mMRC ≤1, CAT <10 ***D*** >1 moderate exacerbation OR any exacerbation leading to hospitalization + mMRC >1, CAT ≥10	mMRC ≤1, CAT <10 ***B*** ≤1 moderate exacerbations + mMRC >1, CAT ≥10 ***E*** >1 moderate exacerbation OR any exacerbation leading to hospitalization
Group A Treatment Selection	Short-acting bronchodilator alone	Long-acting bronchodilator
Group B and E Treatment Selection	Initial treatment with single long-acting bronchodilator alone	Initial treatment with dual long-acting bronchodilator therapy

References:

- Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martinez FJ, de Oca MM, Mortimer K, Papi A, Pavord I, Roche N, Salvi S, Sin DD, Singh D, Stockley R, Varela MVL, Wedzicha JA, Vogelmeier CF. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. Respirology. 2023 Mar 1. doi: 10.1111/resp.14486. Epub ahead of print. PMID: 36856440.
- Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Chen R, Decramer M, Fabbri LM, Frith P, Halpin DM, López Varela MV, Nishimura M, Roche N, Rodriguez-Roisin R, Sin DD, Singh D, Stockley R, Vestbo J, Wedzicha JA, Agustí A. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. Am J Respir Crit Care Med. 2017 Mar 1;195(5):557-582. doi: 10.1164/rccm.201701-0218PP. PMID: 28128970.

LEGISLATIVE NEWS

A recent federal legislative update from the Substance Abuse and Mental health Services Administration (SAMHSA) removed the requirements for providers to have an approved X-waiver to prescribe buprenorphine for opioid use disorder (OUD). This legislation can be found in the Consolidated Appropriations Act of 2023, Section 1262 – also known as the Omnibus Bill. It officially went into effect on January 12, 2023.

Previously, the Drug Addiction Treatment Act (DATA 2000) required the submission of a waiver and 8-24 hours of training, along with a potentially lengthy review process, to be qualified to prescribe any buprenorphine product in an outpatient setting for the treatment of OUD. This update will make does not take away the requirement for a valid DEA registration number but will potentially improve access to care for patients with OUD to receive treatment.

References:

- H.R.2634 - 106th Congress (1999-2000): Drug Addiction Treatment Act of 2000, H.R.2634, 106th Cong. (2000), https://www.congress.gov/bill/106th-congress/house-bill/2634.
- H.R.2617 - 117th Congress (2021-2022): Consolidated Appropriations Act, 2023, H.R.2617, 117th Cong. (2022), https://www.congress.gov/bill/117th-congress/house-bill/2617.