NEW PRODUCT

Kisunla® Concentrate For Solution For Infusion 350mg/20ml

(Eli Lilly)

edited by Lucilla Leung

Qualitative and Quantitative Composition

Each vial contains 350mg/20ml(17.5mg/ml) donanemab. Donanemab is a recombinant monoclonal humanised antibody produced in Chinese Hamster Ovary(CHO) cells and has a molecular weight of 145kDa.

Indications

KISUNLA is indicated for the treatment of patients with Mild Cognitive Impairment (MCI) due to Alzheimer's disease and Mild Alzheimer's dementia (Early Symptomatic Alzheimer's disease) that are apolipoprotein EƐ4 (ApoEƐ4) heterozygotes or non-carriers.

Beta amyloid evidence consistent with Alzheimer's disease (AD) should be confirmed using a validated test prior to initiating treatment.

ApoE ε4 Genotype

KISUNLA is not indicated in apolipoprotein Eε4 (ApoE ε4) homozygous patients. Patients who are ApoE ε4 homozygotes (approximately 15% of Alzheimer's disease patients) treated with this class of medications, including KISUNLA, have a higher incidence of amyloid-related imaging abnormalities (ARIA) in the brain, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and non-carriers. Testing for ApoE ε4 status is required prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results.

Dose and method of administration

Treatment should be initiated by a physician experienced in the diagnosis and treatment of Alzheimer's disease. KISUNLA should be administered under the supervision of a multidisciplinary team trained in detection, monitoring and management of Amyloid Related Imaging Abnormalities (ARIA) and experienced in detecting and managing infusion related reactions.

The recommended dose of donanemab is 350 mg for the first dose, 700 mg for the second dose, 1050 mg for the third dose (350/700/1050 mg), followed by 1400 mg every 4 week. Treatment should be maintained until amyloid plaques are cleared, as confirmed using a validated method, up to a maximum of 18 months. Treatment should be continued for up to 18 months if monitoring of amyloid plaque clearance with a validated method is not possible. The benefit-risk of treatment should be reassessed at regular intervals on an individual basis and if the patient progresses to moderate Alzheimer's disease.

Monitoring and dosing interruption for amyloid related imaging abnormalities

A recent (within 6 months) baseline brain magnetic resonance imaging (MRI) should be available prior to initiating treatment. An MRI should be performed prior to the second dose (one month), prior to the third dose (two months), prior to the fourth dose (usually three months) and prior to the seventh dose (usually six months). The recommendations for dosing interruptions for patients with amyloid-related imaging abnormalities-oedema/effusions (ARIA-E) and amyloid-related imaging abnormalities haemorrhage/hemosiderin deposition (ARIA-H) are provided in Table 1.

Table 1: Dosing Recommendations for Patients with ARIA-E and ARIA-H

	ARIA-E and ARIA-H Severity on MRI		
Clinical Symptom	**Mild**	**Moderate**	**Severe**
Asymptomatic	Consider suspending dosing	Suspend dosing	Suspend dosing
Symptomatic	Suspend dosing		

Contraindications

Hypersensitivity to donanemab or to any of the excipients listed in the excipients.

Baseline MRI findings of prior intracerebral haemorrhage greater than 1 cm, more than 2 microhaemorrhages, superficial siderosis or vasogenic oedema (ARIA-E), which are suggestive of cerebral amyloid angiopathy (CAA).

Severe white matter disease.

Any finding that could prevent a satisfactory MRI evaluation for safety monitoring.

Interactions

No drug interaction studies have been performed. No pharmacokinetic: drug interactions are expected based on the characteristics of donanemab.

Adverse Effects

Treatment Emergent Adverse Events Occurring in ≥2% of Placebo-Controlled Donanemab-Treated Patients

Gastrointestinal disorders

Nausea

Vomitting

General disorders and administration site conditions

Asthenia

Infections and infestations

Nasopharyngitis

Injury, poisoning and procedural complications

Fall

Infusion related reactions

Skin laceration

Investigations

Weight decreased

Metabolism and nutrition disorders

Dehydration

Musculoskeletal and connective tissue disorders

Arthralgia

Pain in extremity

Neoplasm benign, malignant and unspecified (incl cysts and polyps)

Basal cell carcinoma

Nervous system disorders

Amyloid related imaging abnormality oedema / effusion

Amyloid related imaging abnormality – microhaemorrhages and haemosiderin deposits

Headache

Superficial siderosis of central nervous system

Dizziness

Syncope

Cerebral microhaemorrhage

Psychiatric disorders

Depression

Insomnia

Reproductive system and breast disorders

Benign prostatic hyperplasia

Pharmacological Properties

Pharmacodynamic Properties

Reductions in cerebral amyloid plaques, as measured by amyloid positron emission tomography (PET), were observed among patients receiving donanemab. Donanemab reduced tau pathophysiology, as measured by plasma P-tau217.

Mechanism of action

Donanemab is an immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against an insoluble, pyroglutamate N terminal truncated form of amyloid beta (N3pE Aβ) present only in brain amyloid plaques. Donanemab binds to N3pE Aβ and aids plaque removal through microglial-mediated phagocytosis.

Biomarkers

The percentage of donanemab treated patients with amyloid clearance (that is, less than 24.1 Centiloids or visually negative on an amyloid PET scan) in Study TRAILBLAZER-ALZ2.

Forensic classification

P1S1S3