RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	Monjuvi®
Generic Name	tafasitamab-cxix
Drug Manufacturer	Morphosys us inc.

New Drug Approval

FDA Approval Date: July 31, 2020
Review Designation: Orphan
Type of Review: Biologics License Application 761163

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

It is a type of blood cancer that develops when white blood cells called lymphocytes grow out of control. Lymphocytes are part of your immune system. They travel around your body in your lymphatic system, helping you fight infections. There are two types of lymphocyte: T lymphocytes (T cells) and B lymphocytes (B cells).
There are lots of different types of lymphoma. Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma. It is a fast-growing (high-grade) lymphoma.
Diffuse large B cell lymphoma (DLBCL) is the most common lymphoma and accounts for approximately 25 percent of all NHLs in the developed world. In the United States and England, the incidence of DLBCL is approximately 7 cases per 100,000 persons per year. In Europe as a whole, the incidence is approximately 4.92 cases per 100,000 persons per year. Incidence varies by ethnicity, with Caucasian Americans having higher rates than Blacks, Asians, and American Indian or Alaska Natives, in order of decreasing incidence. By comparison, the incidence in Denmark is approximately 3 cases per 100,000 adults per year [9]. DLBCL appears to be a more frequent subtype of NHL in Central and South America, where it accounts for approximately 40 percent of NHLs

Efficacy

The efficacy of Monjuv in combination with lenalidomide followed by MONJUVI as monotherapy was evaluated in L-MIND, an open label, multicenter single arm trial (NCT02399085). Eligible patients had relapsed or refractory DLBCL after 1 to 3 prior systemic therapies, including a CD20-directed cytolytic antibody, and were not candidates for high dose chemotherapy (HDC) followed by autologous stem cell transplantation (ASCT). Patients received MONJUVI 12 mg/kg intravenously in combination with lenalidomide (25 mg orally on Days 1 to 21 of each 28-day cycle) for maximum of 12 cycles, followed by MONJUVI as monotherapy until disease progression or unacceptable toxicity as follows:

- Cycle 1: Days 1, 4, 8, 15 and 22 of the 28-day cycle;
- Cycle 2 and 3: Days 1, 8, 15 and 22 of each 28-day cycle;
- Cycles 4 and beyond: Days 1 and 15 of each 28-day cycle.

Of the 71 patients with DLBCL confirmed by central laboratory who received the combination therapy, the median age was 71 years (range: 41 to 86 years); 55% were males, and 100% had received a prior CD20-containing therapy. Race was collected in 92% of patients; of these, 95% were White and 3% were Asian. The median number of prior therapies was two; 49% had one prior line of treatment, and 51% had 2 to 4 prior lines. Thirty two patients

(45%) were refractory to their last prior therapy and 30 (42%) were refractory to rituximab. Nine patients (13%) had received prior ASCT. The primary reasons patients were not candidates for ASCT included age (47%), refractoriness to salvage chemotherapy (27%), comorbidities (13%) and refusal of high dose chemotherapy/ASCT (13%). Reference ID: 4650017 Efficacy was established based on best overall response rate, defined as the proportion of complete and partial responders, and duration of response, as assessed by an Independent Review Committee using the International Working Group Response Criteria (Cheson 2007).

Safety

ADVERSE EVENTS

Lymphoma The most common adverse reactions (≥20%) are neutropenia, fatigue, anemia, diarrhea, thrombocytopenia, cough, pyrexia, peripheral edema, respiratory tract infection, and decreased appetite.

WARNINGS & PRECAUTIONS

- Infusion-Related Reactions: Monitor patients frequently during infusion. Interrupt or discontinue infusion based on severity.
- Myelosuppression: Monitor complete blood counts. Manage using dose modifications and growth factor support. Interrupt or discontinue MONJUVI based on severity.
- Infections: Bacterial, fungal and viral infections can occur during and following MONJUVI. Monitor patients for infections.
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS OF ACTION

Tafasitamab-cxix is an Fc-modified monoclonal antibody that binds to CD19 antigen expressed on the surface of pre-B and mature B lymphocytes and on several B-cell malignancies, including diffuse large B-cell lymphoma (DLBCL). Upon binding to CD19, tafasitamab-cxix mediates B-cell lysis through apoptosis and immune effector mechanisms, including antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).

Dose & Administration

ADULTS

Administer premedications prior to starting MONJUVI.

• The recommended dosage of MONJUVI is 12 mg/kg as an intravenous infusion according to the following dosing schedule:

• Cycle 1: Days 1, 4, 8, 15 and 22 of the 28-day cycle.

• Cycles 2 and 3: Days 1, 8, 15 and 22 of each 28-day cycle.

• Cycle 4 and beyond: Days 1 and 15 of each 28-day cycle.

• Administer MONJUVI in combination with lenalidomide for a maximum of 12 cycles and then continue MONJUVI as monotherapy until disease progression or unacceptable toxicity.

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PEDIATRICS

The safety and effectiveness of MONJUVI in pediatric patients have not been established.

GERIATRICS

Among 81 patients who received MONJUVI and lenalidomide in L-MIND, 72% were 65 years and older, while 38% were 75 years and older. Clinical studies of MONJUVI did not include sufficient numbers of patients aged 65 and older to determine whether effectiveness differs compared to that of younger subjects. Patients 65 years and older had more serious adverse reactions (57%) than younger patients (39%).

RENAL IMPAIRMENT

Mild to moderate renal impairment (CLcr 30-89 mL/min estimated by the Cockcroft-Gault equation).

HEPATIC IMPAIRMENT

Mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN, or total bilirubin 1 to 1.5 times ULN and any AST).

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

For injection: 200 mg of tafasitamab-cxix as lyophilized powder in singledose vial for reconstitution.