VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Arzerra (ofatumumab)

Effective Date: 10/22/13

Date Developed: 9/3/13 by Albert Reeves MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

Pharmacologic Category: Antineoplastic Agent, Monoclonal Antibody;

Authorization Criteria: previously untreated CLL (in combination with chlorambucil) when fludarabine-based therapy is considered inappropriate; CLL refractory to fludarabine and alemtuzumab

Dosage: **Adult**

Note: Premedicate with acetaminophen, an antihistamine, and a corticosteroid 30-120 minutes prior to treatment (see Administration).

CLL: I.V. Initial dose: 300 mg week 1, followed 1 week later by 2000 mg once weekly for 7 doses (doses 2-8), followed 4 weeks later by 2000 mg once every 4 weeks for 4 doses (doses 9-12; for a total of 12 doses

. Administration: **Do not administer I.V. push or as a bolus.** Premedicate with acetaminophen, an antihistamine, and a corticosteroid 30-120 minutes prior to administration. Administer with an in-line filter (supplied) and polyvinyl chloride (PVC) administration sets. Do not mix with or infuse with other medications. Flush line before and after infusion with NS. Begin infusion within 12 hours of preparation. The final concentration of dose 1 is 0.3 mg/mL and final concentration of doses 2-12 is 2 mg/mL.

Premedication: Premedicate with oral acetaminophen (1000 mg), an oral or I.V. antihistamine (eg, cetirizine 10 mg orally or equivalent), and an I.V. corticosteroid. Full dose corticosteroid is recommended for doses 1, 2, and 9; in the absence of infusion reaction ≥grade 3, may gradually reduce corticosteroid dose for doses 3-8; administer full or half corticosteroid dose with doses 10-12 if ≥grade 3 did not occur with dose 9.

Doses 1 and 2: Initiate infusion at 12 mL/hour for 30 minutes, if tolerated (no infusion reaction) increase to 25 mL/hour for 30 minutes, if tolerated, increase to 50 mL/hour for 30 minutes, if tolerated, increase to 100 mL/hour for 30 minutes, if tolerated, increase to 200 mL/hour for duration of infusion.

Doses 3-12: Initiate infusion at 25 mL/hour for 30 minutes, if tolerated (no infusion reaction) increase to 50 mL/hour for 30 minutes, if tolerated, increase to 100 mL/hour for 30 minutes, if tolerated, increase to 200 mL/hour for 30 minutes, if tolerated, increase to 400 mL/hour for remainder of infusion.

Major adverse reactions and Black Box Warnings:

>10%:

Central nervous system: Fatigue (15%)

Dermatologic: Skin rash (14%)

Gastrointestinal: Diarrhea (18%), nausea (11%)

Hematologic & oncologic: Neutropenia (≥grade 3: 42%; grade 4: 18%; may be prolonged >2 weeks), anemia (16%; grades 3/4: 5%)

Infection: Infection (70%; includes bacterial, fungal, or viral; ≥grade 3: 29%)

Respiratory: Pneumonia (23%), cough (19%), dyspnea (14%), bronchitis (11%), upper respiratory tract infection (11%)

Miscellaneous: Infusion related reaction (first infusion [300 mg]: 44%; second infusion [2000 mg]: 29%), fever (20%)

1% to 10%:

Cardiovascular: Peripheral edema (9%), hypertension (5%), hypotension (5%), tachycardia (5%)

Central nervous system: Chills (8%), insomnia (7%), headache (6%)

Dermatologic: Urticaria (8%), hyperhidrosis (5%)

Infection: Sepsis (8%), herpes zoster (6%)

Neuromuscular & skeletal: Back pain (8%), muscle spasm (5%) Respiratory:

Nasopharyngitis (8%), sinusitis (5%)

<1% (Limited to important or life-threatening): Angina pectoris, bacteremia, hemolytic anemia, hepatitis B (new onset or reactivation), hepatitis (cytolytic), hypoxia, interstitial pulmonary disease (infectious), intestinal obstruction, peritonitis, progressive multifocal leukoencephalopathy (PML), rigors, sepsis (neutropenic), septic shock, thrombocytopenia

Contraindications

There are no contraindications listed within the manufacturer's labeling.

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References:

1. Coiffier B, Lepretre S, Pedersen LM, et al, "Safety and Efficacy of Ofatumumab, a Fully Human Monoclonal Anti-CD20 Antibody, in Patients With Relapsed or Refractory B-Cell Chronic Lymphocytic Leukemia: A Phase 1-2 Study," *Blood*, 2008, 111(3):1094-100. [PubMed 18003886]
2. Hagenbeek A, Gadeberg O, Johnson P, et al, "First Clinical Use of Ofatumumab, a Novel Fully Human Anti-CD20 Monoclonal Antibody in Relapsed or Refractory Follicular Lymphoma: Results of a Phase 1/2 Trial," *Blood*, 2008, 111(12):5486-95. [PubMed 18390837]
3. Kipps TJ, Osterborg A, Mayer J, et al, "Clinical Improvement With a Novel CD20 mAb, Ofatumumab, in Fludarabine-Refractory Chronic Lymphocytic Leukemia (CLL) Also Refractory to Alemtuzumab or With Bulky Lymphadenopathy," *J Clin Oncol*, 2009, 27(15s):7043 [abstract 7043 from 2009 ASCO Annual Meeting].
4. National Comprehensive Cancer Network® (NCCN), "Clinical Practice Guidelines in Oncology™: Non-Hodgkin's Lymphomas," Version 4.2009. Available at http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf
5. Osterborg A, Kipps TJ, Mayer J, et al, "Ofatumumab (HuMax-CD20), a Novel CD20 Monoclonal Antibody, is an Active Treatment for Patients With CLL Refractory to Both Fludarabine and Alemtuzumab or Bulky Fludarabine-Refractory Disease: Results from the Planned Interim Analysis of an International Pivotal Trial," *Blood*, 2008, 112(11):328 [abstract 328 from 2008 ASH Annual Meeting].
6. Wierda WG, Kipps T, Mayer J, et al, "Activity of Ofatumumab, a Novel CD20 mAb, and Prior Rituximab Exposure in Patients With Fludarabine-and Alemtuzumab-Refractory or Bulky Fludarabine-Refractory Chronic Lymphocytic Leukemia (CLL)," *J Clin Oncol*, 2009, 27(15s):7044 [abstract 7044 from ASCO Annual Meeting].

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Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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