Aetna considers ofatumumab (Arzerra) medically necessary for the treatment of individuals with the following indications:

Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)  
Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma.

Aetna considers ofatumumab experimental and investigational for the treatment of the following criteria:

• Use not approved by the FDA; AND

• The use is unapproved and not supported by the literature or evidence as an accepted off-label use.

See also CPB 0314 - Rituximab (Rituxan) and CPB 0764 - Alemtuzumab (Campath).

Background

Chronic lymphocytic leukemia (CLL), affecting primarily individuals aged 50 years or older, is a type of non-Hodgkin's lymphoma (NHL) that results from an accumulation of partially
differentiated lymphocytes. Each year, approximately 16,000 individuals are diagnosed with CLL in the United States, and about 4,400 succumb to the disease. Chronic lymphocytic leukemia can affect the liver, spleen, and lymph nodes. The disruption of normal lymphocyte production leaves patients with CLL vulnerable to infections; anemia and thrombocytopenia are also common complications. Some CLL cells express a substance called ZAP-70, which is a marker for an aggressive form of CLL that is more likely to progress. Treatments for lymphomas depend on the disease type, stage, and other prognostic markers. Because certain lymphomas are categorized as indolent, "watchful waiting" is an option for some patients with follicular NHL or low-risk CLL. Neither NHL nor CLL has been shown to be curable by any standard treatment.

The Guidelines Working Group of the United Kingdom CLL Forum/British Committee for Standards in Haematology's guidelines on the diagnosis and management of CLL (Oscier et al, 2004) noted that for the majority of patients who are ineligible for a transplant procedure and in whom there is no contraindication to fludarabine (e.g., severe renal impairment or an autoimmune cytopenia), both fludarabine and chlorambucil are therapeutic options. Patients in whom fludarabine is contraindicated and for whom a palliative approach has been adopted should be treated with chlorambucil. Moreover, there is no survival advantage for including an anthracycline with chlorambucil in the initial treatment of advanced CLL. Montserrat (2006) stated that an important area of research in the prognosis of CLL is the identification of markers useful for predicting response to therapy and its duration. Among them, del(17p), reflecting P53 abnormalities, is particularly important. In this regard, Lindhagen and colleagues (2009) noted that cells from patients with unfavorable genomic aberrations [del(11q)/del(17p)] showed lower drug sensitivity to fludarabine and chlorambucil than cells from patients with favorable cytogenetics [del(13q)/no aberration].

Bosch et al (2008) examined fludarabine, cyclophosphamide, and mitoxantrone (FCM) as first-line therapy in CLL. A total of 69 patients under the age of 65 years with active CLL were treated. Patients received 6 cycles of fludarabine 25 mg/m² intravenous (IV) x 3 days, cyclophosphamide 200 mg/m² IV x 3 days, and mitoxantrone 6 mg/m² IV x 1 day. Treatment outcome was correlated with clinical and biological variables. The clinical significance of eradicating minimal residual disease (MRD) was also analyzed. The overall response, MRD-negative complete response (CR), MRD-positive CR, nodular partial response (PR), and PR rates were 90 %, 26 %, 38 %, 14 %, and 12 %, respectively. Severe (grades 3 or 4) neutropenia developed in 10 % of the patients. Major and minor infections were reported in 1 % and 8 % of cases, respectively. Median response duration was 37 months. Patients with del(17p) failed to attain CR. Patients achieving MRD-negative CR had a longer response duration and overall survival (OS) than patients with an inferior response. Low serum lactate dehydrogenase levels, low ZAP-70 expression, and mutated IgV(H) genes predicted longer response duration. Finally, both low ZAP-70 and CD38 expression in leukemic cells correlated with MRD-negativity achievement. The authors concluded that FCM induces a high response rate, including MRD-negative CRs in untreated patients with active CLL. Treatment toxicity is acceptable. Both high ZAP-70 and increased CD38 expression predict failure to obtain MRD-negative response. Patients in whom MRD can be eradicated have longer response duration and OS than those with inferior response. These results indicate that FCM can be an ideal companion for chemo-immunotherapy of patients with CLL.

The National Comprehensive Cancer Network (NCCN)'s Clinical Practice Guidelines in
Ofatumumab (Arzerra)  

Oncology on NHL (2010) noted that the first line therapy for CLL without del(17p) include monotherapy (e.g., alemtuzumab, bendamustine, chlorambucil, fludarabine, and rituximab), purine-analog therapy (fludarabine, cyclophosphamide [FC]), chemotherapeutic agents (e.g., fludarabine, rituximab [FR]; fludarabine, cyclophosphamide, rituximab [FCR]; and pentostatin, cyclophosphamide, rituximab [PCR]), as well as alkylating agent-based chemotherapy (e.g., cyclophosphamide, prednisone and vincristine, [CPV]). For CLL with del(17p) with greater than 20 % cells, the first-line therapy include alemtuzumab, CFAR (FCR + alemtuzumab), FR, FCR and high-dose methylprednisone plus rituximab (HDMP + R).

Christian and Lin (2008) stated that the introduction of rituximab (anti-CD20) and alemtuzumab (anti-CD52) has revolutionized the treatment of CLL. Both antibodies were first studied as single agents in relapsed CLL, but rituximab is increasingly used in combination chemo-immunotherapy regimens in previously untreated patients. Phase II studies demonstrated that the addition of rituximab to fludarabine-based chemotherapy improves CR rates and prolongs progression-free survival, but a long-term survival benefit has not been shown. Alemtuzumab is less commonly used, due to the greater likelihood of infusion toxicity, as well as hematologic and immune toxicities. Subcutaneous administration significantly reduces infusion toxicity, but hematologic and infectious complications, most notably cytomegalovirus reactivation, still occur with subcutaneous dosing. Alemtuzumab's unique clinical properties include its clinical activity in relapsed CLL patients with del(17p13) and its ability to eradicate MRD in bone marrow. Its use as consolidation therapy to eradicate MRD after nucleoside analog therapy is under active study. Several investigational monoclonal antibodies are in pre-clinical or clinical studies, most notably lumiliximab and ofatumumab.

Ofatumumab (HuMax CD20) is a human anti-CD20 monoclonal antibody; CD20 is a transmembrane protein antigen that is expressed on B lymphocytes, from the pre-B-cell stage through the mature stage, but is not expressed on stem cells or plasma cells. Anti-CD20 therapy thus specifically targets B-cells, and induces cell death through antibody dependent cellular cytotoxicity. The first anti-CD20 antibody approved was rituximab (Rituxan), a chimeric mouse-human antibody that has been in use since 1997 and is now commonly used in the management of patients with NHL. Ofatumumab is a fully human monoclonal antibody that may have the advantage of improved efficacy and pharmacokinetics with fewer adverse effects compared to chimeric antibodies. Recent evidence suggested that a fully human anti-CD20 monoclonal antibody binds to unique epitopes on the CD20 antigen and appears to initiate cytotoxic processes not demonstrated by rituximab (Ingenix, 2009).

In a phase I/II clinical study, Hagenbeek et al (2008) evaluated the safety and effectiveness of ofatumumab in relapsed or refractory follicular NHL (FL) grade 1 or 2. Four dose groups of 10 patients received 4 weekly infusions of 300, 500, 700, or 1,000 mg. Patients had a median of 2 prior FL therapies and 13 % had elevated lactate dehydrogenase. No safety concerns or maximum tolerated dose (MTD) was identified. A total of 274 adverse events were reported; 190 were judged related to ofatumumab, most occurring on the first infusion day with Common Terminology Criteria grade 1 or 2. Eight related events were grade 3. Treatment caused immediate and profound B-cell depletion, and 65 % of patients reverted to negative BCL2 status. Clinical response rates ranged from 20 % to 63 %. Median time to progression for all patients/responders was 8.8/32.6 months, and median duration of response was 29.9 months at a median/maximum follow-
up of 9.2/38.6 months. The authors noted that ofatumumab is currently being evaluated in patients with rituximab-refractory FL.

In a phase I/II study, Coiffier et al (2008) analyzed the safety and effectiveness of ofatumumab in a multi-center dose-escalating study including 33 patients with relapsed or refractory CLL. Three cohorts of 3 (A), 3 (B), and 27 (C) patients received 4, once-weekly, infusions of ofatumumab at the following doses: (A) one 100-mg and three 500-mg; (B) one 300-mg and three 1,000-mg; (C) one 500 mg and three 2,000-mg. A total of 67 % of the patients were Binet stage B, and the median number of previous treatments was 3. The MTD was not reached. The majority of related adverse events occurred at first infusion, and the number of adverse events decreased at each subsequent infusion. Seventeen (51 %) of 33 patients experienced infections, 88 % of them of grade 1 to 2. One event of interstitial pneumonia was fatal; all other cases resolved within 1 month. The response rate of cohort C was 50 % (13/26), 1 patient having a nodular partial remission and 12 patients partial remission. The authors concluded that ofatumumab was found to be well-tolerated in patients with CLL in doses up to 2,000 mg. Preliminary data on safety and objective response are encouraging and support further studies on the role of ofatumumab in CLL patients. Furthermore, in a review on modern concepts in the treatment of CLL, Smolej (2009) noted that the monoclonal antibody anti-CD20 ofatumumab is currently undergoing clinical trials with promising results.

On October 26, 2009, Arzerra (ofatumumab) was approved under the Food and Drug Administration (FDA)'s accelerated approval process. Arzerra was approved for patients with CLL whose cancer is no longer being controlled by other forms of chemotherapy, specifically fludarabine and alemtuzumab. The labeling notes that the effectiveness of ofatumumab is based on demonstration of durable objective responses, and that no data demonstrate an improvement in disease-related symptoms or increased survival with ofatumumab. The safety and effectiveness of Arzerra was examined in a single-arm, multi-center study in 154 patients with relapsed or refractory CLL (Study 1). Arzerra was administered by IV infusion according to the following schedule: 300 mg (Week 0), 2,000 mg weekly for 7 infusions (weeks 1 through 7), and 2,000 mg every 4 weeks for 4 infusions (weeks 12 through 24). Patients with CLL refractory to fludarabine and alemtuzumab (n = 59) comprised the efficacy population. Drug refractoriness was defined as failure to achieve at least a PR to, or disease progression within 6 months of, the last dose of fludarabine or alemtuzumab. The main efficacy outcome was durable objective tumor response rate. Objective tumor responses were determined using the 1996 National Cancer Institute Working Group Guidelines for CLL. In patients with CLL refractory to fludarabine and alemtuzumab, the median age was 64 years (range of 41 to 86 years), 75 % were male, and 95 % were White. The median number of prior therapies was 5; 93 % received prior alkylating agents, 59 % received prior rituximab, and all received prior fludarabine and alemtuzumab. Eighty-eight percent of patients received at least 8 infusions of Arzerra and 54 % received 12 infusions. The investigator-determined overall response rate (ORR) in patients with CLL refractory to fludarabine and alemtuzumab was 42 % (99 % confidence interval [CI]: 26 to 60) with a median duration of response of 6.5 months (95 % CI: 5.8 to 8.3). There were no complete responses. Antitumor activity was also observed in additional patients in Study 1 and in a multi-center, open-label, dose-escalation study (Study 2) conducted in patients with relapsed or refractory CLL (SmithKline Beecham Corporation Product Insert for Arzerra, 2009).

Ofatumumab is listed in NCCN's Drug and Biologics Compendium (2015) as: first-line therapy in combination with chlorambucil for CLL/SLL without del(17p) or with or without
del(11q) in patients age ≥70 years or in younger patients with significant comorbidities who have indications for treatment; therapy for CLL/SLL in patients with indications for treatment who are unable to tolerate purine analogs in combination with chlorambucil; therapy for relapsed or refractory CLL/SLL in patients with del(11q) or del (17p); and therapy for relapsed or refractory disease without del(11q) or del(17p) in patients with indications for treatment.

Common side effects of Arzerra include cough, diarrhea, fatigue, fever, nausea, pneumonia, rash, shortness of breath, decreased normal white blood cell and red blood cell counts, as well as bronchitis and upper respiratory tract infections. The most serious side effects of Arzerra are increased chance of infections, including progressive multifocal leukoencephalopathy. Patients at high-risk for hepatitis B should be screened before being treated with Arzerra. Patients with evidence of inactive hepatitis should be monitored for re-activation of the infection during and after completing treatment (SmithKline Beecham Corporation Product Insert for Arzerra, 2009).

In April 2014, the FDA approved ofatumumab in combination with chlorambucil, for the treatment of previously untreated patients with CLL, for whom fludarabine-based therapy is considered inappropriate. This approval was based on the results of a multi-center, randomized, open-label trial comparing ofatumumab in combination with chlorambucil to single agent chlorambucil. The trial enrolled 447 patients for whom fludarabine-based therapy was considered to be inappropriate by the investigator for reasons that included advanced age or presence of co-morbidities. In the overall trial population the median age was 69 years (range: 35 to 92 years). Seventy-two percent of patients had two or more co-morbidities and 48% of patients had a creatinine clearance of less than 70 mL/min. Patients received ofatumumab as an intravenous infusion according to the following schedule: 300 mg administered on cycle 1 day 1, 1000 mg administered on cycle 1 day 8 and 1000 mg administered on day 1 of all subsequent 28 day cycles. In both arms, chlorambucil was given at a dose of 10 mg/m² orally on days 1 to 7 every 28 days. Prior to each infusion of ofatumumab, patients received pre-medication with acetaminophen, an antihistamine, and a glucocorticoid.

The primary endpoint of the trial was progression free survival (PFS) as assessed by a blinded Independent Review Committee (IRC) using the 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) update of the National Cancer Institute Working Group (NCI-WG) guidelines. Median PFS was 22.4 months (95% CI: 19.0, 25.2 months) for patients receiving Arzerra in combination with chlorambucil compared to 13.1 months (95% CI: 10.6, 13.8 months) for patients receiving single-agent chlorambucil [hazard ratio 0.57 (95% CI: 0.45, 0.72), stratified log-rank p-value less than 0.001].

The most common adverse reactions (greater than or equal to 5%) with ofatumumab in combination with chlorambucil (greater than or equal to 2% more than in the control arm) were infusion reactions, neutropenia, asthenia, headache, leukopenia, herpes simplex, lower respiratory tract infection, arthralgia and upper abdominal pain. Overall, 67% of patients who received ofatumumab experienced one or more symptoms of infusion reaction. Ten percent of patients experienced a grade 3 or greater infusion reaction.

The results of this randomized trial were adequate to fulfill the postmarketing requirement for GlaxoSmithKline to verify the clinical benefit of ofatumumab and, therefore, the approval of ofatumumab was converted from accelerated approval to regular approval.
The recommended dose and schedule for the approved regimen for ofatumumab in previously untreated CLL is:

300 mg on Day 1 followed 1 week later by 1,000 mg on Day 8 (Cycle 1) followed by 1,000 mg on Day 1 of subsequent 28 day cycles for a minimum of 3 cycles until best response or a maximum of 12 cycles.

The clinical success of B-cell depletion using the anti-CD20 antibody rituximab has sparked a new era in the therapy of rheumatic diseases. In this regard, ofatumumab has also been studied in the treatment of rheumatoid arthritis (RA) as well as other autoimmune diseases (e.g., Crohn's disease, multiple sclerosis, vasculitis, and Wegener's granulomatosis). Dorner and Burmester (2008) reviewed therapeutic approaches of direct and indirect B-cell targeting in autoimmune diseases and their impact on protective immunity. They noted that beyond recent clinical experiences with rituximab as B-cell-depleting agent, other biologicals targeting CD20, such as ocrelizumab, ofatumumab, hA20, and TRU-015 mainly deplete B cells and are under clinical investigation in different entities. Moreover, anti-CD22 targeting as another approach that has been studied in clinical trials showed a modest depletion, but inhibition of B-cell activation. More indirect innovative B-cell-affecting therapies comprise blockade of cytokines, such as B-cell-activating factor, and their receptors as well as blockade of co-stimulation. Although decreases of immunoglobulin levels were seen, so far no major increases in infections were reported. The authors concluded that the value of certain B-cell-depletion therapies as well as other therapies modulating B-cell functions needs to be further delineated, especially in the therapeutic regimen of RA, specific collagen vascular diseases and vasculitis. They stated that long-term observations of protective immunity are also needed to further evaluate the rate of infections. Furthermore, Castillo et al (2009) stated that phase II clinical trials of ofatumumab for patients with aggressive lymphoma and multiple sclerosis are also under development.

In a phase I/II randomized, double-blind, placebo-controlled, clinical trial, Ostergaard and colleagues (2010) examined the safety and effectiveness of ofatumumab in patients with active RA whose disease did not respond to greater than or equal to 1 disease-modifying anti-rheumatic drug. This study investigated the safety and effectiveness of 3 doses of ofatumumab. In part A (phase I), 39 patients received 2 intravenous (i.v.) infusions of ofatumumab (300 mg, 700 mg, or 1,000 mg) or placebo in a 4:1 ratio 2 weeks apart, using a specified pre-medication and infusion regimen. In part B (phase II), 225 patients received study treatment as per phase I in a 1:1:1:1 ratio. Safety was assessed by adverse events (AEs) and laboratory parameters. Effectiveness was assessed by the American College of Rheumatology 20 % criteria for improvement (ACR20), the Disease Activity Score in 28 joints, and the European League Against Rheumatism (EULAR) response criteria; B cell pharmacodynamics were also investigated. Adverse events were predominantly reported at the first infusion and were mostly mild-to-moderate in intensity. Rapid and sustained peripheral B cell depletion was observed in all dose groups. In phase II, patients in all ofatumumab dose groups had significantly higher ACR20 response rates (40 %, 49 %, and 44 % for the 300 mg, 700 mg, and 1,000 mg doses, respectively) than did patients receiving placebo (11 %) at week 24 (p < 0.001). Overall, 70 % of patients receiving ofatumumab had a moderate or good response according to the EULAR criteria at week 24. The authors concluded that these findings indicate that ofatumumab, administered as 2 i.v. infusions of doses up to 1,000 mg, is clinically effective in patients
with active RA. These findings need to be validated by phase III studies with larger number of subjects and longer follow-up.

Robak and Robak (2009) stated that systemic lupus erythematosus (SLE) is an autoimmune disease characterized by B cell hyperactivity and defective T-cell function, with production of high titer autoantibodies. In recent years, conceptual advances and the introduction of new therapies are yielding improvements in the management of this disease. Clinical studies have been undertaken with selected monoclonal antibodies (mAbs) in the treatment of SLE. The important role of B cells in the pathogenesis of autoimmune disorders has provided a strong rationale to target B cells in SLE. Selective therapeutic depletion of B-cells became possible with the availability of the anti-CD20 antibody rituximab and anti-CD22 antibody epratuzumab. Several clinical studies confirm high activity of rituximab in SLE patients especially with lupus nephritis and neuropsychiatric involvement. Recently, several new mAbs reacting with CD20 have been developed. New mAbs directed against CD20 include fully human mAb ofatumumab, IMMU-106 which has a greater than 90 % humanized framework and GA-101, a novel third-generation fully humanized and optimized mAb. These agents are highly cytotoxic against B-cell lymphoid cells. Pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6 play an important role in propagating the inflammatory process responsible for tissue damage. Blocking of these cytokines by mAbs can be also a successful therapy for patients with SLE.

In a review on the use of ofatumumab for the treatment of B-cell malignancies, Cheson (2010) noted that pre-clinical data suggest improved complement-dependent cytotoxicity and antibody-dependent cellular cytotoxicity of ofatumumab compared with rituximab. In early clinical trials, ofatumumab demonstrated single-agent activity against CLL and a number of histologies of B-cell NHL. This antibody was recently approved by the FDA for the treatment of CLL that is resistant to both fludarabine and alemtuzumab. Additional study is ongoing with ofatumumab in combination with chemotherapy and biologic agents to further enhance its efficacy.

Stedman and colleagues (2010) noted that Waldenstrom macroglobulinemia (WM) is a B-cell disorder characterized by the infiltration of the bone marrow (BM) with lymphoplasmacytic cells, as well as detection of an IgM monoclonal gammapathy in the serum. Waldenstrom macroglobulinemia is an incurable disease, with an overall medial survival of only 5 to 6 years. First-line therapy of WM has been based on single-agent or combination therapy with alkylator agents (e.g., chlorambucil or cyclophosphamide), nucleoside analogs (cladribine or fludarabine), and the monoclonal antibody rituximab. Novel therapeutic agents that have demonstrated efficacy in WM include thalidomide, lenalidomide, bortezomib, everolimus, Atacicept, and perifosine. The range of the ORR to these agents is between 25 to 80 %. Ongoing and planned future clinical trials include those using protein-kinase C inhibitors such as enzastaurin, new proteasome inhibitors such as carfilzomib, histone deacetylase inhibitors such as panobinostat, humanized CD20 antibodies such as ofatumumab, and additional alkylating agents such as bendamustine. These agents, when compared to traditional chemotherapeutic agents, may lead in the future to higher responses, longer remissions and better quality of life for patients with WM.

The NCCN's Drugs & Biologics Compendium (20125) recommends the use of ofatumumab in Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma as a single-agent or combination therapy in rituximab-intolerant patients for previously
treated disease that does not respond to primary therapy or for progressive or relapsed disease.

In a case study, Pranzatelli and associates (2012) used ofatumumab in the treatment of a rituximab-allergic child with severe, chronic-relapsing, opsoclonus-myoclonus syndrome (OMS), characterized by persistent cerebrospinal fluid (CSF) B-cell expansion and T-cell dysregulation. The patient had relapsed despite chemotherapy, plasma exchange with immunoadsorption, and resection of ganglio-neuroblastoma, detected 3 years after OMS onset. The 4 ofatumumab infusions (1,195 mg/m(2) total dose) were well-tolerated, and CSF B-cell expansion was eliminated. No further relapses have occurred in 3 years, but he remains on low-dose adrenocorticotropin hormone with neuropsychiatric residuals of OMS. The effectiveness of ofatumumab in the treatment of OMS needs to be examined in well-designed studies.

Gupta and Jewell (2012) noted that ofatumumab is the first human anti-CD20 monoclonal antibody to be approved for patients in the United States and the European Union. Ofatumumab received accelerated approval from the U.S. FDA in October 2009 and was granted a conditional marketing authorization by the European Medicines Agency in April 2010 for the treatment of patients with CLL refractory to fludarabine and alemtuzumab, based on interim results of a pivotal phase 2 trial. Preliminary positive results for ofatumumab in combination with chemotherapy in patients with CLL are currently being confirmed in larger randomized trials in both the front-line setting as well as the relapsed/refractory setting. Ofatumumab has also shown potential in treating B cell non-Hodgkin's lymphoma, such as follicular lymphoma, diffuse large B cell lymphoma, and Waldenström's macroglobulinemia. The authors stated that additional trials are ongoing to confirm activity of ofatumumab as monotherapy and in combination with chemotherapy in patients with follicular lymphoma or diffuse large B cell lymphoma.

Nicholas et al (2012) stated that the therapeutic landscape for multiple sclerosis (MS) is rapidly changing. Currently, there are 8 FDA-approved disease modifying therapies for MS including: IFN-β-1a (Avonex, Rebif), IFN-β-1b (Betaseron, Extavia), glatiramer acetate (Copaxone), mitoxantrone (Novantrone), natalizumab (Tysabri), and fingolimod (Gilenya). These investigators highlighted the experience to-date and key clinical trials of the newest FDA-approved agents, natalizumab and fingolimod. They also reviewed available safety and effectiveness data on several promising therapies under active investigation including four monoclonal antibody therapies: alemtuzumab, daclizumab, ocrelizumab and ofatumumab and 3 agents: BG12, laquinimod, and teriflunomide.

In a review on "Current standards and future treatments of rheumatoid arthritis", Onysko and Burch (2012) listed ofatumumab as an emerging therapy for RA.

Matasar and colleagues (2013) stated that standard treatment of transplant-eligible patients with relapsed diffuse large B-cell lymphoma (DLBCL) consists of rituximab and platinum-based chemotherapy, either ifosfamide, carboplatin, and etoposide (ICE) or dexamethasone, cytarabine, and cisplatin (DHAP), with autologous transplant consolidation for those with chemosensitive disease. Nonetheless, outcomes are suboptimal for patients failing rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). These researchers performed a multi-center phase II trial investigating the safety and effectiveness of ofatumumab combined with ICE or DHAP second-line therapy in patients with relapsed or refractory DLBCL, grade 3b follicular lymphoma, or transformed follicular lymphoma. A total of 61 patients were treated with either ofatumumab-ICE (n = 35) or ofatumumab-DHAP (n = 26). The ORR was 61 %, and
the CR rate was 37%. In patients with 2 or 3 adverse risk factors according to the second-line, age-adjusted, international prognostic index, the ORR was 59% and CR 31%, and in patients with early-relapsing or primary refractory disease, the ORR was 55% and CR 30%. Toxicity was largely hematologic, and stem cell mobilization was successful in 43 of 45 patients. The authors concluded that substitution of ofatumumab for rituximab in standard second-line regimens following failure of R-CHOP is a promising approach.

CPT Codes / HCPCS Codes / ICD-9 Codes

Other CPT codes related to the CPB:

96365 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour

96379 Unlisted therapeutic, prophylactic, or diagnostic intravenous or intra-arterial injection or infusion

96413 Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug

96415 each additional hour (List separately in addition to code for primary procedure)Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

HCPCS codes covered if selection criteria are met:

J9302 Injection, ofatumumab, 10 mg [Arzerra]

ICD-9 codes covered if selection criteria are met:

204.10 Lymphoid leukemia, chronic, without mention of having achieved remission - failed remission [refractory and previously untreated persons whom fludarabine-based therapy is considered inappropriate]

204.12 Lymphoid leukemia, chronic, in relapse

273.3 Macroglobulinemia [Waldenstrom]

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):

200.20 - 200.48 Burkitt's tumor or lymphoma, marginal zone lymphoma, or mantle cell lymphoma

200.70 - 200.78 Large cell lymphoma

202.00 - 202.08 Nodular lymphoma

202.80 - 202.88 Other lymphomas [diffuse large B cell]

242.0 Toxic diffuse goiter [Graves' disease]
245.2 Chronic lymphocytic thyroditis [autoimmune] [Hashimoto’s disease]
255.41 Glucocorticoid deficiency [Addison’s disease]
279.00 - 279.9 Disorders involving the immune mechanism
287.31 Immune thrombocytopenic purpura
340 Multiple sclerosis
357.0 Acute infective polyneuritis [Guillain-Barre syndrome]
358.00 - 358.1 Myasthenia gravis
379.59 Other irregularities of eye movements [paraneoplastic opsoclonus-myoclonus]
446.21 Goodpasture’s syndrome
446.4 Wegener’s granulomatosis
447.6 Arteritis, unspecified [vasculitis]
555.0 - 555.9 Regional enteritis [Crohn’s disease]
564.1 Irritable bowel syndrome
571.42 Autoimmune hepatitis
579.0 Celiac disease
696.0 - 696.1 Psoriasis
710.0 Systemic lupus erythematosus
710.1 Systemic sclerosis
710.2 Sicca syndrome
714.0 - 714.33 Rheumatoid arthritis

The above policy is based on the following references:


20. Ostergaard M, Baslund B, Rigby W, et al. Ofatumumab, a human anti-CD20 monoclonal antibody, for treatment of rheumatoid arthritis with an inadequate response to one or more disease-modifying antirheumatic drugs: Results of a


