About **Arzerra® (ofatumumab)** and Chronic Lymphocytic Leukemia

**What is Chronic Lymphocytic Leukemia (CLL)?**

Cancers that originate in the blood, bone marrow, spleen or lymph nodes are typically categorized as hematological cancers\(^1,2\). Leukemia represents a class of hematological cancers in which the bone marrow produces abnormal cells, typically white blood cells\(^1,2\). Two factors are the basis for classifying leukemia: 1) whether the leukemia is chronic or acute, and 2) what type of bone marrow cells are affected (myeloid or lymphoid)\(^3\).

Four of the most common types of leukemia are\(^3\):

- chronic lymphocytic leukemia (CLL)
- acute lymphoblastic (also known as lymphocytic) leukemia (ALL)
- chronic myeloid (also known as myelogenous) leukemia (CML)
- acute myeloid (also known as myelogenous) leukemia (AML)

CLL, the most commonly diagnosed adult leukemia in Western countries, accounts for approximately one-third of all cases of leukemia\(^4,5,6\). In the majority of cases of CLL, there is an uncontrolled overproduction of B cell lymphocytes whose normal function is to fight infection. In people with CLL, B cell lymphocytes may appear normal, but do not fight infections correctly in the body. Instead, they progressively accumulate in the bone marrow, blood, spleen and lymph nodes, eventually crowding out healthy blood cells\(^7\). As a result, people with CLL are at an increased risk for infections, which may range from colds to more serious infections including pneumonia\(^7\).

The average age of diagnosis is 72 years old\(^5\), and approximately 90 percent of patients with CLL are estimated to be over the age of 55\(^8\). The majority of patients with CLL have at least one comorbidity, or simultaneously existing condition, such as hypertension, diabetes, cardiovascular disease or chronic obstructive pulmonary disease\(^9\).

**How is CLL Treated?**

There are no drug regimens (monotherapy or combination therapy) that are considered curative for CLL. Available drug regimens help patients control and manage their disease\(^7,10\). When recommending a treatment approach, physicians typically focus on the stage (or advancement) of the disease, its rate of growth, as well as a patient’s genetic and biological risk factors and fitness. Patients without symptoms or low blood counts (cytopenias) may not need therapy. Patients are treated if they develop significant symptoms, low blood counts, or frequent infections\(^7,10\). Patients are often treated with combination therapies, which include monoclonal antibodies as well as chemotherapy\(^7,10\).

**About Arzerra (ofatumumab)**

- Arzerra (ofatumumab) is approved in more than 50 countries worldwide.
- Arzerra is a monoclonal antibody that is designed to attach to a protein called CD20 that is found on the surface of lymphocytes, including the cancerous lymphocytes seen in
CLL. By attaching to CD20, ofatumumab stimulates the body’s immune system to attack the cancerous cells, helping to control the disease.

- Arzerra is indicated as monotherapy for the treatment of patients with CLL refractory to fludarabine and alemtuzumab. It was first approved for this indication in 2009\(^{11}\).
- In 2014, Arzerra was also approved in the United States (US) and European Union (EU), among other Health Authorities, in combination with chlorambucil for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate\(^{11,12}\).
- In the EU, Arzerra is also approved in combination with bendamustine in patients with CLL who were either previously untreated or considered inappropriate for fludarabine-based therapy or had relapsed CLL\(^{11}\).

**Arzerra Important Safety Information**


**Precautions and special populations**

- Arzerra is not recommended for use in children under 18 years of age due to insufficient data on safety and/or efficacy.
- Arzerra is not recommended during pregnancy or lactation, or in women of childbearing potential not using effective contraception during treatment and for 12 months after treatment.
- No formal studies of Arzerra in patients with renal or hepatic impairment have been performed.
  - No dose adjustment is recommended for mild to moderate renal impairment (creatinine clearance >30 mL/min).
  - Patients with hepatic impairment are unlikely to require dose modification.
- Arzerra is contraindicated in patients who demonstrate hypersensitivity to Arzerra or any of its excipients.

**Infusion reactions**

Infusion reactions may result in temporary interruption or withdrawal of treatment. Reactions may include but are not limited to, anaphylactoid events, bronchospasm, cardiac events (e.g. myocardial ischaemia/infarction, bradycardia), chills/rigours, cough, cytokine release syndrome, diarrhoea, dyspnoea, fatigue, flushing, hypertension, hypotension, nausea, pain, pulmonary oedema, pruritus, pyrexia, rash, and urticaria. In rare cases, these reactions may lead to death. Even with premedication, severe reactions including cytokine release syndrome have been reported. Patients with a history of decreased pulmonary function may be at greater risk for pulmonary complications from severe reactions and should be monitored closely during infusion of Arzerra.

**Tumor Lysis Syndrome (TLS)**

Risk factors include a high tumour burden, high concentrations of circulating cells (≥25,000/mm3), hypovolaemia, renal insufficiency, elevated pre-treatment uric acid levels and elevated lactate dehydrogenase levels. Management of TLS includes correction of electrolyte abnormalities, monitoring of renal function, maintenance of fluid balance and supportive care.
Progressive multifocal leukoencephalopathy (PML)
A diagnosis of PML should be considered in any Arzerra patient who reports the new onset of or changes in pre-existing neurologic signs and symptoms. If a diagnosis of PML is suspected Arzerra should be discontinued and referral to a neurologist should be considered.

Hepatitis B
Hepatitis B virus (HBV) infection and reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, has occurred in patients treated with drugs classified as CD20-directed cytolytic antibodies, including Arzerra.

All patients should be screened for HBV infection by measuring HBsAg and anti-HBc before initiation of Arzerra treatment. For patients who show evidence of prior (HBsAg negative, anti-HBc positive) hepatitis B infection, physicians with expertise in managing hepatitis B should be consulted regarding monitoring and initiation of HBV antiviral therapy. Arzerra treatment should not be initiated in patients with evidence of current hepatitis B infection (HBsAg positive) until the infection has been adequately treated.

Patients with evidence of prior HBV infection should be monitored for clinical and laboratory signs of hepatitis or HBV reactivation during treatment with and for 6-12 months following the last infusion of Arzerra. HBV reactivation has been reported up to 12 months following completion of therapy. Discontinuation of HBV antiviral therapy should be discussed with physicians with expertise in managing hepatitis B.

In patients who develop reactivation of HBV while receiving Arzerra, Arzerra and any concomitant chemotherapy should be interrupted immediately, and appropriate treatment instituted.

Cardiovascular
Patients with a history of cardiac disease should be monitored closely. Arzerra should be discontinued if patient experiences serious or life threatening cardiac arrhythmias. It is recommended that patients have electrolytes such as potassium and magnesium measured prior to and during the administration of Arzerra. Electrolyte abnormalities should be corrected.

Sodium Content
This medicinal product contains 34.8 mg sodium per 300-mg dose and 116 mg sodium per 1,000-mg dose. This should be taken into consideration for patients on a controlled sodium diet.

Lab Monitoring
Complete blood counts and platelet counts should be obtained at regular intervals during Arzerra therapy and more frequently in patients who develop cytopenias.

Immunisations
Vaccination with live attenuated or inactivated vaccines during Arzerra treatment has not been studied. The response to vaccination could be impaired when B cells are depleted. Due to the risk of infection, administration of live attenuated vaccines should be avoided during and after treatment with Arzerra, until B-cell counts are normalised.
Bowel obstruction
Bowel obstruction has been reported in patients receiving anti-CD20 monoclonal antibodies, including Arzerra. Patients who present with abdominal pain, especially early in the course of Arzerra therapy, should be evaluated and an appropriate treatment instituted.

HBsAg=hepatitis B surface antigen; HBc=hepatitis B core.