

# Ofatumumab

**Ofatumumab**<sup>[1]</sup> (trade name **Arzerra**, also known as HuMax-CD20) is a fully human monoclonal antibody (for the CD20 protein) which appears to inhibit early-stage B lymphocyte activation. It is FDA approved for treating chronic lymphocytic leukemia that is refractory to fludarabine and alemtuzumab (Campath) and has also shown potential in treating Follicular non-Hodgkin's lymphoma, Diffuse large B cell lymphoma, rheumatoid arthritis and relapsing remitting multiple sclerosis. Ofatumumab has also received conditional approval in Europe for the treatment of refractory chronic lymphocytic leukemia. This makes ofatumumab the first marketing application for an antibody produced by Genmab, as well as the first human monoclonal antibody which targets the CD20 molecule that will be available for patients with refractory CLL.

## 1 Medical uses

Its only indication that has received regulatory approval is Chronic lymphocytic leukaemia (CLL).<sup>[2][3][4]</sup>

## 2 FDA Approval

It first received FDA approval on April 17, 2014, for use in combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate<sup>[2]</sup> MHRA approval on the 19th of April 2010,<sup>[4]</sup>

## 3 EMA Approval

EMA approval on the 14th of June 2010<sup>[3]</sup> and Health Canada approval on the 13th of August 2012.<sup>[5]</sup>

## 4 Adverse effects

**Adverse effects by frequency:**<sup>[2][3][4]</sup>

**Very common (>10% frequency):**

- Lower respiratory tract infection, including pneumonia
- Upper respiratory tract infection

- Rash
- Anaemia
- Neutropenia

**Common (1-10% frequency):'**

- Sepsis
- Herpes virus infection
- Urinary tract infection
- Febrile neutropenia
- Leucopenia
- Thrombocytopenia
- Anaphylactoid reactions
- Hypersensitivity
- Tachycardia
- Hypotension
- Hypertension
- Bronchospasm
- Hypoxia
- Dyspnoea (shortness of breath)
- Chest discomfort
- Pharyngolaryngeal pain
- Cough
- Nasal congestion
- Small bowel obstruction
- Diarrhoea
- Nausea
- Urticaria (hives)
- Itchiness
- Flushing
- Back pain
- Cytokine release syndrome

- Pyrexia (fever)
- Rigors
- Chills
- Hyperhidrosis
- Fatigue

#### Uncommon (0.1-1% frequency):

- Agranulocytosis
- Coagulopathy
- Red cell aplasia
- Lymphopenia
- Anaphylactic shock
- Tumour lysis syndrome

#### Rare (<0.1% frequency):

- Hepatitis B infection or reactivation

Ofatumumab has received a **black box warning** regarding the potential for it to cause **progressive multifocal leukoencephalopathy** and **Hepatitis B reactivation**.<sup>[6]</sup> Likewise it is also advised that doctors watch cautiously for small bowel obstruction, neutropenia, thrombocytopenia, infusion reactions or an increased risk for infection.<sup>[6]</sup>

### 4.1 Contraindications

It is contraindicated in individuals that have hypersensitivity to ofatumumab or any of its excipients.<sup>[4]</sup>

### 4.2 Interactions

No formal drug interaction studies have been conducted with ofatumumab.<sup>[2]</sup> Although it is advised that patients are not administered live virus vaccines (e.g. the oral polio vaccine) while undergoing treatment with ofatumumab due to the compromised ability to fight the attenuated viruses seen in patients being treated with ofatumumab.<sup>[6]</sup>

## 5 Mechanism

Ofatumumab is a humanised anti-CD20 monoclonal antibody whose epitope is distinct from that of rituximab.<sup>[7]</sup> The CD20 antigen is expressed on solely B cell lymphocytes.<sup>[7]</sup> Compared with rituximab, ofatumumab binds more tightly to CD20 with a slower off-rate.<sup>[7]</sup> It causes cytotoxicity in the cells that express CD20 by means of complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC).<sup>[7]</sup>

## 6 Clinical trials

Status of clinical trials of ofatumumab conducted by Genmab and GSK, as of late 2010.

- Relapsed follicular non-Hodgkin's lymphoma (NHL)-Phase II<sup>[8]</sup>
- Rheumatoid arthritis (RA):
  - Phase III – OFA110635/GEN410 – Ofatumumab in adult RA patients who have had an inadequate response to methotrexate<sup>[9]</sup>
  - Phase III – OFA110634/GEN411 – Ofatumumab in adult RA patients who have had an inadequate response to TNF-alpha antagonist therapy<sup>[10]</sup>
- Diffuse large B cell lymphoma (DLBCL) – Phase III<sup>[11]</sup>
- B-cell chronic lymphocytic leukemia (B-CLL) – Phase II<sup>[12]</sup>
- Waldenstrom's Macroglobulinemia - Phase II<sup>[13]</sup>
- Relapsing Remitting Multiple Sclerosis (RRMS)-Phase II<sup>[14]</sup>
- Mantle cell lymphoma (MCL)

## 7 See also

- Rituximab, a chimerical anti-CD20 antibody
- Ocrelizumab, a humanized (90%) anti-CD20 antibody

## 8 References

- [1] Zhang, Bodi (2009). "Ofatumumab". *MAbs*. **1** (4): 326–331. doi:10.4161/mabs.1.4.8895. PMC 2726602. PMID 20068404.
- [2] "ARZERRA (ofatumumab) injection, solution [GlaxoSmithKline LLC]". *DailyMed*. GlaxoSmithKline LLC. September 2013. Retrieved 24 January 2014.
- [3] "Arzerra : EPAR - Product Information" (PDF). *European Medicines Agency*. Glaxo Group Ltd. 7 March 2013. Retrieved 24 January 2014.
- [4] "Arzerra (acetate formulation) -Summary of Product Characteristics (SPC)". *electronic Medicines Compendium*. GlaxoSmithKline UK. 27 November 2013. Retrieved 24 January 2014.
- [5] "Product Information". *Health Canada*. GlaxoSmithKline Inc. 13 August 2012.

- [6] “Arzerra (ofatumumab) dosing, indications, interactions, and more”. *Medscape Reference*. WebMD. Retrieved 24 January 2014.
- [7] Lin, TS (2010). “Ofatumumab: a novel monoclonal anti-CD20 antibody” (PDF). *Pharmacogenomics and personalized medicine*. **3**: 51–59. PMC 3513208. PMID 23226042.
- [8] <http://clinicaltrials.gov/ct2/show/NCT00394836?term=nct00394836&rank=1>
- [9] Clinical trial number *NCT00611455* for “Investigating Clinical Efficacy of Ofatumumab in Adult RA Patients Who Had an Inadequate Response to MTX Therapy” at ClinicalTrials.gov
- [10] Clinical trial number *NCT00603525* for “Investigating Clinical Efficacy of Ofatumumab in Adult RA Patients Who Had an Inadequate Response to TNF- $\alpha$  Antagonist Therapy” at ClinicalTrials.gov
- [11] Clinical trial number *NCTNCT01014208* for “Ofatumumab Versus Rituximab Salvage Chemoimmunotherapy Followed by Autologous Stem Cell Transplant in Relapsed or Refractory Diffuse Large B Cell Lymphoma (ORCHARRD)” at ClinicalTrials.gov
- [12] Clinical trial number *NCT00349349* for “HuMax-CD20 in B-Cell Chronic Lymphocytic Leukemia (B-CLL) Patients Failing Fludarabine and Alemtuzumab” at ClinicalTrials.gov
- [13] <http://clinicaltrials.gov/ct2/show/NCT00811733?term=nct00811733&rank=1>
- [14] <http://clinicaltrials.gov/ct2/show/NCT00640328?term=nct00640328&rank=1>
- Coiffier B, Lefebvre S, Pedersen LM, et al. (February 2008). “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*. **111** (3): 1094–100. doi:10.1182/blood-2007-09-111781. PMID 18003886.
  - Zhang B (July 2009). “Ofatumumab”. *MAbs*. **1** (4): 326–31. doi:10.4161/mabs.1.4.8895. PMC 2726602. PMID 20068404.
  - ClinicalTrials.gov: HuMax-CD20 search results

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