Patent expiry dates for biologicals: 2016 update

Biosimilars have been approved in Europe since 2006 and in the US since 2015. With patents on originator biologicals expiring and ever-tightening healthcare budgets, biosimilars are expected to take an increasing share of the biologicals market. In light of these facts, this paper gives estimated patent expiry dates for just some of the best-selling biologicals.

Keywords: Biological, biosimilar, patent

With biologicals making up a larger share of the new drugs approved in both Europe and the US, the pricing of drugs, and the impact of those prices on healthcare budgets, is poised to become a big issue. One way to offset these costs is to introduce biosimilars for biologicals where the patents and exclusivity periods have expired.

The European Medicines Agency (EMA) approved its first biosimilar, Omnitrope (somatropin), back in 2006 [1]. Since then, EMA has approved 24 biosimilars within the product classes of human growth hormone, granulocyte colony-stimulating factor (G-CSF), erythropoesis stimulating agent, insulin, follicle-stimulating hormone (FSH), parathyroid hormone, and tumour necrosis factor (TNF)-inhibitor, for use in the European Union (EU).

Many blockbuster biologicals are already, or will soon be, facing competition from biosimilars due to patent expiries and loss of exclusivity. There are also more than 200 new biotechnology products in the pipeline (phase II to registered), all of which could be future targets for biosimilars. With the increasing price of new biologicals and continuing pressure on healthcare budgets, biosimilars are expected to make up an increasing share of the biologicals market.

Table 1: Estimated patent and exclusivity expiry dates for best-selling biologicals: not humanized antibodies

Biological	Approval date*	European Union (EU)	US
Adcetris (brentuximab vedotin)	25 Oct 2012	1 Aug 2023	2015–2031
	19 Aug 2011		
Aranesp (darbepoetin alfa)	6 Aug 2001	6 Jul 2016	15 May 2024
	17 Sep 2001		
Avonex/Rebif (interferon beta-1a)	19 Mar 2009	2015	2015
	7 Feb 2003		
Betaferon/Betaseron (interferon beta-1b)	30 Nov 1995	6 Jul 2024	7 May 2013
	23 Jul 1993		
Bexxar (tositumomab)	Withdrawn	Data not available	Jan 2029
	27 Jun 2003		
Prostascint (capromab)	-	Data not available	Nov 2036
	28 Oct 1996		
Enbrel (etanercept)	3 Feb 2000	1 Aug 2015 ##	22 Nov 2028
	2 Nov 1998		
Erbitux (cetuximab)	29 Jun 2004	29 Jun 2014	13 Feb 2016
	12 Feb 2004		
Orthoclone OKT3 (muromonab-CD3)	-	Data not available	2021
	14 Sep 1992		
Remicade (infliximab)	13 Aug 1999	13 Feb 2015	4 Sep 2018
	24 Aug 1998		
Removab (catumaxomab)	20 Apr 2009	May 2020	Data not available
	-		
Rituxan/MabThera (rituximab)	2 Jun 1998	12 Nov 2013	22 Sep 2016
	26 Nov 1997		
Reopro (abciximab)	-	Data not available	Jun 2015
	16 Dec 1993		
Simulect (basiliximab)	9 Oct 1998	Apr 2013	Data not available
	12 May 1998		
Sylvant (siltuximab)	22 May 2014	Jul 2034	1 Aug 2027
	23 Apr 2014		
Zevalin (ibritumomab)	16 Jan 2004	2013	19 Feb 2016
	19 Feb 2002		

*EU provides 10 years of exclusivity (8 years data exclusivity and 2 years market exclusivity + 1 year possible extension), US Biologics Price Competition and Innovation Act of 2009 (BPCI Act) provides 12 years exclusivity (4 years data exclusivity and 8 years market exclusivity); ##Includes 6-month paediatric extension.

Source: GaBI Online (www.gabionline.net), Sheppard et al. [1], Bernstein Research [2]

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Table 2: Estimated patent and exclusivity expiry dates for best-selling biologicals: humanized antibodies

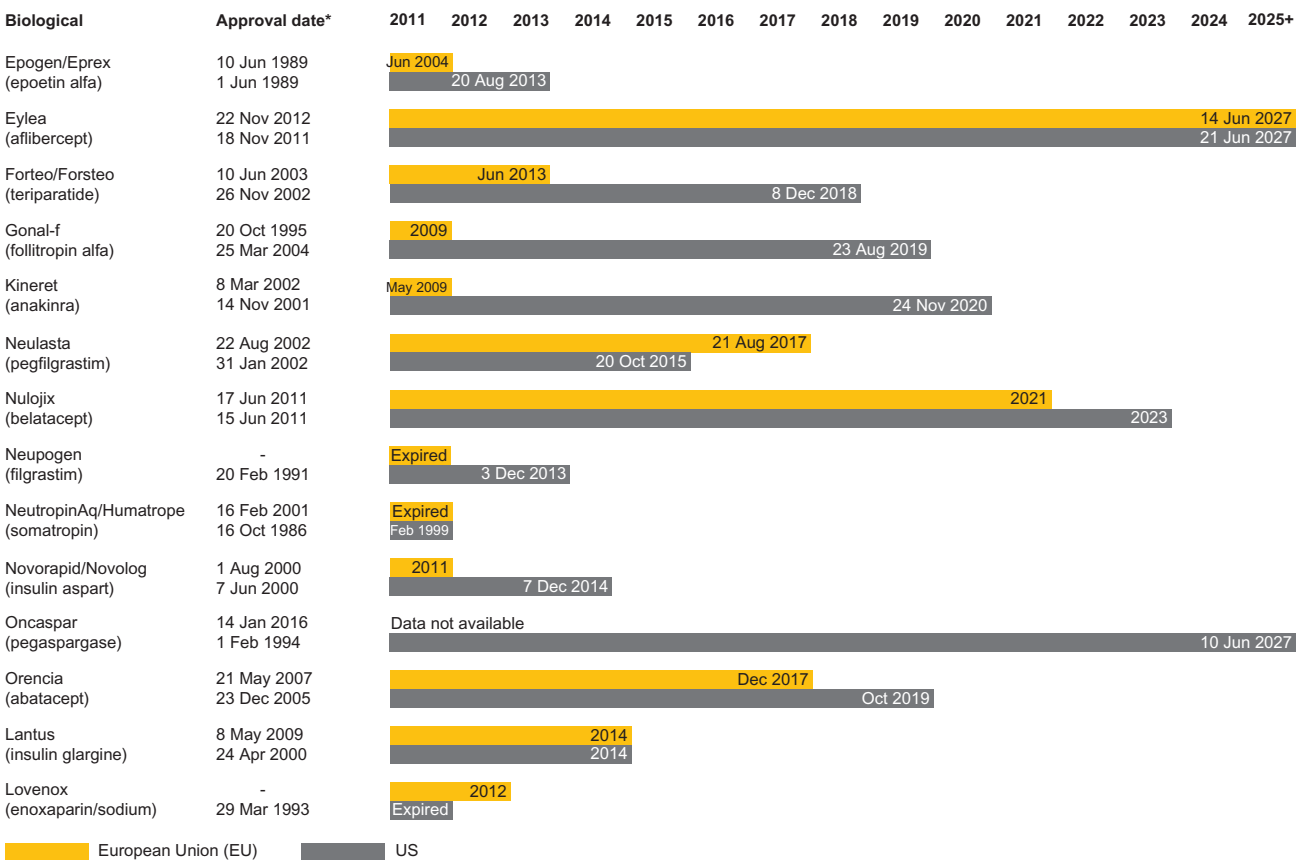
Biological	Approval date*	EU	US
Abthrax (raxibacumab)	15 Oct 2014	Data not available	2026
Actemra/RoActemra (tocilizumab)	16 Jan 2009 8 Jan 2010	23 Apr 2017 #	22 Dec 2015
Avastin (bevacizumab)	12 Jan 2005 26 Feb 2004	21 Jan 2022	4 Jul 2019
Arzerra (ofatumumab)	19 Apr 2010 26 Oct 2009	Data not available	2023
Benlysta (belimumab)	13 Jul 2011 9 Mar 2011	2021	2023
Campath/Lemtrada (alemtuzumab)	12 Sep 2003 7 May 2001	7 May 2021	6 Jul 2021
Cimzia (certolizumab pegol)	1 Oct 2009 22 Apr 2008	5 Jul 2021	13 Feb 2024
Cyramza (ramucirumab)	19 Dec 2014 21 Apr 2014	May 2023	Nov 2025
Cosentyx (secukinumab)	15 Jan 2015 21 Jan 2015	Data not available	8 Oct 2020
Entyvio (vedolizumab)	22 May 2014 20 May 2014	Data not available	24 Jul 2017
Gazyva/Gazyvaro (obinutuzumab)	23 Jul 2014 1 Nov 2013	5 Nov 2024	Jan 2035
Herceptin (trastuzumab)	28 Aug 2000 25 Sep 1998	28 Jul 2014**	18 Jun 2019
Humira (adalimumab)	8 Sep 2003 31 Dec 2002	15 Jun 2017	25 Nov 2017
Ilaris (canakinumab)	23 Oct 2009 17 Jun 2009	Data not available	Data not available
Kadcyla (trastuzumab emtansine)	15 Nov 2013 22 Feb 2013	23 Jun 2020	8 Sep 2026
Keytruda (pembrolizumab)	17 Jul 2015 4 Sep 2014	13 Jun 2028	Nov 2036
Lucentis (ranibizumab)	22 Jan 2007 30 Jun 2006	2022	30 Jun 2020
Opdivo (nivolumab)	19 Jun 2015 22 Dec 2014	2 May 2026	19 Jun 2027
Perjeta (pertuzumab)	4 Mar 2013 8 Jun 2012	Feb 2024	Jun 2026
Poteligeo (mogamulizumab)	11 Jan 2012 -	Jun 2033	Dec 2035
Prolia/Xgeva (denosumab)	26 May 2010 1 Jun 2010	Data not available	2016
Simponi (golimumab)	1 Oct 2009 24 Apr 2009	Oct 2024	Feb 2004
Soliris (eculizumab)	20 Jun 2007 16 Mar 2007	1 May 2020	16 Mar 2021
Stelara (ustekinumab)	16 Jan 2009 25 Sep 2009	Jan 2024	Sep 2023
Synagis (palivizumab)	13 Aug 1999 19 Jun 1998	9 Aug 2015	20 Oct 2015
Tysabri (natalizumab)	27 Jun 2006 23 Nov 2004	Aug 2015	Mar 2015
Vectibix (panitumumab)	3 Dec 2007 27 Sep 2006	2018	8 Apr 2020
Xolair (omalizumab)	25 Oct 2005 20 Jun 2003	Aug 2017	20 Jun 2017
Yervoy (ipilimumab)	13 Jul 2011 25 Mar 2011	2021	2023
Zenapax (daclizumab)	26 Feb 1999 10 Dec 1997	Mar 2013	Data not available

European Union (EU) US

*EU provides 10 years of exclusivity (8 years data exclusivity and 2 years market exclusivity + 1 year possible extension), US Biologics Price Competition and Innovation Act of 2009 (BPCI Act) provides 12 years exclusivity (4 years data exclusivity and 8 years market exclusivity); #Based on Supplementary Protection Certificate; **In the UK. Other major EU markets follow on 28 August 2015; patent protecting the cells that make certain levels of erythropoietin lasts until 26 May 2015.

Source: GaBI Online (www.gabionline.net), Sheppard et al. [1], Bernstein Research [2]

Table 3: Estimated patent and exclusivity expiry dates for best-selling biologicals: not antibodies



*EU provides 10 years of exclusivity (8 years data exclusivity and 2 years market exclusivity + 1 year possible extension), US Biologics Price Competition and Innovation Act of 2009 (BPCI Act) provides 12 years exclusivity (4 years data exclusivity and 8 years market exclusivity).
Source: GaBI Online (www.gabionline.net), Sheppard et al. [1], Bernstein Research [2]

There has been significant harmonization across the globe with respect to patents, mainly as a result of the World Trade Organization's TRIPS agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights). This has resulted in most patent laws nowadays giving the term of a patent as 20 years from the filing date of the application. This is the case both in Europe and the US, where patents have a term of 20 years from the date of filing [2].

For both Europe and the US, exclusivity periods should also be considered (see footnote in Tables 1 to 3).

Estimated patent and exclusivity period expiry dates for just some of the best-selling biological molecules are shown in Tables 1 for not humanized antibodies, Table 2 for humanized antibodies, and Table 3 for biologicals that are not antibodies.

Although the EU previously defined a period of 10 years data exclusivity, this was revised at the latest review of pharmaceutical EU legislation to the following:

Ten years if the reference product is centrally approved or application to the centralized procedure has been made before 20 November 2005. Or eight years data exclusivity + 2 years market exclusivity + 1 year possible extension if a full dossier is submitted on or after 30 October 2005 via a national procedure or after 20 November 2005 via the centralized procedure [3].

The expiration of patents and other intellectual property rights for originator biologicals over the next decade opens up opportunities for biosimilars to enter the market and increase industry competition. Price reduction strategies should increase adoption among physicians and patients alike, spurring increases in the biosimilars market share.

According to a report by Grand View Research, the global market for biosimilars will experience rapid growth from 2016 to 2024. The biosimilars market is expected to reach US$41.7 billion in 2024, with the most significant factor contributing to this growth being patent expiries on major biologicals. Demand is also being fuelled by governments around the world turning to biosimilars as a cheaper option to reduce healthcare costs.

Although the US is the largest biologicals market globally, it is still playing catch up when it comes to biosimilars. The US

Food and Drug Administration (FDA) only approved its first biosimilar in 2015 and to date (January 2017) has approved four biosimilars [3], compare to 24 biosimilars currently approved in the EU [1]. The US therefore currently accounts for only a small part of the global biosimilars market, while Europe is the largest contributor to biosimilar revenues worldwide.

The EU, however, is not without its problems. Uptake of biosimilars varies significantly between the different countries of the EU, with some, such as Italy and Spain, having quite low biosimilars use compared to countries where there is high acceptance of biosimilars, e.g. Austria, Germany, The Netherlands and Sweden [4]. However, favourable clinical outcomes demonstrated through clinical trials of biosimilars, including in the NOR-SWITCH trial of switching from the originator biological to biosimilar infliximab, are expected to increase confidence and boost uptake of biosimilars [5].

Major companies investing in the biosimilars market include Amgen, Biocad, Biocon, Celltrion, Dr Reddy's Laboratories, Hospira, Intas Biopharmaceutical, Mylan, Pfizer, Sandoz, Stada Arzneimittel and Teva Pharmaceutical Industries.

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