

Aprovel faces European generic approvals

Aprovel (irbesartan), Sanofi's blockbuster antihypertensive, lost protection in several western European countries with the expiry of supplementary protection certificates (SPCs) during August (see Figure 1). In the UK, Actavis took full advantage and launched on 'day one' after patent expiry with list prices for 28-tablet packs of £4.85 (US\$7.67) for the 75mg strength, £5.92 for 150mg tablets and £7.97 for the 300mg version. Arrow Génériques was among the first entrants in France, while Ranbaxy's Basics and Stada announced launches in Germany. Sandoz' 1A Pharma and Hexal secured marketing authorisations for irbesartan in time for prompt launches as did Teva's AbZ, CT Arzneimittel and Ratiopharm, along with Actavis, Pfizer, Krka's Tad Pharma and Sanofi's Winthrop.

Global sales of Aprovel and the CoAprovel combination with hydrochlorothiazide declined by 20.2% to €786 million (US\$985 million) in the first half of 2012, including €339 million in western Europe. The global sales decline can be attributed to the loss of patent protection for Avapro/Avalide in the US in late-March 2012, and the subsequent launch of generic irbesartan, along with its fixed-dose combination with hydrochlorothiazide. Teva has enjoyed 180-day exclusivity for its tablets, but that six-month period is now drawing to a close, and almost a dozen players holding tentative approvals are waiting in the wings (**Generics bulletin**, 6 April 2012, page 19).

Additional SPCs have been awarded for the fixed-dose combination in the European Union that may constrain generic competition until October 2013. However, patent expert GenericsWeb notes that the claims of the basic patent, EP0,454,511, do not specify all components of the combination, and therefore may be found invalid. It calculates, following the Medeva decision by the European Court of Justice (ECJ), that up to a third of all combination SPCs could be invalid (**Generics bulletin**, 6 April 2012, page 24). However, the mechanisms available to generic competitors wishing to challenge SPCs at national patent offices are uncertain. SPCs for the combination have already been rejected in Norway and the Czech Republic.

August also brought the expiry of SPCs for Merck's blockbuster asthma and allergy remedy Singulair (montelukast), which generated global sales of US\$2.77 billion in the first half of 2012. However,

protection has been extended by a further six months due to the grant of a paediatric extension after the successful completion of an agreed paediatric investigation plan (PIP). In Belgium, GenericsWeb observes, no paediatric extension has been granted.

In the US, the first generic rivals to Singulair have just entered the market after a six-month paediatric patent extension. Apotex, Aurobindo, Dr Reddy's, Endo and Kudco secured US Food and Drug Administration (FDA) approval for montelukast standard and chewable tablets, as did Mylan, Roxane, Sandoz, Teva and Torrent. Teva uniquely also received approval for the asthma treatment in granule form, whilst Glenmark only received approval for standard tablets.

In terms of data exclusivity (see Figure 2), August saw the expiry of 10-year protection awarded in European Union states via a national procedure for Daiichi Sankyo's antihypertensive Olmetec (olmesartan). Several SPCs protect olmesartan and its combinations, but the validity of SPCs for combinations remains in doubt following the ECJ's Medeva decision concerning combination SPCs. In the UK, the country's patent office has rejected an SPC for olmesartan plus hydrochlorothiazide. **G**

SPC expiries in August

INN	Country
Candesartan	Switzerland
Irbesartan	Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Norway, Spain, Sweden, Switzerland, UK
Mometasone	Switzerland
Montelukast	Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Norway, Slovenia, Spain, Sweden, UK
Rivastigmine	Greece, Portugal

Figure 1: Molecules for which supplementary protection certificates (SPCs) expired in certain markets during August 2012 (Source – GenericsWeb)

Data exclusivity expiries in August

INN	Country/Region
Alglucosidase alfa	Canada*
Deferasirox	Turkey
Dexmedetomidine	European Union
Drotrecogin alfa (activated)	European Union
Ethinylestradiol/Norelgestromin	European Union
Fosaprepitant	Australia
Hvt lbd vaccine	European Union
Lanreotide	US
Maraviroc	Israel, US
Morphine/Naltrexone	US
Olmesartan	Belgium, France, Germany, Italy, Luxembourg, Netherlands, Sweden, UK
Paricalcitol	Belgium, France, Germany, Italy, Luxembourg, Netherlands, Sweden, UK
Pegfilgrastim	European Union
Rasagiline	Canada*
Rotavirus vaccine	Canada*
Sitaxentan	Turkey
Sulfur hexafluoride	Switzerland
Telmisartan/Hydrochlorothiazide	Switzerland
Tulathromycin	Canada*

* This will be followed by a no-marketing period of two years during which a notice of compliance will not be granted to a generic manufacturer. In addition, a further six months data protection will be added to the 8-year term for studies of Alglucosidase alfa and Rotavirus vaccine in paediatric populations.

Figure 2: Molecules for which data exclusivity expired in certain markets during August 2012 (Source – GenericsWeb)

Want more?

This data is extracted from the monthly update for Pipeline Scope, an online intelligence tool that provides fast access to reliable information on key patent, SPC and data-protection expiries, covering 44 countries and over 1,500 INNs.

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