Dexilant depicts drama of US first-to-file

As the US Food and Drug Administration (FDA) does not make public most details of the abbreviated new drug application (ANDA) filings it receives – and the parties to paragraph IV patent litigation often choose to disclose little additional information – Hatch-Waxman cases often present themselves as serial dramas played out over time, the characters and conflicts revealing themselves bit by bit with each episode. The early phases of the conflict over Takeda's acid-reflux treatment Dexilant (dexlansoprazole) – which is available as 30 mg and 60mg delayed-release capsules – have been one such drama.

Having initially launched dexlansoprazole in the US under the Kapidex brand name in February 2009, Takeda subsequently changed the name of its successor to Prevacid (lansoprazole) to avoid confusion with Casodex (bicalutamide) and Kadian (morphine sulfate). Takeda reported Dexilant sales of US$92 million in the year ended 31 March 2010, although sales of the proton-pump inhibitor have since risen.

Information about an ANDA with a paragraph IV certification of patent invalidity, unenforceability or non-infringement for a rival to the 60mg strength of Dexilant first appeared on the FDA's website on 17 January 2011. The agency reported a submission date of 25 August 2010. Just over a month after details on the 60mg version appeared, the FDA posted on 21 February further information about the 30mg strength, for which it reported a submission date of 30 November 2010.

Takeda sued Handa Pharmaceuticals in the US District Court for the Northern District of California on 23 February 2011. The complaint indicated that Handa initially submitted its ANDA with a paragraph IV certification for the 60mg strength in August 2010 and then amended it to include the 30mg strength in January 2011, more than a month after the first reported paragraph IV submission for the 30 mg version. "Indeed," observes Thomson Reuters, which maintains a database of paragraph IV challenges, "Handa's press release from 2 March 2011 confirmed the impression that the company had been first-to-file only for the 60mg strength." At that time, California-based Handa mentioned in its release only the 60mg version, which it said had US sales of around US$300 million in 2010, according to IMS Health data (**Generics *bulletin***, 18 March 2011, page 17).

The identity of other filers was a mystery to observers, and remained so for another month.

On 31 March 2011, Dr. Reddy's Laboratories was the next company sued by Takeda in the same California court that will rule on Takeda's complaint against Handa. A similar suit was filed against Dr. Reddy's on 1 April in the US District Court for the Southern District of New York. Also on 1 April, Takeda filed separate suits against Anchen and Impax in the Northern California court.

Impax subsequently announced its belief that it was first-to-file for the 30mg strength. "Based on the filing data of the ANDA, the company believes that it is the first-to-file an ANDA with a paragraph IV certification on the 30mg capsule, and expects to be entitled to 180 days of market exclusivity," stated Impax. The generics company – which is based in Hayward, California – cited Wolters Kluwer data that showed Dexilant 30mg and 60mg capsules had US sales of US$20 million and US$261 million respectively in the 12 months ended January 2011.

The FDA's Orange Book lists five patents covering Dexilant delayed-release capsules. US patents 6,462,058 and 6,664,276 include claims to the drug substance and drug product as well methods of its use; while US patent 6,939,971 includes method-of-use claims; and US patent 7,285,668 includes claims directed to the drug substance. The six-month pediatric exclusivity associated with those four patents will expire on 15 December 2020.

However, also listed in the Orange Book is US patent 7,790,755, which includes claims to the drug product. The pediatric exclusivity associated with the '755 patent does not expire until 2 February 2027.

According to Thomson Reuters, the initial complaint against Handa alleged infringement of all five patents listed against Dexilant in the Orange Book. In an amended complaint, Takeda added infringement allegations concerning US patent 7,732,282, which does not appear in the entry for Dexilant in the Orange Book. Takeda also alleges infringement of the same six patents in its suit against Anchen.

The suit against Impax alleges infringement of the five Orange Book patents. But its litigation with Dr. Reddy's only alleges infringement of the '276 and '755 patents. According to Takeda, the notice letter sent by Dr. Reddy's did not provide information about any certification regarding the '755 patent. However, the letter did include a paragraph IV certification to the '276 patent, as well as paragraph III certifications not challenging three other Orange Book patents listed for Dexilant.

"Even as many of the basic details are known, observers must now wait and watch as the story unfolds," Thomson Reuters comments.

KEY DETAILS: DEXILANT

Brand:	Dexilant
Active ingredient:	dexlansoprazole
Delivery form:	30mg and 60mg delayed-release capsules
Brand owner:	Takeda
Annual US brand sales:	Approximately US$300 million in 2010
First paragraph IV filing submitted to FDA:	25 August 2010 – 60mg 30 November 2010 – 30mg
Known paragraph IV filers:	Anchen Pharmaceuticals Dr Reddy's Laboratories Handa Pharmaceuticals Impax Laboratories
Patents at issue – expiry dates:	6,462,058 – 15 December 2020* 6,664,276 – 15 December 2020* 6,939,971 – 15 December 2020* 7,285,668 – 15 December 2020* 7,790,755 – 2 February 2027* 7,732,282 – 15 June 2020
District court location:	Northern District of California Southern District of New York

* includes a six-month paediatric extension

Figure 1: Key details of paragraph IV challenges to Takeda's Dexilant (dexlansoprazole) acid-reflux treatment in the US (Source – Thomson Reuters)