

Cholesterol-Lowering Drugs

Ranbaxy and Teva team up on atorvastatin

Ranbaxy will pay Teva a portion of its profits on US sales of atorvastatin calcium during a 180-day exclusivity period after the two firms struck a deal to ensure that the Indian firm got to market promptly. Ranbaxy's version entered the market on 30 November at the same time as Watson started shipping its authorised generic of Pfizer's Lipitor blockbuster. On the same day, Mylan – also through a patent-litigation settlement with Pfizer – introduced its rivals to the brand firm's Caduet (atorvastatin/amlodipine) tablets in 11 strengths.

Three-and-a-half years ago, Ranbaxy and Pfizer settled atorvastatin patent litigation with a deal that allowed the Indian firm to launch on 30 November 2011 with 180-day exclusivity (*Generics bulletin*, 4 July 2008, page 15). However, Ranbaxy's ability to secure the necessary regulatory approval from the US Food and Drug Administration (FDA) to enjoy that exclusivity was thrown into doubt when the agency a few months later imposed an alert barring imports of 30 generics from Indian plants in Batamandi, Dewas and Paonta Sahib (*Generics bulletin*, 3 October 2008, page 5). The FDA then invoked its Application Integrity Policy (AIP) to stop reviews of applications from the Paonta Sahib site after Ranbaxy "falsified data and test results" (*Generics bulletin*, 6 March 2009, page 1).

Having to date failed fully to address the FDA's concerns, Ranbaxy is making its atorvastatin tablets in the US at its Ohm Laboratories facility in New Brunswick, New Jersey. A company spokesperson declined to comment on whether the partnership with Teva included the Israeli company supplying the active pharmaceutical ingredient (API) for the tablets, while Teva said the "terms of the agreement will not be disclosed".

Teva does not have US approval for finished-dose atorvastatin, but it does hold drug master files (DMFs) for atorvastatin calcium APIs made in both Beer Sheva and Petah Tikva, Israel.

"Information about the availability of generic atorvastatin can be obtained from Ranbaxy," the FDA stated. A few weeks before generic entry, Watson's president and chief executive officer, Paul Bisaro, had predicted a "full launch" by Ranbaxy (*Generics bulletin*, 18 November 2011, page 7). Pfizer, he believed, would retain around a 40% market share during the 180-day exclusivity period, not least due to defensive tactics such as striking deals with pharmacy benefit managers and offering a card that reduces patient co-payments for Lipitor to US\$4 per month (*Generics bulletin*, 18 November 2011, page 26). **G**

Biogenerics

EMA floats idea of accepting biogenerics

Allowing a biosimilar to be authorised on the basis of a generic bioequivalence study is floated for discussion by the European Medicines Agency (EMA) in a concept paper for revising its ‘overarching’ biosimilars guideline.

Stressing that it is talking about “exceptional situations” – for a “very simple biological” that had been “fully characterised on the quality level” – the EMA says discussion is needed on whether a biological medicinal product could be authorised “based on a bioequivalence study only combined with an extensive quality comparability exercise”.

“Recent improvements in analytical technologies allow and support this approach for certain biologicals,” commented Suzette Kox, the European Generic medicines Association’s (EGA’s) senior director of scientific affairs. Discussing the feasibility of following the generic legal basis for some biological products was a “major step forward”, she added.

Revising the biosimilars guideline – which came into force in 2005 – provided a “unique opportunity”, Kox continued, finally to address the issue of sourcing of the reference product. “The wording on the choice of reference product should be refined to allow global development of biosimilars,” she said. “Given the economic crisis we are in, and the increasing pressure on national healthcare budgets, we urgently need a regulatory framework which avoids repetition of unnecessary clinical trials.”

Noting that in some ways the threshold for a biosimilar-product applicant was “currently higher than for an originator-product applicant” – “who can seek approval in all territories based on the same data set from one global development programme” – Kox said the EGA also supported several of the EMA’s less dramatic proposals. One of these is to define the word ‘biosimilar’. “Numerous terms are in use for ‘biosimilar’, or ‘similar biological medicinal product’,” says the agency, “and often the term has been used in an inappropriate way.”

Comments on the concept paper are requested by 29 February 2012 with the aim of releasing a draft revised guideline for consultation in the first half of 2012. This timetable will be running in parallel with the EMA’s schedule for revising its guideline on non-clinical and clinical issues for authorising biosimilars, for which a concept paper was issued in October with a 31 December deadline for comment (*Generics bulletin*, 14 October 2011, page 1). **G**

Mergers & Acquisitions

Actavis acquires all of PharmaPack

Actavis has acquired 100% of the shares in Dutch packaging specialist PharmaPack International for an undisclosed amount. “This acquisition gives Actavis much greater flexibility in tender markets and allows for minimum order quantities for smaller markets,” stated Claudio Albrecht, Actavis’ chairman and chief executive officer.

At present, Actavis buys a large number of tablets from third-party manufacturers. “The lead times are sometimes between six and nine months, and are therefore much too long. With the acquisition of PharmaPack International we will be able to reduce these lead times by more than 50%,” stated Albrecht.

One of the Dutch company’s future roles will be the bulk packaging of drugs produced at Actavis’ facility in Alathur, India. The Icelandic company anticipates “a significant reduction in freight costs”, helping to “increase the group’s cost competitiveness” and make a positive impact on Actavis’ working capital.

Based in Zoetermeer, the Netherlands, PharmaPack aims to offer a “one-stop-shop” for packaging pharmaceutical and biotech products, including cytostatic, hormone and opiate products. It has 10 blister-packaging lines, and can also handle bottles, vials and other containers. **G**

Cough/Cold Remedies

Perrigo gets US nod for Mucinex rival

Perrigo plans to launch a US rival to Reckitt Benckiser’s Mucinex (guaifenesin) 600mg extended-release tablets by the end of June 2012 after receiving final approval from the US Food and Drug Administration (FDA) for a generic version of the OTC cough and cold brand.

Acknowledging that Perrigo was still “working through litigation” with Reckitt over Mucinex, the generics firm’s chairman and chief executive officer, Joseph Papa, said Perrigo nonetheless “expects to begin shipping this product in our retail and wholesale customers’ store-brand packaging in the second half of our fiscal year” ending in June. Mucinex 600mg tablets had annual sales of around US\$146 million, Perrigo indicated. **G**

Mergers & Acquisitions

Vivimed adds APIs through Uquifa

India's Vivimed Labs has strengthened its position in active pharmaceutical ingredients (APIs) and intermediates by acquiring Spanish group Uquifa from Yule Catto for £35.0 million (US\$55.0 million), of which £6.4 million is deferred for three years.

Yule Catto – which intends to focus on speciality polymers – said sales by its non-core Uquifa Pharma Chemicals division increased by 4.7% to £35.4 million in the first half of this year. But deferring orders into July and “persistent pressure on margins from Asian competition” contributed to the division’s operating profit falling by 22.8% to £2.29 million.

Uquifa – which employs 390 staff – has two facilities in Spain, as well as a former SmithKline Beecham plant in Cuernavaca, Mexico. All three have been approved by regulators including the US Food and Drug Administration (FDA). The Spanish firm has made more than 150 filings worldwide, including around 50 drug master files (DMFs) in the US, and holds more than 20 certificates of suitability (CoS) in Europe.

“Deftly combining the supply-side efficiencies and market penetration of Vivimed with the enviable expertise of Uquifa in APIs” would present “a range of synergistic opportunities”, Vivimed insisted. The Spanish producer would also provide a “robust pipeline of filings to accelerate growth across Europe and the Americas in the next five years”. **G**

Pricing & Reimbursement

France delists 80 treatments

France has delisted from reimbursement around 80 products from today after their therapeutic value was judged to be “insufficient” by the government’s transparency commission, following the guidance of the country’s *Haute Autorité de Santé* (HAS).

Buflomedil 150mg tablets and tetrazepam 50mg tablets made by several generics firms are included on the list of products losing reimbursement. Mylan and Sandoz’ etidronate 200mg and 400mg tablets are also included, along with EG Labo and Teva’s nimesulide 100mg tablets. **G**

Intellectual Property

SPCs depend on basic patent claims

Supplementary protection certificates (SPCs) can only be granted to products containing active ingredients that are specified in the claims of a basic patent, the European Court of Justice (ECJ) has ruled. This means originators will not be able to rely on SPCs based on patents covering just one active ingredient to protect their combination products.

The ECJ ruled in response to vaccine disputes referred by a UK court, however, that it was possible to obtain an SPC for a combination of at least two ingredients where that product also contained ingredients not covered by the basic patent.

Medeva had appealed against the UK Patent Office's refusal to grant five SPCs for a range of vaccines, each of which contained pertactin and filamentous haemagglutinin along with other ingredients. In four of the SPC applications, the Patent Office objected that more active ingredients were specified in the applications than had been identified in the claims of the basic patent. And regarding the fifth application, the Patent Office said the marketing authorisations submitted in support related to vaccines that contained more active components than the ingredients listed in the SPC application and the patent claim.

On appeal, the Court of Appeal for England and Wales stayed proceedings and asked the ECJ for a ruling on six questions. The first five questions revolved around the meaning of the phrase "the product is protected by a basic patent in force" as cited in Article 3(a) of the European Union's SPC Regulation 469/2009. The sixth question was whether Article 3(b) of that Regulation permitted granting SPCs to combination products that contained active ingredients not specified in the basic patent.

Taking the first five questions together, the ECJ noted that the Latvian, Lithuanian and Portuguese governments had argued that the wording of the patent claims was the crucial factor, whereas the UK government and Medeva had maintained that "a product protected by a basic patent in force" corresponded to "any combination of substances of a medicinal product directly infringing the patent".

The ECJ pointed out that Article 5 of the 469/2009 Regulation said an SPC conferred the same rights as the basic patent, and was subject to the same limitations and obligations. "It follows that Article 3(a) of the Regulation precludes the grant of a SPC relating to active ingredients which are not specified in the wording of the claims of the basic patent," it stated. **G**

Reproductive Health

Draft guideline covers r-hFSH biosimilar

Requirements for approving a biosimilar containing recombinant human follicle stimulating hormone (r-hFSH) are covered by the latest draft guideline from the European Medicines Agency (EMA). The product-specific guidance presents the current view of the EMA's committee for human medicinal products (CHMP) on the non-clinical and clinical requirements for demonstrating comparability of two r-hFSH-containing medicines.

Noting that FSH is used in assisted reproductive therapy (ART) for women to stimulate growth and recruitment of ovarian follicles – as well as in men to induce and maintain spermatogenesis – the guideline states in its non-clinical section that FSH is a highly glycosylated protein, and that *in vitro* studies “may not fully reflect the more complex situation *in vivo*”. It says therefore that additional comparative *in vivo* studies should be performed.

As far as clinical studies are concerned, the guideline says that “at least one” adequately-powered, randomised, parallel group clinical trial will be required to demonstrate clinical comparability regarding efficacy between the biosimilar and its reference product. The recommended model, it adds, is stimulating multifollicular development in patients undergoing superovulation for ART, such as *in vitro* fertilisation.

Interested parties have until 31 May 2012 to comment on the draft guideline.

One of those parties may be Watson Pharmaceuticals, which has an exclusive, worldwide licensing agreement with Itero Biopharmaceuticals to develop and commercialise Itero's FSH product. This is currently in pre-clinical development as a biosimilar for treating female infertility. **G**

Subscriptions to News@Genericsbulletin

Subscribers to **Generics bulletin** – The Business Newsletter for the Generic Medicines Industry supplied in hard-copy format – receive **News@Genericsbulletin** most weeks free-of-charge as part of their subscription.

Contacting News@Genericsbulletin

If you need any information or help regarding subscriptions or editorial please contact:
Aidan Fry, Editor, **Generics bulletin** and **News@Genericsbulletin**, OTC Publications Ltd,
54 Creynolds Lane, Shirley, Solihull, West Midlands B90 4ER, United Kingdom. Tel: +44
1564 777550. Fax: +44 1564 777524. E-mail: info@generics-bulletin.com.

About News@Genericsbulletin

News@Genericsbulletin is published by OTC Publications Ltd. No part of this publication may be stored in a retrieval system, reproduced, transmitted, abstracted or sold without prior permission of the publisher. Copyright OTC Publications Ltd. All rights reserved.

Company registered in England No 2765878.

Registered office: 54 Creynolds Lane, Shirley, Solihull, West Midlands B90 4ER, UK.