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MOVERS AND SHAKERS

A PHARMA MATTERS REPORT

A REVIEW OF OCTOBER-DECEMBER 2012. PUBLISHED FEBRUARY 2013.

The Thomson Reuters quarterly report on the US generics industry using strategic intelligence and competitive analysis information from *Newport Premium*™, the critical product targeting and global business development system from the industry authority on the global generics market.

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IN THIS ISSUE

In this quarterly report, we look at a few of the companies beginning to make their marks on the US generics market either with their finished dose products or active ingredients, and analyze trends and statistics relating to the market as a whole.

SECTION I: INTRODUCTION

2012 may be remembered as the year of the Generic Drug User Fee Act (GDUFA). During the first half of the year, the US generic drug industry pressed its campaign for the implementation of user fees, which it hoped would provide the FDA with additional resources to meet the needs of the industry. June saw congressional authorization of GDUFA as part of the larger Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA). While The Generic Pharmaceutical Association (GPhA) actively advocated for the passage of the act and publicly applauded its passage, the generic industry awaited further details of its implementation, which became public over the course of the following months.

GDUFA funds should allow the FDA to reduce the review time for applications, cut review backlogs, and increase overseas inspection and monitoring of finished dose and active ingredient manufacturing facilities supplying products to the US market. However, some observers have suggested that the fees could also have negative impacts if they turn out to be a significant barrier for smaller companies or limit generic interest in products with small markets or slim margins.

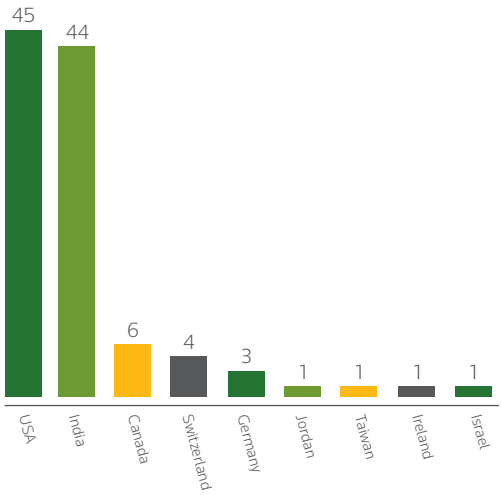
ANDA approvals in 2012 reflected the international nature of the US generics market. For the year, 92 corporate groups from 16 countries received a total of 506 final ANDA approvals. That was down somewhat from 2011, when the FDA approved 547 ANDAs submitted by 99 groups from 19 countries. Indian companies continued to increase their presence in the US generic market in 2012, with 205 approvals going to 29 groups. 41 US-based groups received 171 approvals in 2012.

Given that the US generics market has become increasingly crowded, it is not surprising that much of the deal making by generic drug manufacturers and marketers in 2012 seemed to be motivated by the need to diversify product lines and capabilities and the ongoing push to expand into markets outside of the US. The year also saw continuing consolidation in the industry with Watson's acquisition of Actavis as well as smaller, but significant, acquisitions such as the purchase of Fougera (formerly Nycomed) by Novartis. The line between innovator and generic companies blurred further with Takeda's acquisition of URL Pharma early in the year, but the Japanese company divested itself of the URL generic business in a fourth-quarter deal with Sun, although Takeda retained URL's successful Colcrys gout treatment.

But now, let's take a look at the developments in the last quarter of 2012.

SECTION II: ANDA APPROVALS

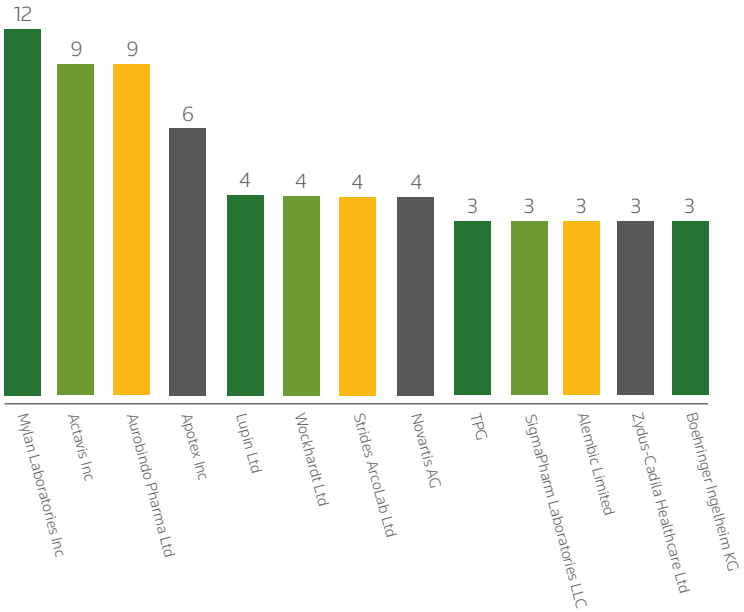
TOTAL 'A'-RATED ANDAs BY COUNTRY OF ORIGIN OF APPLICANT FOR OCTOBER TO DECEMBER 2012



During the fourth quarter of 2012, 45 companies from 9 countries received a total of 106 final ANDA approvals. US-based groups received the most approvals, with 45 approvals granted among 18 corporate groups. India-based companies were close behind, with 20 corporate groups receiving a total of 44 approvals.

In comparison, during the third quarter of 2012, 58 companies from 12 countries received a total of 168 final ANDA approvals, with 71 approvals going to 18 corporate groups from India, and 55 approvals going to 28 groups from the US.

GROUPS WITH THE MOST 'A'-RATED ANDA APPROVALS FOR OCTOBER TO DECEMBER 2012



During the fourth quarter of 2012, US-based Mylan received 12 ANDA approvals, the most of any company. Actavis/Watson of the US and India's Aurobindo were next in line with 9 approvals each.

In comparison, during the third quarter of 2012, Mylan, Aurobindo, and Israel's Teva led the field, with 11 ANDA approvals each. India's Dr. Reddy's was next in line with 9 approvals.

SECTION III: PARAGRAPH IV CHALLENGES

In the fourth quarter of 2012, the FDA posted information on first Paragraph IV patent challenges to 3 new active ingredients or combinations. This is up slightly from 2 during the previous quarter, but lower than the fourth quarter of 2011, when we learned of first challenges to 6 new active ingredients or combinations.

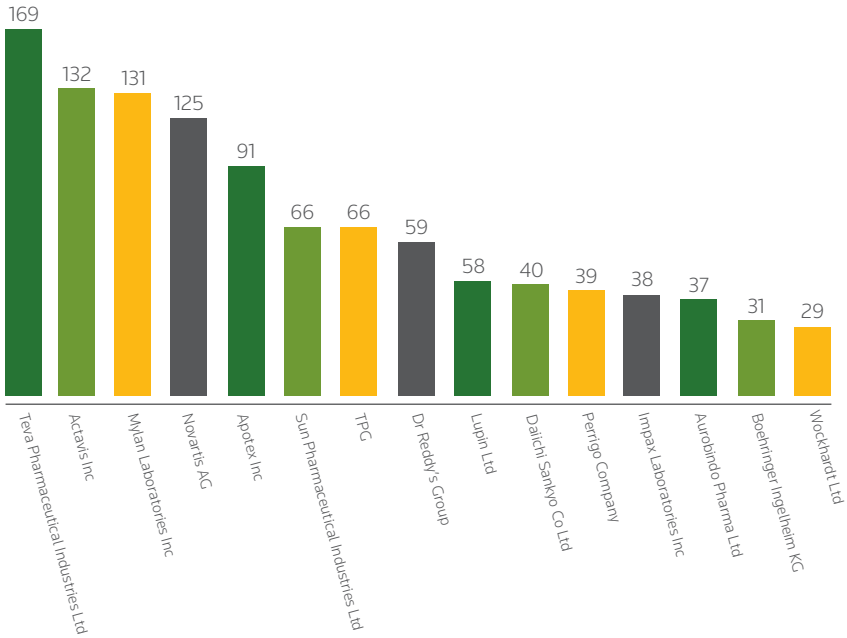
Thomson Reuters is aware of 44 new Paragraph IV patent infringement lawsuits, concerning 24 different compounds or combinations, filed during the fourth quarter of 2012. This total includes complaints filed in more than one court for jurisdictional purposes as well as suits concerning ANDAs that may be the subject of earlier litigation. During the third quarter, the US District Court for the District of Delaware was the most frequent venue chosen for Hatch-Waxman litigation with 18 new suits filed. The US District Court for the District of New Jersey was the second most popular venue with 12 new cases. The Southern District of New York was third with 8 new cases.

Teva continues to be the most prolific filer of ANDAs with Paragraph IV certification. At the time of writing this report, we linked the company to challenges on 169 compounds or combinations.

The combined Actavis/Watson is now in second place, linked to 132 challenged compounds or combinations.

Mylan and Novartis (Sandoz) drop to third and fourth place on the list with challenges on 131 and 125 products, respectively.

GROUPS WITH THE MOST PATENT CHALLENGES ON RECORD THROUGH DECEMBER 2012



PRODUCTS FIRST EXPOSED TO PARAGRAPH IV CHALLENGES, AS REPORTED BY THE FDA BETWEEN OCTOBER AND DECEMBER 2012

ACTIVE INGREDIENT:
ixabepilone

POSTED BY FDA:
31 October 2012

BRAND NAME:
Ixempra® Kit

NDA HOLDER:
Bristol-Myers Squibb

- Dr. Reddy's Laboratories has submitted an ANDA with Paragraph IV certification for a generic version of Ixempra Kit (ixabepilone) for injection.
- The Orange Book currently lists six patents covering Ixempra Kit:

  US Patent 6,670,384 has been granted pediatric exclusivity expiring on July 23, 2022.

  US Patent 7,022,330 has been granted pediatric exclusivity expiring on July 23, 2022.

  US Patent 7,125,899 has been granted pediatric exclusivity expiring on November 26, 2018.

  US Patent 7,312,237 has been granted pediatric exclusivity expiring on February 21, 2025.

  US Patent RE41,393 has been granted pediatric exclusivity expiring on August 8, 2022.

  US Patent RE41,911 has been granted pediatric exclusivity expiring on March 28, 2021.

  In litigation with Dr. Reddy's, Bristol-Myers has alleged infringement of US Patent 6,670,384, US Patent 7,022,330, and US Patent RE41,393.
- At the time of the first ANDA submission for a generic version of Ixempra Kit, Formosa Laboratories held the only active DMF for ixabepilone reported by the FDA.

PRODUCTS FIRST EXPOSED TO PARAGRAPH IV CHALLENGES, AS REPORTED BY THE FDA BETWEEN OCTOBER AND DECEMBER 2012

ACTIVE INGREDIENTS:
lubiprostone

POSTED BY FDA:
27 December 2012

BRAND NAME:
Amitiza®

NDA HOLDER:
Sucampo

- Anchen has submitted an ANDA with Paragraph IV certification for a generic version of Amitiza (lubiprostone) capsules.
- The Orange Book lists numerous patents covering Amitiza capsules, expiring between July 14, 2014 and October 25, 2027.

  In litigation with Anchen, Sucampo, R-Tech Ueno, and Takeda have alleged infringement of six patents.

  US Patent 6,414,016 will expire on September 5, 2020.

  US Patent 7,795,312 will expire on September 17, 2024.

  US Patent 8,026,393 will expire on October 25, 2027.

  US Patent 8,071,613 will expire on September 5, 2020.

  US Patent 8,097,653 will expire on November 14, 2022.

  US Patent 8,338,639 will expire on January 23, 2027.
- At the time the first ANDA with Paragraph IV certification was submitted for a generic version of Amitiza capsules, Apotex, Dr. Reddy's Laboratories, Everlight, PHF, and Teva held active DMFs for lubiprostone.

PRODUCTS FIRST EXPOSED TO PARAGRAPH IV CHALLENGES, AS REPORTED BY THE FDA BETWEEN OCTOBER AND DECEMBER 2012

ACTIVE INGREDIENT:
sitagliptin phosphate, simvastatin

POSTED BY FDA:
10 December 2012

BRAND NAME:
Juvisync™

NDA HOLDER:
Merck

- At least one company has submitted an ANDA with Paragraph IV certification for a generic version of Juvisync (sitagliptin phosphate/simvastatin). We do not yet know the identity of the filer.
- The Orange Book lists eight patents covering Juvisync tablets.

  US Patent 6,303,661 will expire on April 24, 2017.

  US Patent 6,699,871 will expire on July 26, 2022.

  US Patent 6,890,898 will expire on February 2, 2019.

  US Patent 7,078,381 will expire on February 2, 2019.

  US Patent 7,125,873 will expire on July 26, 2022.

  US Patent 7,326,708 will expire on April 11, 2026.

  US Patent 7,459,428 will expire on February 2, 2019.

  US Patent 8,168,637 will expire on June 26, 2022.
- At the time the first ANDA with Paragraph IV certification was submitted for a generic version of Juvisync tablets, there were several active DMFs for each component of the combination on file with the FDA.

SECTION IV: BIOSIMILARS WATCH

Uncertainty as to the future of biosimilar competition in the US market continued at the close of 2012, with the news that two biosimilar development programs had been halted. Teva announced it had suspended its late stage trial for TL011, a biosimilar rituximab. Similarly, one of the most intriguing players in the global biosimilars market, South Korea's Samsung, halted development on its version of a biosimilar rituximab (SAIT101). Samsung originally planned to deliver biosimilar therapies by 2015, and it is unknown if the decision to stop development will delay the expected launch date.

Alfred E. Tiefenbacher's AET Biotech entered into an agreement with BioXpress Therapeutics S.A. of Switzerland focused on the development and manufacturing of an adalimumab biosimilar. AET Biotech is also responsible for commercialization and required long-term investment. One of the top selling products worldwide, adalimumab is expected to attract multiple biosimilar competitors in regulated markets such as the EU and US.

Two US-based companies, Boston Oncology and Oncobiologics, have partnered to bring biosimilar products to Middle Eastern and North African markets. The strategic deal permits Boston Oncology to license, manufacture, and commercialize four Oncobiologics' biosimilar therapies. Boston Oncology will also manage development of clinical programs manufacturing facilities for the target markets.

Another US-based company, STC Biologics, was awarded a Small Business Innovation Research contract from the National Cancer Institute to continue development of a biosimilar monoclonal antibody. The contract, along with additional funding from US-based Ligacept LLC, will provide finance required to scale up manufacturing and commence clinical work on their STC101 candidate.

In late November, the Alliance for Safe Biologic Medicines (ASBM), whose members include Genentech, Amgen, and the Biotechnology Industry Organization (BIO), released the paper "It's all about the name: what is the imperative of adopting a unique names for biologic and biosimilar therapeutics?" which provided insight to the ASBMs views on the topic of nomenclature for biosimilars approved in the US. The paper included the recommendation that interchangeable products should receive a distinct name from the reference product for which they are considered interchangeable.

SECTION V: NOTABLE DEALS

Deal making in the generic drug industry continued apace during the fourth quarter of 2012, with deals driven by the need to strengthen growth, diversify product lines, and expand in growing global markets. We also saw divestments, acquisitions, and partnerships undertaken during the quarter in efforts to realign assets and focus to correspond with current strategy.

Watson's Moves

Moves made by Watson (known as Actavis as of January 2013) during the quarter exemplified many of the motives mentioned above. Most significantly, the company completed its acquisition of the Actavis group of companies for €4.25 billion. The addition of Actavis will strengthen Watson's business outside of the United States, particularly in established and emerging markets in Europe. In order to secure FTC approval for the acquisition, Watson agreed to divest a number of products to Par and Sandoz.

As part of an effort to realign its global corporate structure and assets in the wake of the Actavis acquisition, Watson sold its $47 million minority stake in Moksha8. Moksha8 has established operations in Brazil and Mexico and aims to become a leader across Latin America. While Watson divested itself of its stake in Moksha8, the two companies also expanded an ongoing sales and marketing collaboration involving a portfolio of branded generic CNS products.

In another move to focus on core business priorities, in late October, Watson announced the sale of its Rugby OTC products and trademarks to the Harvard Drug Group for approximately $117 million. Watson did, however, retain ownership of ANDAs and manufacturing facilities for the nicotine gum products sold by Rugby, and will supply nicotine gum products to Harvard Drug as part of a related supply agreement.

Expanding Capabilities

In October, contract manufacturer Patheon announced a deal to acquire Banner Pharmacaps from Netherlands-based VION for $255 million. Headquartered in North Carolina, with additional research and manufacturing facilities in the Netherlands, Canada, and Mexico, Banner specializes in gelatin based formulations. Patheon noted that the deal provided it with products and state-of-the-art facilities, along with an expanded geographical presence. The deal was completed in December.

In a move to expand beyond its generic drug focus, India's Sun Pharmaceutical Industries announced an agreement to acquire Wilmington, Massachusetts based DUSA Pharmaceuticals, which developed and markets the Levulan (aminolevulinic acid HCl) photodynamic therapy platform. The $230 million acquisition will provide Sun entry into the dermatological treatment device market as well as FDA-approved manufacturing facilities.

Mylan added to its Indian holdings, striking a deal with SMS Pharmaceuticals to acquire the Indian company's Visakhapatnam facility for the manufacture of oncology bulk drugs and formulations. The purchase price has been reported to be roughly $32 million.

In a deal involving domestic US players, Pernix Therapeutics, a Texas-based specialty pharmaceutical company, agreed to acquire Cypress Pharmaceuticals, a privately-owned generic drug company, and Hawthorn Pharmaceuticals, a privately-owned branded drug company, both based in Mississippi. The deal is worth approximately $101 million and will significantly broaden Pernix's generic and branded offerings and product pipeline.

In December, we learned of a major deal in which Sun's Caraco subsidiary will acquire the URL Pharma generic business from Takeda. The deal does not include URL's Colcrys (colchicine) gout treatment. The value of the transaction was not disclosed. Takeda acquired URL in April 2012.

Cooperation, Reorganization, and Shifting Focus

While Watson was divesting its interest in Moksha8, Forest entered into an alliance with the Latin American company. Under the agreement announced in October, Moksha8 will receive an exclusive Latin American license to Forest's Viibryd (vilazodone HCl) antidepressant, and potentially other products, as well as up to $125 million in financing. After two years, Forest will have the option to acquire Moksha8. Forest hopes the deal will provide it with a commercial footprint in the region.

In October, US-based Alvogen agreed to take a majority stake in South Korea's Kunwha Pharmaceuticals through a purchase of existing stock and newly issued shares in an effort to enhance access to the growing markets in the Asia-Pacific region.

In November, India's Orchid Chemicals & Pharmaceuticals announced that it would end its Chinese joint venture for the production of cephalosporin antibiotics in the face of growing competition in China. Orchid's interest in the joint venture will be transferred to its partner, North China Pharmaceutical Corporation, for $13.9 million.

Also in November, it was announced that India's Panacea Biotec and Kremers Urban of the US will cooperate to launch 11 drugs in the US, the first of which is expected to be tacrolimus capsules. Kremers Urban will market and distribute the products, while Panacea will be responsible for the research, development, registration, and supply.

In November, Impax and Perrigo, two US-based companies, announced an agreement to collaborate on the development, manufacturing, and commercialization of an unspecified topical generic drug product with first to market potential.

Eli Lilly and Strides Arcolab of India recently announced an agreement under which Agila Specialties, a division of Strides, will manufacture oncology products to be marketed by Lilly in several emerging markets. The deal specifies that Lilly will have the option to add branded generic oncology drugs to the initial portfolio of 10 products. The collaboration will allow Strides to take advantage of Lilly's strong distribution network, while Lilly will benefit by the expansion of its oncology portfolio in emerging markets.

In mid-December, Teva established a joint venture in South Korea with Handok Pharmaceuticals. Teva will have a controlling stake in the venture and will be responsible for manufacture and supply of products, while Handok will use its expertise in the South Korean market to fulfill its sales, marketing, and regulatory role.

In late December, Perrigo closed the year by announcing that it would acquire the remaining stake in Cobrek Pharmaceuticals, a privately-held, US-based drug development company, in an all cash deal worth approximately $45 million. Perrigo previously held an 18.5% minority stake in the company.

SECTION VI: OPENING MOVES

LOTUS PAHRMACEUTICAL COMPANY, LTD.

Headquartered in Taiwan, Lotus Pharmaceutical Company, is a specialty pharmaceutical company primarily dedicated to the development of oral solid drugs for the local and international markets. Lotus prides itself on its clinical trial based drug development and has invested heavily to strengthen its R&D capabilities since 2005. In 2006, the company expanded its focus outside of Taiwan, seeking to develop the expertise necessary to do business in China and the regulated markets of North America, Europe, and Japan. The company claims the submission of several ANDAs in the US since 2008 and it passed an FDA inspection in 2010. Lotus also completed the construction of a facility for the manufacture of anti-tumor drugs in 2010.

Lotus plans to build its worldwide presence by pursuing technically difficult products, including controlled-release formulations, and has strategic alliances for capsule and patch formulation development with Taiwan Fisherman Pharmaceutical Group and Taiwan Patron Chemical & Pharmaceutical Company.

The company hopes to derive more than 50% of its revenue through exports within three years and has begun to implement a patent challenge strategy in the US market. In December 2012, Lotus announced its submission of an ANDA with Paragraph IV certification for a generic version of Xenical (orlistat) capsules. According to Lotus, it notified Hoffman La Roche of its ANDA with Paragraph IV certification at the end of September 2012, but no litigation has yet resulted.

SIDMARK LABORATORIES (INDIA) PVT. LTD.

Founded in 1984 in collaboration with US partners, India's Sidmak Laboratories has long been developing and manufacturing a range of formulations for the domestic Indian market. Sidmak's US partner, Sidmak Laboratories, Inc., was acquired by Pliva in 2002. The Indian company can manufacture a variety of tablets, soft and hard gelatin capsules, granules, and transdermal patches in its own cGMP-compliant facilities.

Sidmak's products include antianginal, analgesic, antiasthmatic, antidiabetic, and haematinic drugs along with antioxidants and multivitamins. The company has devoted resources to the development of novel drug delivery systems and has successfully developed oral modified release systems for a number of drugs.

In its efforts to expand its business internationally, Sidmak has focused first on the US market. The company claims to be in the process of developing a wide portfolio of products for registration with the FDA. This effort came to our attention in December 2012 when Medicis filed a patent infringement suit against Sidmak in the U.S. District Court for the District of Delaware in response to Sidmak's ANDA with Paragraph IV certification for a generic version of Solodyn (minocycline HCl) extended-release tablets.

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