Bloomberg BNA

Pharmaceutical Law & Industry Report®

VOL. 14, NO. 15 PAGES 501–534 APRIL 8, 2016

HIGHLIGHTS

Pfizer, Celltrion Win U.S. Approval for Copy of J&J's Remicade

Pfizer Inc. and Celltrion Inc. win approval to market a low-cost copy of Johnson & Johnson's best-selling arthritis treatment, Remicade. It's the second biosimilar approved in the U.S. **Page 520** . . . The FDA's approval of the second U.S. biosimilar was a very big step for these less-expensive biologic drugs because it shows the agency is comfortable reviewing more complex biosimilars, an attorney and pharma association say. **Page 520**

Amgen, Apotex Debate When a Biosimilar Can Be Released

In arguments before the Federal Circuit, attorneys for Amgen and Apotex disagree on what advance notice the biosimilar statute requires before Apotex's biosimilar of Amgen's chemotherapy-related treatment Neulasta can go to market. **Page 505**

FDA Draft: Label Must State Product Is a Biosimilar

In other biosimilar news, the FDA issues a new draft guidance saying biosimilar product labels must include a statement that the product is a biosimilar and may rely on the data submitted for FDA approval by the originator biologic. **Page 511**

BNA INSIGHTS: Jurisdiction for ANDA Patent Cases

Attorneys from Sterne Kessler examine the recent Federal Circuit *Acorda* decision on where abbreviated new drug application cases can be heard. They say that, for the time being, ANDA plaintiffs can rest easy on their choice of forum. In the meantime, ANDA defendants should prepare to face litigation anywhere in the U.S. **Page 530**

Hospira Can't Get Helsinn's Patent Suit Dismissed

In the wake of the *Acorda* decision, Hospira fails in its bid to get Helsinn Healthcare SA's patent infringement suit against it over the anti-nausea drug Aloxi thrown out. The U.S. District Court for the District of New Jersey finds the case can't be dismissed on jurisdictional grounds. **Page 506**

Colorado House Panel Kills Drug Price Bill

The sponsor of a Colorado bill (H.B. 1102) to require drug manufacturers to submit a report to the state on the cost of producing prescription drugs says she will introduce the measure again next year, after a legislative committee kills the bill. **Page 519**

CMS Delays Part of Medicaid Outpatient Drug Rule

The CMS has delayed the effective date for part of a final rule that changes how the government pays for outpatient prescription drugs in the Medicaid program. **Page 516**

ALSO IN THE NEWS

FRAUD AND ABUSE: Citing a decline in major pharmaceutical settlements with the government, a consumer group calls for stronger enforcement to deter pharmaceutical manufacturers from breaking the law. **Page 512**

FRAUD AND ABUSE: DOJ announces a one-year pilot program to encourage companies, including health-care companies that sell products abroad, to self-report violations of the Foreign Corrupt Practices Act. **Page 514**

DRUG DEVELOPMENT: A Senate committee approves five medical innovation bills during the final markup of companion legislation to the House's 21st Century Cures bill. **Page 510**

MEDICAID: Two whistle-blowers fail to prove Solvay's alleged off-label marketing for its drugs caused false Medicaid claims. **Page 507**

ADVERTISING AND MARKETING: The FDA tells Shionogi Inc. that its copayment assistance voucher for a head lice treatment omits important risk information. **Page 522**

LITIGATION TABLE

PATENTS: A table lists recent Hatch-Waxman case filings against generic companies. **Page 533**

 ISSN 1542-9547

Bloomberg BNA

PHARMACEUTICAL LAW & INDUSTRY REPORT

THE BUREAU OF NATIONAL AFFAIRS, INC., 1801 S. BELL STREET, ARLINGTON, VA 22202-4501 (703) 341-3000

PHARMACEUTICAL LAW & INDUSTRY REPORT (ISSN: 1542-9547) is published weekly except for the week before Labor Day and the weeks of Thanksgiving and Christmas, at the annual subscription rate of $2,623 for a single print copy, by The Bureau of National Affairs, Inc., 1801 S. Bell St., Arlington, VA 22202-4501. Periodical postage rates paid at **Periodicals Postage Paid at** Arlington, VA and at additional mailing offices. POSTMASTER: Send address changes to Pharmaceutical Law & Industry Report, BNA Customer Contact Center, 3 Bethesda Metro Ctr, Suite 250, Bethesda, MD 20814.

   ISSN 1542-9547

In This Issue

COURT PROCEEDINGS

FEDERAL NEWS

STATE NEWS

INDUSTRY NEWS

INTERNATIONAL NEWS

BNA INSIGHTS

LITIGATION TABLE

TABLE OF CASES

COMPANY NAMES INDEX

  PLIR ISSN 1542-9547

Court Proceedings

Biosimilars

Amgen, Apotex Argue What Advance Notice Is Needed Before Neulasta Biosimilar Release

Attorneys for Amgen and Apotex disagreed on what advance notice the biosimilar statute requires before Apotex's biosimilar of Amgen's chemotherapy-related treatment Neulasta can go to market, in arguments before the Federal Circuit April 4 (*Amgen, Inc. v. Apotex, Inc.*,Fed. Cir., No. 16-1308, *oral arguments* 4/4/16).

Apotex is appealing an order issued by the U.S. District Court for the Southern District of Florida that under the statute, Apotex must wait 180 days from the date when the Food and Drug Administration approves the biosimilar before it can put it on the market (13 PLIR 1759, 12/18/15). The district court strictly interpreted the U.S. Court of Appeals for the Federal Circuit's decision in *Amgen v. Sandoz* (13 PLIR 1051, 7/24/15).

Preventing 'Chaos.' Kerry B. McTigue of Cozen O'Connor PC, representing Apotex in oral arguments before the appeals court, argued that the *Sandoz* court had ''carved out a distinction'' between that case and Apotex's situation.

He noted that the *Sandoz* court had emphasized that its ruling on the 180-day notice period was influenced by Sandoz's refusal to engage in the information exchange under the Biologics Price Competition and Innovation Act (BPCIA). Apotex, in contrast, had exchanged the information and then told Amgen that it wouldn't be notifying it as to when the Neulasta biosimilar would be released to market.

''If there was ever a case to be distinguished from *Sandoz*, this is it,'' McTigue said.

Nicholas P. Groombridge of Paul Weiss Rifkind Wharton & Garrison LLP, representing Amgen, responded by citing an amicus brief by the Biotechnology Innovation Organization that predicted situations where a biosimilar would be released to market and then pulled back as a result of successful patent litigation by the biologic's originator, also known as the reference product sponsor (RPS).

''The purpose of the 180-day notice is to prevent this kind of chaos'' by ''allowing both parties to resolve patent disputes before the launch of the biosimilar,'' Groombridge said.

***Sandoz* Interpretation.** Neulasta (pegfilgrastim) is a biologic used to treat neutropenia, a lack of certain white blood cells caused by cancer chemotherapy. A biologic is a complex, large molecule, such as a monoclonal antibody or a cell-signaling protein. A product designed to resemble an FDA-approved biologic can only be approved by the agency as biosimilar to the reference product with no clinically meaningful differences, and, if it meets additional requirements, as interchangeable without the approval of a physician.

The BPCIA, signed into law in 2010 as part of the Affordable Care Act, provides an abbreviated approval pathway for a biosimilar that partly relies on the data originally submitted to the FDA by the RPS for approval. The BPCIA balances this benefit to the biosimilar applicant with provisions aimed at preserving incentives to develop innovative biologics.

The statute provides 12 years of data exclusivity for the RPS and outlines information exchange procedures, commonly referred to as the ''patent dance'' (42 U.S.C. § 262(l)(2)(A)), in which the applicant provides the RPS with its abbreviated biologic license application (aBLA), information about how its proposed product is manufactured and a mutually developed list of patents for which the sponsor believes it could reasonably assert an infringement claim.

The statute also says in Paragraph (l)(8)(A) that the applicant must notify the RPS not less than 180 days before the date of the first commercial marketing of the biosimilar product.

In *Sandoz*, the Federal Circuit held that the ''patent dance'' wasn't mandatory and that the 180-day notice began from the date the FDA approved the biosimilar and not, as Sandoz argued, from the date when the agency agreed to review the biosimilar.

In Amgen's complaint against Apotex, it said that Apotex had provided it with a copy of its aBLA for a Neulasta biosimilar and engaged in the ''patent dance.'' But Amgen also alleged that Apotex told it in a letter that because it had agreed to comply with the information exchanges, it could opt out of providing the 180-day notice of commercial marketing.

BPCIA Choices. Amgen asked the district court to order Apotex to delay marketing of its biosimilar of Neulasta for 180 days after the FDA approved it for market, and the district court issued the preliminary injunction.

In his oral argument before the Federal Circuit, McTigue, representing Apotex, said, ''The BPCIA created choices. With Apotex's interpretation, if you choose to engage in the (l)(2)(a) information exchange, what you get is the benefit of not using the notice of commercial marketing. Some applicants may want the certainty of the patent information exchange, as Apotex did, and some may want the certainty of using the notice of commercial marketing, and some may not.''

Amgen's reading would make Section (l)(9)(c), which allows the RPS, and not the biosimilar applicant, to file a declaratory judgment action if notice isn't given ''superfluous,'' McTigue said.

''Under Amgen's reading, an RPS could bring a declaratory judgment action on any patent because notice was not given,'' he said. ''But the important thing to remember is, we're not here on patents, we're here on notice.''

McTigue concluded by noting that the *Sandoz* court had been concerned that, without the 180-day notice

and because Sandoz hadn't engaged in the patent information exchange, Amgen would have no way of knowing what patents the biosimilar might have infringed. But Apotex had provided the patent exchange information, he said.

''For the same reason, because there is a specific remedy, we must honor Apotex's right [to get its product to market]. We move that the court vacate the preliminary injunction,'' McTigue said.

Notice Gives Clarity. Groombridge, representing Amgen, said Paragraph (l)(8)(A) says that the applicant ''shall'' provide the 180-day notice. ''What Apotex is asking the court to do is to re-write (l)(8)(A) and put in language that occurs elsewhere in the statute.''

He said, ''If you take away the 180-day notice period what you say to the RPS is, 'You have to seek a preliminary injunction immediately when you file a lawsuit because you have no idea when the biosimilar will launch.' ''

Amgen is represented by Groombridge, Catherine Nyarady, Jennifer H. Wu, Jennifer Gordon, Eric Alan Stone, Stephen Accursio Maniscalco and Peter Sandel of Paul Weiss Rifkind Wharton & Garrison LLP, New York; John F. O'Sullivan, Allen P. Pegg and Jason Sternberg of Hogan Lovells, Miami; and Wendy A. Whiteford, Lois M. Kwasigroch and Kimberlin Morley of Amgen, Thousand Oaks, Calif. Apotex is represented by McTigue, W. Blake Coblentz, Barry P. Golob, Aaron S. Lukas and Donald R. McPhail of Cozen O'Connor PC, Washington, and David Charles Frederick, John Christopher Rozendaal and Miles J. Sweet of Kellogg Huber Hansen Todd Evans & Figel PLLC, Washington.

BY JOHN T. AQUINO

To contact the reporter on this story: John T. Aquino in Washington at jaquino@bna.com

To contact the editor responsible for this story: Randy Kubetin at rkubetin@bna.com

An audio recording of the oral argument can be downloaded from the Federal Circuit website at http://www.cafc.uscourts.gov/. Click on ''Oral Argument Recordings'' and search for arguments on April 4, 2016.

Patents

Hospira Fails to Get Helsinn Aloxi Suit Dismissed; Court Finds Jurisdiction Exists

Hospira Inc. failed in its bid to get Helsinn Healthcare SA's patent infringement suit against it over the anti-nausea drug Aloxi thrown out (*Helsinn Healthcare S.A. v. Hospira, Inc.*, 2016 BL 107238, D.N.J., No. 3:15-cv-02077-MLC-DEA, 4/5/16).

In an April 5 opinion, Judge Mary L. Cooper of the U.S. District Court for the District of New Jersey found that the case couldn't be dismissed on jurisdictional grounds because Hospira and its subsidiary, Hospira Worldwide Inc. (Worldwide), had sufficient minimum contacts with the New Jersey forum to enable the court to hear the case.

Patent litigators told Bloomberg BNA that this case may be the first district court case to apply the Federal Circuit's recent holding in Acorda Therapeutics, Inc. v. Mylan Pharmaceuticals, Inc., 2016 BL 83256, No. 15-1456, No. 15-1460, (Fed. Cir. March 18, 2016) (14 PLIR 437, 3/25/16). The rule the Federal Circuit announced in *Acorda* effectively establishes jurisdiction in all forums over any filer of an abbreviated new drug application (ANDA) seeking approval to make and sell a generic version of a drug.

Court Cites *Acorda*. In her opinion, Cooper held that ''specific jurisdiction may be asserted over Hospira and Worldwide because of Defendants' suit-related contacts'' with the New Jersey forum, and relied heavily on the U.S. Court of Appeals for the Federal Circuit's March ruling in *Acorda*.

Cooper observed that *Acorda* addressed the same jurisdictional issues and a similar set of facts.

In *Acorda*, the Federal Circuit held that abbreviated new drug application (ANDA) filings establish a substantial connection with a forum state and the ANDA filer, because they predict the filer's future activities in the state, such as manufacturing or marketing a generic product.

Although Hospira and Worldwide aren't incorporated and don't have their principal places of business in New Jersey, at least one of Helsinn's subsidiaries and its distributor do have principal places of business there, Cooper said. In addition, both Hospira and Helsinn have litigated Hatch-Waxman ANDA cases in New Jersey federal court, she said.

Moreover, Worldwide is registered to do business in New Jersey and intends to market the proposed generic Aloxi in the state, the opinion said.

''Under the rationale set forth in *Acorda*, the Court finds that Hospira's marketing of generic Aloxi will, at least in some part, take place in New Jersey because Hospira identifies itself as 'the world's leading provider of injectable drugs and infusion technologies', '' Cooper wrote.

''These facts lean even more strongly toward a finding of minimum contacts than in *Acorda*, where the court held that Mylan's 'network of independent wholesalers and distributors' alone constitutes a minimum contact with the state,'' she said.

''[U]nder *Acorda*'s guidance, these facts establish sufficient minimum contacts to find specific jurisdiction over both Hospira and Worldwide with respect to the pending ANDA,'' Cooper wrote.

Jurisdiction Isn't Unfair. The court also found that asserting specific jurisdiction over Hospira and Worldwide wouldn't be unfair or unreasonable.

''The Court does not find any unfairness here that would override the minimum contacts that Hospira and Worldwide have with New Jersey,'' the court concluded.

Hospira has litigated Hatch-Waxman lawsuits in this court and has initiated at least two of those actions, she said. In addition, New Jersey has an interest in adjudicating the parties' dispute because it has adjudicated or is adjudicating many similar Hatch-Waxman cases over generic Aloxi products.

''This only weighs more in favor of judicial economy and efficiency, as the ANDA actions currently pending in this Court involve the same Aloxi patents as the ones at issue here,'' Cooper said.

Accordingly, the judge said, the Hospira defendants didn't make a compelling argument as to why asserting jurisdiction in this case would be unfair or unreasonable.

  PLIR ISSN 1542-9547

First Decision to Apply *Acorda*? Attorney Jake M. Holdreith, of Robins Kaplan LLP in Minneapolis, told Bloomberg BNA April 6 that the ruling in the Helsinn case may be the first time a district court has applied the Federal Circuit's holding in the *Acorda* case.

''This is one of the first decisions applying the Federal Circuit's *Acorda* ruling, in which the Federal Circuit may have put an end to the personal jurisdiction arguments that ANDA filers have been making for the last several years,'' he said.

Before the Federal Circuit decided *Acorda*, ANDA filers had been arguing, with some success, that if the forum lacked general jurisdiction over them and the generic product at issue hadn't been developed or sold there, that forum also lacked specific jurisdiction over them.

But *Acorda* held that generic drug manufacturers are subject to personal jurisdiction throughout the country as a result of filing an abbreviated new drug application with the FDA.

''The New Jersey court's decision in *Helsinn v. Hospira* is predictably in line'' with the Federal Circuit's latest ruling in *Acorda*,'' attorney Paul A. Ainsworth, of Sterne, Kessler, Goldstein & Fox P.L.L.C. in Washington, told Bloomberg BNA April 6. The result in the case is not surprising because the Federal Circuit's analysis relied on facts that are typical to most, if not all, ANDA filers, he said.

''We expect this to be trend for ANDA filers seeking to challenge personal jurisdiction so long as the *Acorda* decision remains good law,'' he said.

''It seems apparent that patent holders will regain substantial control over the choice of forum in Hatch-Waxman cases for now,'' Holdreith told Bloomberg BNA. It is likely that most of these cases will continue to be heard in Delaware, New Jersey and, to a lesser extent New York, he said. Patent holders perceive those forums to be more favorable to protecting patents in Hatch-Waxman cases.

Things Could Change. But things are far from settled in the jurisdictional arena, Holdreith said. For example, he said, the U.S. Supreme Court could wind up reviewing the venue rule announced in *Acorda* or Congress could pass legislation that affects choice of venue in patent cases . And, he said, arguments have been raised in the *In Re: TC Heartland* case, now before the Federal Circuit, that the patent venue provisions should be interpreted to narrow the available venues for patent suits.

''Any of these could result in yet another change in the battle for control of venue in Hatch-Waxman cases,'' Holdreith said.

Claim Plausible. In addition to addressing jurisdiction, Judge Cooper's ruling also addressed whether Helsinn's complaint sufficiently stated a plausible claim for relief.

Among other things, Hospira argued that Helsinn didn't state a claim against Worldwide because Worldwide didn't submit the ANDA to make and sell a generic version of Aloxi to the Food and Drug Administration.

But Cooper said that Section 271(b) of the Patent Act doesn't explicitly require that a defendant must sign the ANDA in order for it to be a properly named defendant in a Hatch-Waxman case.

And, Cooper said, irrespective of whether Worldwide signed or submitted the ANDA, it is undisputed that it will be the sole U.S. marketer, seller, and distributor of Hospira's generic version of Aloxi and will benefit if the application is approved. Moreover, Cooper said, Helsinn alleged that Worldwide acts as Hospira's subsidiary, agent and alter ego, and that both Hospira and Worldwide will infringe the Aloxi patents by making, selling or offering the proposed generic product for sale.

Accordingly, Helsinn's allegations sufficiently demonstrate a plausible claim for relief, Cooper said, and denied Hospira's motion dismiss the complaint for failure to state a claim.

Aloxi (palonosetron hydrochloride) injection is approved for use in adults to help prevent nausea and vomiting when it happens right away or later (up to five days) with certain anticancer medicines. It's also approved to help prevent acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy in both adults and children.

Helsinn is based in Switzerland. Hospira is now part of New York-based Pfizer Inc.

Paul Hastings LLP in New York represented Helsinn. Jenner & Block LLP in New York represented Hospira.

BY DANA A. ELFIN

To contact the reporter on this story: Dana A. Elfin in Washington at delfin@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

A copy of the opinion is at http://www.bloomberglaw.com/public/document/Helsinn_Healthcare_SA_v_Hospira_Inc_No_152077_MLC_2016_BL_107238_.

Medicaid

Solvay Beats Medicaid False Claims Case; Court Finds Lack of Evidence From Relators

Two private whistle-blowers for Solvay Pharmaceuticals Inc. couldn't prove the company's alleged off-label marketing for its drugs caused false Medicaid claims, a federal judge has ruled (*United States ex rel. King v. Solvay S.A.*, 2016 BL 101294, S.D. Tex., No. 4:06-cv-2662, 3/31/16).

The court's decision ends almost 13 years of litigation in which two former sales managers for Solvay, John King and Tammy Drummond, had alleged that the drug manufacturer urged physicians to use three of the company's drugs for uses not approved by the Food and Drug Administration.

In his March 31 opinion, Judge Gray H. Miller of the U.S. District Court for the Southern District of Texas, ruled that the Medicaid claims data from Texas and New York that the whistle-blowers relied on wasn't admissible as evidence at trial in the case.

As a result, the court found that King and Drummond were unable to show that alleged off-label marketing by the drug manufacturer actually caused a false claim for the drug under any government-sponsored program.

Sarah M. Frazier of Berg & Androphy in Houston, who represented the whistle-blowers in the case, told Bloomberg BNA that the court's order was premised ''on technical issues, easily resolved at trial, relating to authentication of large Medicaid claims datasets, even though the court acknowledged it had no reason to doubt their authenticity.''

She faulted the district court for disregarding ''overwhelming evidence of illegal and deceptive off-label marketing'' by Solvay and indicated that her clients intended to appeal the decision to the U.S. Court of Appeals for the Fifth Circuit.

''We anticipate that the Fifth Circuit will elevate substance—in the form of rigorously collected proof—over form, and refer these claims, as well as erroneously dismissed AndroGel claims, back to the district court for trial,'' she said.

Attorneys for Solvay didn't respond to Bloomberg BNA's request for comment.

Long-Standing Litigation. The False Claims Act suit alleged that Solvay sought to increase prescriptions of its drugs Aceon, Luvox and AndroGel through alleged kickbacks and by promoting off-label uses for the drugs to physicians who sat on Medicaid pharmaceutical and therapeutics committees.

In a series of rulings over the past few years, the court has dismissed every part of the lawsuit, including a Feb. 8 decision dismissing allegations that the drug company attempted to improperly influence physicians in an effort to get the drugs listed on state Medicaid preferred drug lists (14 PLIR 201, 2/12/16).

In the March 31 ruling, the court examined Medicaid claims data presented by the whistle-blowers and determined that it didn't meet the federal court requirements for admissibility at trial. Additionally, the court found that the notes made by Solvay sales representatives of their calls to physicians didn't include sufficient admissible evidence that the representatives were soliciting off-label uses for the drugs.

Berg & Androphy represented the whistle-blowers. Hogan Lovells US LLP represented Solvay.

BY MATTHEW LOUGHRAN

To contact the reporter on this story: Matthew Loughran in Washington at mloughran@bna.com

To contact the editor responsible for this story: Janey Cohen at jcohen@bna.com

The court's opinion is at http://www.bloomberglaw.com/public/document/United_States_v_Solvay_SA_No_CIVIL_ACTION_H062662_2016_BL_101294_.

Product Liability

Maker of Depakote Must Face Birth Defects Lawsuit, Court Says

Abbott Laboratories must face a suit by a family alleging the mother's use of Depakote during pregnancy caused their son to be born with spina bifida, even though the drug carried a black box warning about that birth defect (*B.F. v. Abbott Labs, Inc.*, E.D. Mo., No. 4:12-cv-01760-CAS, 3/31/16).

The plaintiffs raised fact questions whether the warning was adequate and whether a stronger warning would have prevented the injury, Judge Charles A. Shaw of the U.S. District Court for the Eastern District of Missouri said March 31.

Beth Forbes used Depakote to treat bipolar disorder from 2003 until January 2005, when she learned she was pregnant. The label included a black box warning in all caps, that said, in part, ''Valproate (Depakote) can produce teratogenic effects such as neural tube defects (e.g., spina bifida).''

A black box warning is the strongest the Food and Drug Administration can require. The agency says such a warning appears on a drug's label and is designed to call attention to serious or life-threatening risks.

A separate warning said the Centers for Disease Control and Prevention estimated the risk of valproate acid-exposed women having a child with spina bifida to be about 1 to 2 percent.

Spina bifida is an incomplete closing of the backbone and membranes around the spinal cord.

Unresolved issues included whether the label should have said Depakote should only be used as a last line of treatment in women of childbearing potential, whether Abbott understated the risk of congenital malformations and whether the warning failed to advise about the importance of contraceptive use, the opinion said.

Forbes's physician testified she might not have prescribed Depakote if Abbott had provided this additional information, the court said.

AbbVie, a company that was created in 2013, now markets Depakote, according to an Abbott spokeswoman.

Aubuchon, Raniere & Panzeri, P.C. represents the plaintiffs.

Bryan Cave and others represent Abbott Labs.

BY JULIE STEINBERG

To contact the reporter on this story: Julie A. Steinberg in Washington at jsteinberg@bna.com

To contact the editor responsible for this story: Nicholas Datlowe at ndatlowe@bna.com

Full text is at http://www.bloomberglaw.com/public/document/BF_et_al_v_Abbott_Laboratories_Inc_et_al_Docket_No_412cv01760_ED_.

Product Liability

Lipitor Plaintiffs Consider Options After Evidence Barred

Women alleging Lipitor caused their diabetes are evaluating options after a ruling that excluded nearly all their evidence linking drug and disease (*Lipitor (Atorvastatis Calcium) Mktg., Sales Prac. & Prod. Liab. Litig., In re*, D.S.C., No. 14-02502, 3/30/16).

Testimony from Dr. Michael Quon, Dr. Barbara Roberts and Dr. Edwin Gale—three experts who sought to connect Lipitor to diabetes in female patients at dosages of 10, 20 and 40 milligrams—was barred by Judge Richard M. Gergel of the U.S. District Court for the District of South Carolina March 30.

The court allowed testimony by Dr. Sonal Singhs that the cholesterol drug can cause diabetes at an 80 milligram dose.

The ruling, in combination with prior decisions excluding plaintiffs' evidence, ''has had a profound impact on all plaintiffs within this litigation,'' plaintiffs' lead counsel in the federal multidistrict litigation H. Blair Hahn told Bloomberg BNA April 1.

''Plaintiffs strongly disagree with the court's rulings and all legal options are being considered,'' Hahn said.

  PLIR ISSN 1542-9547

On the other side, ''Pfizer is pleased the Court has decided that there is no reliable general causation evidence to support plaintiffs' claims regarding Lipitor at the 10, 20 and 40 mg. doses,'' the company said in a statement e-mailed to Bloomberg BNA April 1.

Plaintiffs ''have failed to meet this essential burden of proof for the doses taken by the vast majority of patients prescribed the medicine,'' Pfizer said.

Earlier, Gergel excluded opinions of biostatistician Nicholas Jewell in all pending cases. And the judge barred the opinion of Dr. Elizabeth Murphy, who said Lipitor was a substantial contributing factor in bellwether plaintiff Juanita Hempstead's development of type 2 diabetes (14 PLIR 244, 2/19/16).

Plaintiffs were given an opportunity to advise the court of any cases in the MDL that could survive summary judgment under the ruling in *Hempstead*, and they didn't identify any case.

Hahn is with Richardson Patrick Westbrook and Brickman.

DLA Piper US LLP represents Pfizer.

BY JULIE STEINBERG

To contact the reporter on this story: Julie A. Steinberg in Washington at jsteinberg@bna.com

To contact the editor responsible for this story: Jeffrey D. Koelemay at jkoelemay@bna.com

The order is available at http://www.bloomberglaw.com/public/document/In_Re_Lipitor_Atorvastatin_Calcium_Marketing_Sales_Practices_and_/5.

Product Liability

Pfizer Wins Dismissal In Zoloft Birth-Defect Warning Cases

Pfizer Inc. won dismissal of more than 300 lawsuits attempting to link the antidepressant Zoloft to heart defects in newborns (*In re Zoloft Prod. Liab. Litig.*, E.D. Pa., No. 12-02342, 4/5/16).

Judge Cynthia M. Rufe of the U.S. District Court for the Eastern District of Pennsylvania granted Pfizer's motion for summary judgment April 5. Rufe presides over the Zoloft federal multidistrict litigation.

Plaintiffs alleged Pfizer failed to warn about possible birth defects in children born to women who used Zoloft while pregnant.

Evidentiary Rulings. The decision follows Rufe's earlier rulings that barred plaintiffs' expert evidence.

The plaintiffs were granted a ''Daubert do-over'' after the exclusion of testimony from four experts who sought to testify that Zoloft could cause birth defects.

But in December 2015, Rufe barred statistician Nicholas Jewell's causation testimony (13 PLIR 1737, 12/11/15).

Without admissible expert testimony based on epidemiological evidence, plaintiffs instead ''have cobbled together evidence of biological plausibility, specific causation opinions based on an assumption that general causation has been established, and anecdotal evidence,'' the court said. This is insufficient, the opinion said.

The latest ruling affirms that the plaintiffs failed to produce reliable scientific evidence that Zoloft causes the injuries the plaintiffs alleged, Pfizer said in a statement.

''There is extensive science supporting the safety and efficacy of Zoloft, and the medicine carries accurate, science-based and FDA-approved information on its benefits and risks,'' the company said.

New York-based Pfizer reaped about $3.3 billion in Zoloft sales in 2005, making it the best-selling antidepressant on the market at the time. The company lost patent protection on the drug the next year and generic versions are now made by other drugmakers, including Mylan NV. Under U.S. law, the label on generic versions of the drug must contain the same warnings as Pfizer's label.

The drug currently generates about $375 million in revenue for the company or about 0.8 percent of the company's total sales in 2015.

Mark Robinson, a lawyer for the plaintiffs, didn't immediately respond to phone and an e-mail messages seeking comment on the ruling.

Pfizer won two jury trials in 2015 in cases brought by women making similar claims in Philadelphia and St. Louis (13 PLIR 874, 6/19/15).

BY KARTIKAY MEHROTRA

—Julie A. Steinberg contributed reporting.

To contact the reporter on this story: Kartikay Mehrotra in San Francisco at kmehrotra2@bloomberg.net

To contact the editors responsible for this story: Michael Hytha at mhytha@bloomberg.net, Andrea Tan

The opinion is available at http://www.bloomberglaw.com/public/document/IN_RE_ZOLOFT_SERTRALINE_HYDROCHLORIDE_PRODUCTS_LIABILITY_LITIGATI/8.

Federal News

Drug Development

Senate Panel Approves 'Cures' Bills, But Several Issues Wait for Floor Action

A Senate committee approved five medical innovation bills April 6 during the final markup of companion legislation to the House's 21st Century Cures bill.

The five bills—which include language to deter the FDA from relying too heavily on guidance documents and to address privacy protection for research participants' genetic data—are the last bills the Senate Health, Education, Labor and Pensions Committee will mark up in an effort to accelerate the development of new drugs and devices. The committee has now approved a total of 19 bills with 50 proposals over three markup sessions as part of the legislative package.

However, HELP Committee Chairman Lamar Alexander (R-Tenn.) said the Senate still has more work to do, most notably reaching a bipartisan agreement on mandatory funding for the National Institutes of Health.

"Without that agreement, we don't get this bill. But without this bill, we don't get mandatory funding either."

—HELP Chairman Lamar Alexander (R-Tenn.) on mandatory funding for NIH

''The House has done its job. We've done most of ours,'' Alexander said, reiterating statements that the medical innovation effort is the most important legislation that can move through Congress this year. ''It has the promise of improving the health of virtually every American. We should make certain we finish this, and the sooner the better.''

The House approved its cures measure, H.R. 6, in 2015.

Floor Action Next. Senate Majority Leader Mitch McConnell (R-Ky.) has agreed to hold a floor vote on 21st Century Cures once the HELP committee has completed its work, Alexander said.

The committee has made progress on the issue of mandatory NIH funding, Alexander said, adding that the House's bill would provide $8.75 billion in mandatory funding for both the NIH and the Food and Drug Administration.

HELP Democrats, particularly Sens. Elizabeth Warren (Mass.) and ranking member Patty Murray (D-Wash), have said they won't support the medical innovation package without additional, mandatory NIH funding. Alexander said he favors a one-time funding surge to support specific projects in precision medicine, the cancer ''moonshot'' initiative, brain research, support for young scientists and big ''biothink'' awards for large, innovative projects (14 PLIR 376, 3/11/16).

''I can assure that you I don't have any intention of taking the work product of this committee to the floor without a bipartisan agreement with Senator Murray and others about the surge of funding for the National Institutes of Health,'' Alexander said. ''Without that agreement, we don't get this bill. But without this bill, we don't get mandatory funding either.''

HELP Committee leaders have consulted with the chairman and ranking member of the Senate Finance Committee as well as Health and Human Services Secretary Sylvia Mathews Burwell, he said.

Murray said she believes the committee can reach a bipartisan agreement, and once that's reached, ''we'd be able to make a real difference in the lives of patients and families across the country.''

Besides funding, Alexander said, other issues that still need to be resolved are:

- appropriate language for regenerative medicine legislation;
- monitoring medical devices after they're approved, an issue for which Murray has advocated strongly;
- a rare-disease or orphan drug bill (S. 1421) known as the OPEN Act, which would extend the exclusivity period by six months on an FDA-approved drug or biological product that is approved to prevent, diagnose or treat a new indication for a rare disease or condition; and
- oversight of laboratory-developed tests, an area where the FDA has proposed taking a stronger role.

''These are some of the remaining issues, but the fact remains that we began with 50 bipartisan issues,'' Alexander said. ''So we've made substantial progress.''

Bills Approved. The bills approved by the committee during the April 6 markup were:

- S. 2700, the FDA and NIH Workforce Authorities Modernization Act, which is designed to make it easier for the NIH and the FDA to recruit top scientists (14 PLIR 444, 3/25/16);
- S. 185, the Promise for Antibiotics and Therapeutics for Health (PATH) Act, which would permit the FDA to accelerate an antibacterial drug's approval for an identifiable, limited patient population if the drug treats a serious or life-threatening condition and addresses an unmet need;
- S. 2713, the Advancing Precision Medicine Act of 2016, which supports the White House's ongoing Precision Medicine Initiative to advance an emerging model of health-care delivery that targets treatments to patient subgroups identified by their genetic makeup;

  PLIR ISSN 1542-9547

■ S 2742, the Promoting Biomedical Research and Public Health for Patients Act, which aims to cut the time scientists spend on administrative tasks so they can focus more on developing medical treatments; and

■ S. 2745, the NIH Strategic Plan and Inclusion in Clinical Research.

Four of the five bills moved forward on a voice vote. Senators approved the precision medicine bill (S. 2713) by a 20-2 vote, with Warren and Sen. Rand Paul (R-Ky.) voting against the bill.

Too Many FDA Guidances? The HELP Committee also approved several amendments to the bills, including one from Sen. Pat Roberts (R-Kan.) over concern that the FDA is relying too heavily on guidance documents instead of using the rulemaking process. Roberts' amendment would require the FDA to justify why it's issuing a guidance document as opposed to formal rulemaking, whenever the FDA issues a new guidance that provides initial interpretations of new significant regulatory requirements.

The committee approves an amendment requiring the FDA to justify why it's issuing a guidance document as opposed to formal rulemaking in certain cases.

''My intent is not to prohibit the agency from issuing guidance. They aren't all bad. They are vital to industries the FDA regulates,'' Roberts said. ''But they must be used appropriately—to guide, not to implement new policies and avoid the requirements of the formal rulemaking process.''

Murray said she couldn't support Roberts' amendment because FDA Commissioner Robert M. Califf expressed concerns that such a requirement would slow the FDA's ability to relay information quickly and efficiently, especially when there is a public health risk.

The FDA guidance language was one of two amendments HELP members attached to S. 2700. The other amendment from Sens. Richard Burr (R-N.C.) and Robert P. Casey Jr. (D-Pa.) would waive the Department of Health and Human Services' requirements under the Paperwork Reduction Act during a public health emergency.

Privacy. The committee also approved an amendment to S. 2713 to protect the genetic privacy of research participants. Warren, who sponsored the amendment with Sen. Michael B. Enzi (R-Wyo.), said the privacy laws need to be updated as researchers are collecting more and more information to help understand diseases and develop the next generation of cures.

''It will give more people reassurance that participation in clinical trials won't compromise their privacy,'' she said.

Warren, who has said she won't vote in favor of any medical innovation bills without guaranteed mandatory funding for the NIH, voted in favor of the amendment but against S. 2713.

The committee also approved an amendment to S. 2742 from Burr that would require the NIH's National Center for Advancing Translational Sciences to include in its annual report any methods and tools that have been developed with NCATS-supported research.

BY JEANNIE BAUMANN

To contact the reporter on this story: Jeannie Baumann in Washington at jbaumann@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

More information on the markup is available at http://www.help.senate.gov/.

Warren and Enzi's genetic privacy amendment is at https://www.congress.gov/bill/114th-congress/senate-bill/2744.

Roberts' amendment on FDA guidance is at http://src.bna.com/dUR.

Burr's NCATS amendment is at http://src.bna.com/dVh.

Biosimilars

Label Must State Product Is a Biosimilar, May Rely on Originator's Data, FDA Says

Biosimilar product labels must include a statement that the product is a biosimilar and may rely on the data submitted for FDA approval by the originator biologic, according to a new FDA draft guidance document.

The draft guidance was released March 31 and is the subject of a notice in the April 4 Federal Register (81 Fed. Reg. 19,194). Attorneys told Bloomberg BNA that the guidance document is relatively consistent with the labeling the Food and Drug Administration authorized for the first biosimilar approved under the Biologics Price Competition and Innovation Act in March 2015—Sandoz's Zarxio, a biosimilar of Amgen's Neuopogen.

''The big news about the draft guidance is that they got it out, and this alone will end some uncertainty for both the biosimilar applicant and the originator of the biologic, also known as the reference product sponsor (RPS),'' said Siegmund (Sige) Gutman, chair of Proskauer's life sciences patent practice.

He added, ''In it, there is something for everyone.''

However, a few organizations, including the Patients for Biologics Safety and Access and the American College of Rheumatology, released statements indicating that the clinical trial data for the biosimilar should be included in the labeling and that the label should specify whether the supporting clinical data for each indication are derived from studies of the biosimilar or the reference biologic.

Splitting the Baby. A biologic is a complex, large molecule, such as a monoclonal antibody or a cell signaling protein, that is different from the small molecules of chemically derived drugs. Generics of chemically derived drugs are identical to the brand product, while a product designed to resemble an FDA-approved biologic can only be approved by the FDA as biosimilar to the RPS with no clinically meaningful differences, and, on further FDA approval, as interchangeable without the approval of a physician.

The BPCIA, signed into law in 2010 as part of the Affordable Care Act, provides an abbreviated approval pathway for a biosimilar that partly relies on the data originally submitted to the FDA by the RPS for approval.

Thomas H. Wintner, an attorney with Mintz Levin, noted in an April 1 phone interview that reference product sponsors should be pleased that the draft guidance requires the label to have a clear statement that the product is a biosimilar, although some RPSs would have preferred that the label reference data from clinical studies the biosimilar applicant submitted to the FDA to establish biosimilarity.

''And from the biosimilar manufacturer's perspective, the FDA will still permit reliance in the labeling on the RPS' clinical studies, even if the biosimilar applicant's data shows some differences with the RPS', which wouldn't be surprising since FDA is approving the product as similar, not identical, to the reference product,'' Wintner said.

Premier Inc., a performance improvement alliance of hospitals and other health-care providers, issued a statement March 31 praising the draft guidance, saying ''it will help ensure that prescribers and pharmacists understand which drugs can be grouped and substituted for one another, avoiding the potential for error that would happen if biosimilars had wholly unique names that made no reference to the branded equivalent. Moreover, in avoiding distinguishable names for every biosimilar, we believe the FDA's guidance will improve patient access and speed the uptake of these cost saving products.''

FDA Says It Didn't Want to Stir Confusion. In an FDA ''From Our Perspective'' posting online, FDA's Leah Christl addressed the FDA's reasoning behind its decision to rely on the RPS's data in the labeling.

''While we recommend that biosimilar labeling include biosimilar product-specific data necessary to inform safe and effective use of the product, we generally do not recommend that comparative data supporting the demonstration of biosimilarity be included in biosimilar product labeling. We've taken this approach to avoid potential confusion or misinterpretation of the comparative data,'' she said. Christl is associate director for therapeutic biologics and lead of the therapeutic biologics and biosimilars staff in the FDA's Office of New Drugs.

Christl wrote that, rather than essentially repeat the reference product's demonstration of safety or effectiveness, comparative clinical studies are intended to demonstrate that there are no clinically meaningful differences between the proposed biosimilar product and the reference product.

''Indeed, comparative clinical studies in a biosimilar development program may use endpoints or study populations that are different from those used to support approval of the reference product. Due to the potential for differences in clinical study parameters, we think that including comparative clinical data in biosimilar product labeling would be confusing or even potentially misleading to health care providers,'' Christl wrote.

Ultimately, Christl said, the comparative data are useful for the FDA to make a decision about biosimilarity, but aren't likely to be relevant to a provider's prescribing considerations.

Looking Ahead. Wintner noted that the draft guidance says that clinical studies from the biosimilar applicant might need to be included on the label if needed to ''inform safe and effective use.''

The draft guidance also touches on the ''naming issue,'' discussing when biosimilar sponsors should use their biosimilar's name, the reference product's proprietary name and the ''core name'' of the product—the part of the proper name that doesn't include the four-letter suffix proposed in the FDA's draft guidance on biologics naming.

Gutman noted that the draft labeling guidance shouldn't be interpreted to be a definitive reflection of the FDA's position on the naming of biosimilars.

The draft guidance doesn't address AbbVie's request that the labeling of a biosimilar note that it isn't approved for all the indications of the reference sponsor.

Wintner repeated that there were no real surprises in the draft guidance. ''This will be more interesting when we have five or six biosimilar products on the market and we have two or three years in and we have some experience from when physicians actually prescribe biosimilars,'' he said.

After the April 4 publication of the notice, there is a 60-day comment period on the guidance ending June 3. Comments may be submitted electronically on http://www.regulations.gov. The docket number is FDA-2016-D-0643.

BY JOHN T. AQUINO

To contact the reporter on this story: John T. Aquino in Washington at jaquino@bna.com

To contact the editor responsible for this story: Lee Barnes at lbarnes@bna.com

The draft guidance is at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM493439.pdf. Text of the Federal Register notice is at http://src.bna.com/dNr or https://www.gpo.gov/fdsys/pkg/FR-2016-04-04/html/2016-07611.htm.

Fraud and Abuse

Consumer Group Wants Stronger Enforcement for Drug Industry

Citing a decline in major pharmaceutical settlements with the government, a consumer group March 31 called for stronger enforcement to deter pharmaceutical manufacturers from breaking the law and defrauding federal and state health programs.

Public Citizen's new report found that drugmakers entered into 373 state and federal settlements totaling $35.7 billion in criminal and civil penalties from 1991 through 2015, but that both the number and size of settlements decreased significantly in 2014 and 2015.

Of the 373 settlements, 140 were federal settlements totaling $31.9 billion and 233 were state settlements totaling $3.8 billion. From 1991 through 2015, 31 companies entered into repeat settlements with the federal government.

The violation resulting in the most federal penalties was unlawful promotion, usually off-label marketing.

  PLIR ISSN 1542-9547

Attorneys told Bloomberg BNA that the decline in settlements in 2014 and 2015 was a result of clearer rules and the pharmaceutical industry becoming better at complying with those rules.

The pharmaceutical industry said the report is misleading because, among other things, it aggregates all settlements involving the industry with little regard to whether the companies actually broke the law.

Decrease in Settlements, Penalties. Just $2.4 billion in federal financial penalties was recovered in 2014 and 2015, which is less than one-third of the $8.7 billion recovered in 2012 and 2013 and the lowest two-year total since 2004 and 2005, Public Citizen said. There were also only 20 state settlements in 2014-2015, which is the lowest two-year total since 2006-2007.

The report said there are several possible reasons for this decrease in settlement activity, including:

- a decline in federal enforcement;
- a shift in the focus of federal prosecutions away from off-label marketing and toward other forms of illegal activity;
- changes in state Medicaid pharmaceutical reimbursement strategies; and
- shifts in industry marketing strategies.

''We don't yet know why there were fewer and smaller settlements in the 2014 to 2015 period,'' Sammy Almashat, researcher with Public Citizen's Health Research Group and lead author of the report, said in a statement. ''But we do know that, in addition to the rarity of executive accountability, previous penalties never have been large enough to deter the most common types of pharmaceutical fraud. So it would be surprising if the industry suddenly decided, of its own accord, to comply with laws it has routinely violated for decades.''

''Much larger penalties and successful prosecutions of company executives that oversee systemic fraud, including jail sentences if appropriate, are necessary to deter future unlawful behavior.''

—PUBLIC CITIZEN

In one large settlement, Johnson & Johnson paid $2 billion in 2013 after pleading guilty to off-label promotion of its antipsychotic drug Risperdal for use in elderly patients with dementia, the report said (11 PLIR 1333, 11/8/13). Risperdal brought in $11.7 billion in sales for the company in just the first 12 years after its approval (1994-2005), nearly six times the total settlement amount.

Public Citizen said the Johnson & Johnson case ''demonstrates the stark imbalance between the penalties for and the profits made on implicated products.''

''Much larger penalties and successful prosecutions of company executives that oversee systemic fraud, including jail sentences if appropriate, are necessary to deter future unlawful behavior,'' the report said. ''Otherwise, these illegal but profitable activities will continue to be part of companies' business model.''

Legislation Introduced. Responding to the report, Democratic presidential candidate Sen. Bernie Sanders (I-Vt.) said in a statement that ''time and time again, drug companies defraud American taxpayers while making billions off government-granted monopolies.''

''Enough is enough. The greed of the pharmaceutical industry must end,'' Sanders said. ''I urge my colleagues to stand up to the pharmaceutical industry and pass legislation to send a clear message that crime will no longer pay.''

Sanders and Rep. Elijah Cummings (D-Md.) introduced a bill (S. 2023, H.R. 3513) in September 2015 that would, among other things, terminate any remaining market exclusivity period on any product found in violation of criminal or civil law through a federal fraud conviction or settlement (13 PLIR 1294, 9/11/15).

Attorneys Cite Better Compliance. Daniel Kracov, head of the health-care practice at Arnold & Porter LLP in Washington, told Bloomberg BNA April 1 that the report ''has a pretty obvious flaw'' in that it doesn't take into account that over the time period studied ''almost the entire industry has instituted and now has very well-developed compliance programs.''

Kracov said the industry has spent hundreds of millions of dollars on compliance, so that has had an impact on the number of violations and the number of lawsuits.

Also, Kracov said the whole First Amendment debate over what companies can say has led to fewer cases being brought against companies.

''There were a whole class of cases that were predicated on the notion that speech related to off-label uses is per se unlawful. That is now in question,'' Kracov said. ''Why would a prosecutor bring a case if that was the only basis for the case? So, I think you're going to see a natural caution with respect to those cases.''

Kevin McAnaney, with the Law Offices of Kevin G. McAnaney in New York, told Bloomberg BNA in a March 31 e-mail that ''the obvious explanation for the decline is that as the rules have become clearer, the industry has become better at complying.''

''These cases are driven by relators, not the government, and if there are fewer settlements, it is because there are fewer alleged violations,'' McAnaney said.

Paul E. Kalb, of Sidley Austin LLP in Washington, told Bloomberg BNA in a March 31 e-mail that he believes ''that the trend described reflects the fact that over the past decade the industry has focused intensively on conducting business in a compliant manner.''

''Among many other steps, most companies have invested heavily in progressively sophisticated compliance programs. I believe that is the reason, not a failure of governmental oversight or prosecutorial zeal, for the decline in the number and aggregate value of settlements in the industry,'' Kalb said. ''In short, I believe that the report reflects positive developments and that Public Citizen's alarm at this trend and plea for even more draconian punishments is misplaced.''

Laurence Freedman, an attorney with Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC, Washington, told Bloomberg BNA in a March 31 e-mail that while the statistics in the report are interesting, ''the conclusion that there is less enforcement is off-base.''

"Attempted regulation through litigation costs everyone more especially taxpayers."

—KIRK OGROSKY, FORMER FEDERAL PROSECUTOR

The Department of Justice ''and the relators' bar are as vigorous as ever, it could be that the wave of enforcement for over a decade has led to the desired deterrence and compliance in the industry as to off-label marketing,'' Freedman said. ''There is a fundamental flaw in the assumption that there is widespread illegal conduct that may escape enforcement. DOJ has been hyper-aggressive in its pharma enforcement, as demonstrated precisely by these statistics, and there has been no policy shift by DOJ.''

Kirk Ogrosky, an attorney with Arnold & Porter in Washington and a former federal prosecutor, told Bloomberg BNA in an e-mail that ''the conclusion that there should be more DOJ litigation and enforcement against pharmaceutical manufacturers misses the mark entirely.''

False Claims Act ''litigation is an after-the-fact tool that rarely should be used in a highly regulated market. The taxpaying public would be much better served by [the Centers for Medicare & Medicaid Services] and the FDA doing a better job on the front end,'' Ogrosky said. ''Attempted regulation through litigation costs everyone more especially taxpayers.''

For example, Ogrosky said that ''of the money identified by Public Citizen, over $5 billion went to whistleblowers and their attorneys, not to mention the cost that companies have incurred dealing with the hundreds of frivolous allegations.''

''We need to address structural flaws in our healthcare system, not simply encourage more litigation and enforcement action,'' Ogrosky said.

Industry: 'Misleading Conclusions.' The Pharmaceutical Research and Manufacturers of America (PhRMA) said in a March 31 statement to Bloomberg BNA that it is ''disappointed at the report's misleading conclusions.''

''Biopharmaceutical companies are committed to legal and ethical conduct that serves the best interests of patients. The report makes scant mention of the tens of millions of dollars companies spend annually to develop and maintain state-of-the-art legal compliance programs,'' PhRMA said. ''Among its many methodological flaws, the report aggregates all settlements involving the pharmaceutical industry, with little regard as to whether the companies actually broke the law.''

PhRMA said ''civil settlements rarely resolve the question of guilt, yet the report glosses over its own finding that 88 percent of the settlements reported were civil, not criminal.''

''Conversations about how to direct health care enforcement to promote ethical corporate conduct, patient safety, innovation, and security of the public fisc are important and necessary,'' PhRMA said. ''Those conversations are ill-served by slapdash conclusions based on faulty reasoning shown in this report.''

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Janey Cohen at jcohen@bna.com

The report is at http://www.citizen.org/hrg2311.

Fraud and Abuse

DOJ Unveils New Pilot Program to Encourage Companies to Self-Report Foreign Bribes

The Justice Department announced April 5 that it's beginning a one-year pilot program to encourage companies, including health-care companies that sell products abroad, to self-report violations of the Foreign Corrupt Practices Act.

The FCPA, which covers companies that list their securities in the U.S., prohibits offering or paying bribes to foreign government officials at any level of government. The DOJ enforces the statute along with the Securities and Exchange Commission.

The new program is designed to incentivize companies to ''come to us earlier than they do now,'' Assistant Attorney General Leslie Caldwell, who heads DOJ's Criminal Division, said in a conference call with reporters. Currently, she said, many FCPA violations never even come to the government's attention .

The pilot program's incentives for companies who self-disclose before they're caught include significantly lower penalties of as much as 50 percent below the federal sentencing guidelines for criminal cases, avoiding appointment of a corporate monitor or even the DOJ declining to prosecute the self-reported violation, DOJ officials said.

The guidelines make a ''clear distinction between voluntary self-disclosure versus companies that may decide they want to wait until after they're caught and then cooperate,'' Andrew Weissmann, chief of the fraud section at the DOJ's Criminal Division, said.

''If a company opts not to self-report, the pilot program makes it clear that the outcome will be significantly different and significantly more severe than if it had self-reported,'' Caldwell said.

The DOJ predicts the increased FCPA resources will increase the number of prosecutions.

The DOJ said it will assess the pilot program after a year. It also announced that it was beefing up its resources in the FCPA area, including hiring 10 new prosecutors devoted solely to foreign corruption cases and adding three new squads in the overseas corruption area at the Federal Bureau of Investigation. ''Given our increased resources, we will increase the number of prosecutions'' in the FCPA area, Caldwell predicted.

Attorney Tim Purdon, a former U.S. attorney, told Bloomberg BNA, ''More agents and more prosecutors mean more cases.'' Purdon, with the firm of Robins Kaplan in Bismarck, N.D., and a former U.S. attorney for North Dakota, said, ''There is no question that this is not business as usual. The key fact here is the dedica-

  PLIR ISSN 1542-9547

tion of new resources in the form of a 50 percent increase in the number of prosecutors'' and the establishment of three new FBI squads devoted to FCPA investigations.

The plan sets forth ''a clear DOJ leadership direction to work with foreign counterparts and mutually share information, including documents and witnesses,'' attorney Katie McDermott, of Morgan, Lewis & Bockius LLP's Washington office, told Bloomberg BNA in an April 5 e-mail.

''If this direction is successful, it will assure expedited investigations but also potentially more complicated settlements that will involve many stakeholders, not simply DOJ,'' she said, adding that many countries have their own anti-bribery statutes that will be affected in parallel investigations. McDermott is a former DOJ official.

Focus on Life Sciences. For life sciences companies, the DOJ's new guidance and increased transparency in the self-disclosure area will help them better navigate the often murky FCPA waters, health-care fraud attorneys told Bloomberg BNA.

''The pilot program is a positive step by having a publicly articulated benefit,'' Kirk Ogrosky, with Arnold & Porter LLP in Washington and a former DOJ official, told Bloomberg BNA April 5.

McDermott said the new plan provides ''a very clear and thought-out strategy of providing incentives for voluntary self-disclosure if defined mandates are met, including requiring companies to arrange interviews of its officers and employees here and abroad.''

Guidance is likely welcome because the government has already been scrutinizing pharmaceutical and medical device companies for FCPA violations and other potential corruption in connection with the sales and marketing of their products overseas, particularly in emerging markets.

''This is a high-risk area for pharmaceutical and device companies, particularly those who operate [in countries] where the risk is higher,'' Stephen G. Sozio, of Jones Day in Cleveland, told Bloomberg BNA in an April 5 telephone call.

''There was a real question in the mind of industry and in the mind of those who advise industry clients in terms of whether there was a discernible benefit from self-disclosure,'' Sozio, a former DOJ official, said. ''This makes clear there is a discernible benefit.''

''Because this is a risk for them, any program that the government comes up with that formalizes the benefit of self-disclosure and makes it transparent as to what benefit can be obtained and what is expected to obtain that benefit is a good thing for the industry,'' he added.

Jacqueline Wolff of Manatt, Phelps & Phillips LLP's New York office and a former DOJ official, told Bloomberg BNA April 5 that the DOJ's goal of ''providing greater transparency on charging decisions for companies is laudable.''

But Wolff said some of the program's aspects could actually lead to fewer companies self-disclosing.

These aspects include capping how much penalties can be reduced by, adding restrictions on overseas interviews of employees and requiring companies to prove that ''overseas'' legal restrictions prevent them from completing some of the required tasks under the program.

''Time will tell,'' Wolff said.

Attorney Advises Caution. But Ogrosky advised companies to look before they leap because prosecutors and agents still have wide discretion in FCPA cases. ''Even with the newly announced pilot program, I would caution against running to DOJ without a complete understanding of the issues,'' he said.

''While a 50 percent decrease in the penalty coupled with no monitor is promising, the decision to disclose still requires stepping into an arena where a company subjects itself to the discretion of the prosecutor and agents handing the matter,'' he said.

''While it seems intuitive that those who self-disclose would receive better treatment, the fact remains that there is a remarkable amount of variability in the justice system,'' Ogrosky said. ''Everyone should understand how DOJ has treated those who self-disclosed versus those who did not, and current public information makes it difficult to assess.''

''Factors such as the completeness of the disclosure, the level of required follow-up, and the seriousness of the underlying conduct will still take center stage,'' Ogrosky said. ''Without full transparency, the program may not have the desired impact.''

Corporate Self-Policing Inadequate? Meanwhile, Robert Weissman, president of the Washington-based consumer group Public Citizen, criticized the new program as a ''step back.''

Corporate self-policing has a dismal track record, Weissman told Bloomberg BNA in an April 5 telephone interview. ''The premise of the DOJ's pilot program is 'If you come clean, we won't prosecute you on the premise that you won't break the law in the future,' '' he said. ''Yet they do it anyway, all the time.''

In the pharmaceutical industry, he said, the industry's business and pricing models create ''the climate for corruption. As that model is exported overseas, there's a lot of reason to anticipate more pervasive bribery.''

''To the extent companies are looking at emerging markets as areas for their growth potential, there's good reason to be worried about unethical behavior as they try to expand and gain market share,'' he added.

''We need more enforcement and tougher penalties, not less enforcement and weaker penalties,'' Weissman said.

McDermott was more hopeful about the program. She said that DOJ's new FCPA plan mirrors a successful 1997 Health Care Fraud Program that required agency coordination of remedies and information and enhanced resources for investigations, and included incentives for voluntary self-disclosure and government guidance on compliance and anti-fraud prevention.

This model has been successful for the government's health-care fraud enforcement priorities, McDermott said. The DOJ is likely ''expecting similar success on an international scale, especially with self-disclosures, for FCPA enforcement,'' she added.

BY DANA A. ELFIN

To contact the reporter on this story: Dana A. Elfin in Washington at delfin@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

DOJ's enforcement plan and guidance is available at https://www.justice.gov/opa/file/838386/download.

A DOJ blog post about the program is at https://www.justice.gov/opa/blog/criminal-division-launches-new-fcpa-pilot-program.

Medicaid

CMS Delays Implementation of Part Of Medicaid Outpatient Drug Rule

The CMS has delayed the effective date for part of a final rule that changes how the government pays for outpatient prescription drugs in the Medicaid program.

The delay affects certain drugs, such as those that are injected or inhaled, and responds to a request from drug industry groups for more time.

On Jan. 21, the Centers for Medicare & Medicaid Services released the final rule on outpatient drugs (CMS-2345-FC; RIN 0938-AQ41) (14 PLIR 145, 1/29/16). The final rule implements provisions in the Affordable Care Act, which revised the formula for reimbursing pharmacies for generic and multiple-source drugs in Medicaid by using the average manufacturer price (AMP) to set the federal upper limit or FUL. FUL, a type of cost-containment strategy, is the maximum Medicaid reimbursement rate for multiple-source drugs.

The final rule establishes a definition of AMP for so-called 5i drugs: inhalation, infusion, instilled, implanted or injectable drugs. This part of the final rule was set to take effect on April 1, but the CMS said in a March 31 announcement that it has delayed the effective date until July 1.

The CMS said in its March 31 statement that ''it is our understanding that the greatest challenges for manufacturers'' related to determining the AMP for 5i drugs ''that are not generally dispensed through retail community pharmacies.''

The Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO) requested the extension of the effective date in a Feb. 26 letter to the CMS, saying the extension was needed to ''give manufacturers enough time to take the steps necessary to calculate Medicaid rebates according to the final rule's requirements.''

Details From Attorneys. Stephanie Trunk, of Arent Fox LLP in Washington, told Bloomberg BNA in an April 5 e-mail that the CMS ''is delaying the effective date for a very limited portion of the final AMP rule related to the implementation of changes to the AMP calculation for 5i drugs that are not generally dispensed at retail.''

Trunk said that until July, manufacturers can use ''existing approaches as documented in their reasonable assumptions to determine whether a 5i drug is generally dispensed by retail community pharmacies, which dictates whether a 5i AMP methodology or retail community pharmacy focused AMP methodology should be'' used.

The PhRMA and BIO letter noted that under the CMS's final rule, a 5i drug will be considered ''not generally dispensed through a retail community pharmacy'' if 70 percent or more of its sales are to entities that aren't retail community pharmacies, in what's known as the 70/30 test. The industry groups' letter detailed the lengths that companies would have to go through to make a monthly 70/30 determination.

Donna Lee Yesner, of Morgan Lewis & Bockius LLP in Washington, told Bloomberg BNA in an April 5 e-mail that most of the requirements in the final rule ''necessitating significant system changes involve 5i AMP, particularly how to apply the 70/30 ratio for determining on a monthly basis whether a drug is not generally sold to retail community pharmacies and a smoothing mechanism to reduce the likelihood of switching back and forth from retail to non-retail.''

''The calculation of 5i AMP is also unique so manufacturers need to set up a third calculation which incorporates the statute and final rule and certain assumptions where the final rule is unclear,'' Yesner said. ''For these reasons, CMS is rightly deferring enforcement of the 5i AMP portion of the rule.''

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Janey Cohen at jcohen@bna.com

The CMS announcement is at http://src.bna.com/dTo.

The final rule is at http://src.bna.com/cat.

Medicare

Patient Advocates, Medical Professionals Oppose MedPAC Recommendations on Part D

Patient advocacy and medical professional groups are fighting recommendations being considered by Congress's Medicare advisers urging modifications to the Part D drug benefit, including the low-income subsidy and protected classes of drugs.

Hundreds of advocates and medical groups have sent letters to the Medicare Payment Advisory Commission asking the members to nix recommendations such as increased cost sharing for low-income beneficiaries and allowing plans to remove drugs from their formularies in two of the six protected classes. A vote is planned for April 7.

MedPAC has said that the decade-old benefit is firmly established and it's time for the government to relax requirements, some of which were originally designed to draw plans to the popular program.

''The current structure of Part D reflects a system of federal subsidies and regulations that was designed to encourage broad participation of Medicare beneficiaries and private plan sponsors in a new program,'' according to MedPAC's brief on the April 7 session.

''Now at the start of Part D's eleventh year, the market for Medicare Advantage prescription drug plans has grown substantially and the market for stand-alone prescription drug plans is firmly established,'' it said.

Three Groups of Recommendations. At their March meeting, the commissioners considered a slate of three groups of draft recommendations.

The first group would ask Congress to change the Part D benefit to lower Medicare's individual reinsurance subsidy, exclude manufacturers' discount in the coverage gap from enrollees' true out-of-pocket spending and eliminate estimated cost sharing above the out-of-pocket threshold.

The second group would ask Congress to change Part D to modify the low income subsidy (LIS) copayment

  PLIR ISSN 1542-9547

for beneficiaries to encourage the use of generic drugs; reduce or eliminate cost-sharing for generics; and have therapeutic classes reviewed at least every three years.

MedPAC has contended that beneficiaries who receive the LIS and who use high-cost drugs have substantially lower use of generics in many drug classes.

The third group would recommend that Congress remove antidepressants and immunosuppressants for transplant rejection from the six protected classes; streamline the process for midyear formulary changes; require prescribers to provide more rigorous supporting statements when applying for exceptions; and permit plan sponsors to use certain tools to manage specialty drug benefits.

Low Income Subsidy, Protected Classes. The groups are most concerned about the recommendations that would call upon Congress to make changes to the LIS and protected classes.

In a March 24 letter to Commission Chairman Francis J. Crosson, more than 260 patient groups said the changes to cost sharing could limit access for low income beneficiaries to needed medications and shouldn't be approved.

Contrary to MedPAC's contention that LIS beneficiaries use more brands, the groups said that generic utilization is already high among Part D beneficiaries.

If LIS enrollees have to pay higher cost sharing for brand name drugs, they might not be as likely to adhere to their prescribed treatment, they said.

Instead, the letter said it encourages improvements to the appeals process for denied coverage of specific drugs. ''Recent findings of the CMS' audits of plan sponsors revealed ongoing challenges related to coverage determinations, appeals and grievances (CDAG) as well as formulary and benefits administration.''

The groups included the American Psychiatric Association, American Psychological Association, Easter Seals, Multiple Sclerosis Foundation, National Alliance on Mental Illness, NAACP and state and local groups representing patients with various conditions.

Appeals Improvements Needed. Similarly, the Medicare Rights Center, in its letter to MedPAC, said the current state of the appeals process could worsen implementation of some of the recommendations.

''In the absence of needed improvements to the Part D appeals process, we are deeply concerned that the proposed formulary flexibilities, specifically the changes to the protected classes, could limit beneficiary access to needed medications,'' the center said.

If these particular recommendations are approved, MedPAC should condition them to improvements to the Part D coverage determination and appeals processes, the center said.

A March 30 letter from more than two dozen medical and patient groups, including the American Society of Transplant Surgeons and the American Society of Transplantation, Anxiety and Depression Association of America and the Association for Ambulatory Behavioral Healthcare, asked that MedPAC abandon its draft recommendation weakening the protected classes.

The groups, called the Partnership for Part D Access, said removing antidepressants and immunosuppressants from the protected classes would not lead to Medicare program cost savings, contrary to MedPAC staff assumptions, but would have serious health implications for beneficiaries.

''Historically, due to the unique and variable ways in which patients respond to different drugs, and the complicated interplay of co-morbidities and drug interactions, it has been widely recognized that doctors need to have complete discretion to prescribe the most appropriate medicines for patients with these and other conditions addressed by the protected classes,'' they said.

Access to Medicines. Another umbrella group, the Medicare Access for Patients Rx, told MedPAC March 25 that some of its proposals would harm beneficiaries' access to needed medicines.

''Specifically, we ask that MedPAC reject proposals to: make changes to true out-of-pocket costs (TrOOP); increase copays for low-income subsidy (LIS) beneficiaries; and eliminate any of the protected classes,'' it said.

Among the groups signing the letter were the American Society of Consultant Pharmacists, the National Community Pharmacists Association, the Epilepsy Foundation and the National Organization for Rare Disorders.

Drug manufacturers are concerned that many of the proposals ''would significantly harm beneficiaries by shifting costs to vulnerable patients and jeopardizing their access to needed medicines.''

''Given that there is often a medical need for certain brand medicines and the very modest income and resources of LIS beneficiaries (below approximately $1,336 monthly income for an individual in 2016), this policy unfairly targets the most vulnerable Part D beneficiaries.''

Drug Manufacturers' Views. The Pharmaceutical Research and Manufacturers of America indicated agreement with the groups.

A spokeswoman told Bloomberg BNA April 4 that drugmakers are concerned that many of the proposals ''would significantly harm beneficiaries by shifting costs to vulnerable patients and jeopardizing their access to needed medicines.''

She said she hopes MedPAC ''will thoughtfully consider feedback from stakeholders on these important issues in advance of their vote.''

BY MINDY YOCHELSON

To contact the reporter on this story: Mindy Yochelson in Washington at myochelson@bna.com

To contact the editor responsible for this story: Janey Cohen at jcohen@bna.com

Research and Development

NIH Names Pfizer, Johns Hopkins Leaders To Panel to Set Cancer Moonshot Agenda

Pfizer Inc. and Johns Hopkins University leaders are among the 28 members of a new panel that will set the scientific agenda for Vice President Joe Biden's cancer ''moonshot'' initiative, the NIH announced April 4.

The formation of the Blue Ribbon Panel, which is a working group of the presidentially appointed National Cancer Advisory Board (NCAB), will serve as the forum for public input while informing the scientific direction and goals of the ''moonshot'' initiative to double the rate of progress on cancer treatments and prevention.

''This Blue Ribbon Panel will ensure that, as NIH allocates new resources through the Moonshot, decisions will be grounded in the best science,'' Biden said in an April 4 statement.

National Institutes of Health Director Francis S. Collins said the vice president's call to action, including the establishment of this panel, comes at just the right time for all the right reasons. ''Thanks to advances in science, we are now in a historically unique position to make profound improvements in the way we treat, detect, and prevent cancer,'' Collins said.

The panel is a complementary group to the White House Cancer Moonshot Task Force, whose members were announced in January (14 PLIR 175, 2/5/16). While the task force consists entirely of federal agency representatives, the panel members primarily work outside the federal government, with some input by the NIH.

Recommendations on Horizon. Findings of the panel will be reported to the NCAB, which in turn will make its recommendations to the NIH's National Cancer Institute and contribute to the overall approach of the initiative.

The Blue Ribbon Panel is expected to hold its first meeting in the next few weeks, and will deliver its recommendations later this summer, the NIH said in announcing the panel members. The recommendations won't likely be presented during the NCAB's June meeting as previously expected, an NIH spokeswoman told Bloomberg BNA, because of the amount of time it took to assemble the 28-member panel. The task force is expected to produce and deliver a final report by the end of the year.

The panel will be led by current NCAB Chairman Tyler Jacks, who is the director of the Massachusetts Institute of Technology Koch Institute for Integrative Cancer Research; along with Elizabeth Jaffee, professor and deputy director for translational research in cancer at Johns Hopkins University; and Dinah Singer, the NCI's acting deputy director and division of cancer biology director. Other members comprise representatives from patient advocacy groups, industry and academia. Industry representatives include Mikael Dolsten, president of Pfizer Worldwide Research and Development, and Angel Pizarro, technical business development manager, Amazon Web Services Scientific Computing and Research Computing.

Proposed Themes. The panel will consider how to advance the themes that have been proposed for the initiative:

- the development of cancer vaccines,
- highly sensitive approaches to early detection,
- advances in immunotherapy and combination therapies,
- single-cell genomic profiling of cancer cells and cells in the tumor microenvironment,
- enhanced data sharing and
- new approaches to the treatment of pediatric cancers.

Bloomberg Philanthropies provides financial support for the moonshot cancer initiative.

The cancer community, including the American public, will be given a forum to post comments and insights to help inform the panel's deliberations.

NEJM Perspective. In a New England Journal of Medicine perspective that was released in concert with the announcement of the panel, Collins and NCI Director Douglas Lowy went into detail about the scientific rationale for these proposed themes as well as the possible activities that could take place under these themes.

''Although key actions and deliverables remain a work in progress, one aim of this new initiative is certain: to inspire a new generation of American visionaries to defy the boundaries of current knowledge about cancer. Unleashing the talents of the scientific community by providing a strong, steady stream of resources should enable biomedical research to accelerate progress in the fight against cancer,'' the NEJM perspective said. ''We expect these efforts to build a firm foundation for the development of better means of prevention, treatment, and cure for all types of cancer.''

BY JEANNIE BAUMANN

To contact the reporter on this story: Jeannie Baumann in Washington at jbaumann@bna.com

To contact the editor responsible for this story: Randy Kubetin at rkubetin@bna.com

More information on the Blue Ribbon Panel is available at http://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel.

The NEJM perspective is available at http://www.nejm.org/doi/full/10.1056/NEJMp1600894.

   ISSN 1542-9547

State News

Colorado

Opposition From Pharmaceutical Industry Halts Colorado's Price Transparency Bill

The sponsor of a bill (H.B. 1102) to require drug manufacturers to submit a report to the state on the cost of producing prescription drugs said she will introduce the measure again next year, after a legislative committee killed the bill.

State Rep. Joann Ginal (D) told Bloomberg BNA April 1 the bill was the latest attempt by a state to require the pharmaceutical industry to provide information about what goes into pricing of prescription drugs. However, stiff opposition to the bill by the industry, as well as dissent from the state's leading bioscience association, prompted the House Committee on Health, Insurance, & Environment to kill it on a 12-1 vote March 10. Ginal was the lone supporter of the measure.

Ginal told Bloomberg BNA the issue is an important one to health consumers, and she plans to work with industry representatives to bring an improved bill to the Colorado General Assembly 2017 session. ''When I came out of the committee hearing I went up to them and said, 'I hope you guys know this isn't the end. I intend to work with you to make sure this is something we can all agree on.' ''

During committee debate on the bill, representatives of the industry presented statements expressing their opposition to the concept. The bill, which Ginal introduced Jan. 19, would have required drug manufacturers to submit a one-time report to the Colorado Commission on Affordable Health Care outlining certain information about drugs made available in Colorado for which the wholesale acquisition cost is $50,000 or more per year or per course of treatment.

R&D Cost Reporting. Companies would have been required to provide information on drug research and development costs; clinical trials and regulatory costs; material, manufacturing and administration costs attributable to the drug; and acquisition costs, including patents and licensing. Ginal called it a ''reasonable approach towards understanding the underlying costs behind production drug prices'' (14 PLIR 293, 2/26/16).

However, she said, industry representatives told her the bill would ''hurt them terribly.''

Frank Seagrave, president and CEO of Silvergate Pharmaceuticals Inc., said the bill would ''only result in additional administrative costs requiring extensive reporting provisions that would provide absolutely no transparency to the public.'' The resources the bill would require ''would be better used to continue the efforts of the industry in creating new cures and treatments for patients and their families,'' he said.

The reporting requirement ''would place an undue burden on bioscience companies,'' said Ralph Christoffersen, general partner with Lightstone Ventures, a life science investment team that manages a portfolio of more than 50 medical device and biotechnology companies. ''It is also concerning that the information being requested could be proprietary in nature, impossible for companies to compose and offer no additional transparency for the consumer,'' he said.

'Inaccurate Calculation.' When computing the costs of research and development into one medicine, companies must take into account the failure of several others, he said, ''and failure to recognize the expense associated would result in an inaccurate calculation of the investment these companies are making.''

The resulting report would provide inaccurate information to the legislature ''and ultimately offer no benefit to the patients we are trying to serve,'' Christoffersen said.

Ginal said she ''emphatically made certain'' the bill would not result in companies giving away trade secrets. ''I'm not trying to regulate them, I'm trying to get the information for consumers and policymakers to find out what's really happening with drug pricing.''

The bill has ''run its course this year,'' she said, but next year she will ''start working with the various pharmaceutical companies and health insurance companies to look at why the cost of drugs is so high.''

Support From Health Plans. Testimony in opposition to the bill also was provided by Pfizer, PhRMA, the Colorado BioScience Association and the Liver Health Connection.

Testifying in favor were Kaiser Permanente, the National Federation of Independent Business, the United Food and Commercial Workers Union Local 7, Healthier Colorado, the Colorado Association of Health Plans and the Colorado Consumer Health Initiative.

BY TRIPP BALTZ

To contact the reporter on this story: Tripp Baltz in Denver at abaltz@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

More information on the bill is available from the Colorado General Assembly at http://www.leg.state.co.us/CLICS/CLICS2016A/csl.nsf/MainBills?openFrameset.

Industry News

Biosimilars

Pfizer, Celltrion Win U.S. Approval for Copy of J&J's Remicade

Pfizer Inc. and Celltrion Inc. won approval to market a low-cost copy of Johnson & Johnson's best-selling arthritis treatment, Remicade.

The drug, Inflectra, is just the second in the U.S. in a class of cheaper versions of brand-name biotechnology drugs known as biosimilars. The Food and Drug Administration cleared the intravenous infusion for seven conditions treated by Remicade, including rheumatoid arthritis and plaque psoriasis, according to a statement from the agency April 5.

Remicade generated $4.5 billion in U.S. sales last year for J&J, competing with AbbVie Inc.'s blockbuster Humira. Amgen has applied to the FDA for approval of a biosimilar version of Humira.

Developed by Celltrion, the copycat of J&J's Remicade was authorized for sale in 2013 by the European Medicines Agency, where it is called Remsima. Celltrion has applied for approval of another biosimilar to treat breast cancer and is studying a third in non-Hodgkin's lymphoma, according to its website. It has an agreement with Pfizer's Hospira unit to market Inflectra.

The only biosimilar approved for U.S. sale is Novartis AG's copy of Amgen Inc.'s Neupogen immune booster, which gained clearance in March 2015 (13 PLIR 351, 3/13/15), and went on sale later in 2015 (13 PLIR 1298, 9/11/15).

Biosimilars are copies of complex biologic drugs, which are made from living organisms. Typically injected or infused, biologics are often more expensive than simple pills made from chemicals. Until recently, they had never faced U.S. competition from cheaper, generic versions.

BY ANNA EDNEY

To contact the reporter on this story: Anna Edney in Washington at aedney@bloomberg.net

To contact the editors responsible for this story: Drew Armstrong at darmstrong17@bloomberg.net, John Lauerman, Cecile Daurat

Biosimilars

Attorney Says Second U.S. Biosimilar Shows FDA's Confidence; Patients' Group Worried

The FDA's approval of the second U.S. biosimilar was a very big step for these less-expensive biologic drugs because it shows the agency is comfortable reviewing more complex biosimilars, an attorney and pharma association said.

The Food and Drug Administration approved Pfizer's and Celltrion's Inflectra as a biosimilar of Johnson & Johnson's blockbuster arthritis treatment Remicade (infliximab) on April 5. The approval came a year and two days after the agency approved the first U.S. biosimilar under the Biologics Price Competition and Innovation Act (BPCIA)—Zarxio, Sandoz's biosimilar of Amgen's cancer treatment Neupogen (13 PLIR 351, 3/13/15).

''This signals that the Food and Drug Administration has confidence in its approval process and confidence to okay something as complex as a biosimilar of a monoclonal antibody as well as extrapolations across seven indications of the original biologic or reference product,'' Stacie Ropka, counsel at Axinn Veltrop & Harkrider, Hartford, Conn., told Bloomberg BNA in an April 6 phone interview. Zarxio is a biosimilar of a relatively straightforward protein (13 PLIR 353, 3/13/15); Remicade has seven indications, and Inflectra may be used for any of them.

Remicade generated $4.5 billion in U.S. sales in 2015 for J&J, competing with AbbVie Inc.'s blockbuster drug Humira. Amgen Inc. has applied to the FDA for approval of a biosimilar version of Humira.

Big Step, Some Concerns. Ropka said, ''Since the FDA now knows the type of data it requires for biosimilars of both straight-forward and complex biologics, I would think it would say to other biosimilar applicants, 'This type of data has worked for us.' That is not to say that it's still not going to be on a case-by-case basis. But there's no denying this is a big step forward for biosimilars in that it should encourage other biosimilar developers.''

Mark Merritt, president and chief executive officer of the Pharmaceutical Care Management Association (PCMA), said in a statement, ''The FDA is taking important steps toward approving more biosimilars in the United States. Increasing competition through the approval of brand and generic drug competitors is the key to lowering prescription drug costs for consumers, employers, government programs and others. To further advance the use of biosimilars, the FDA should finalize an interchangeability policy that will allow for greater patient access to these important drugs.''

But not everyone was excited about the FDA's decision.

J&J issued a statement comparing Remicade to its new competitor, Inflectra, noting that Inflectra hasn't

  PLIR ISSN 1542-9547

yet been found to be interchangeable, and a patients' group expressed concern that the FDA continues to approve biosimilars without having first put in place critical policies that safeguard patients.

Market Availability. How quickly Inflectra gets to market is unclear. In the stipulation of dismissal of J&J's litigation against Celltrion concerning Inflectra, Celltrion indicated to the U.S. District Court for the District of Massachusetts on March 22 that it wouldn't sell the biosimilar in the U.S. before June 30, which is when the patents-at-issue will expire.

The release of Inflectra may also depend on a decision by the U.S. Court of Appeals for the Federal Circuit in *Amgen, Inc. v. Apotex, Inc.*, for which a three-judge panel heard oral arguments on the day before the FDA's approval of Inflectra *(see related item)*. The question in that case is whether a biosimilar applicant always has to give 180 days' notice to the original or reference product sponsor, starting on the day the FDA approves the biosimilar, of its intent to commercially market the product. If the Federal Circuit concludes that the notice is always required, that could push Inflectra's release date to October.

J&J, Patients' Group Reactions. A biologic is a complex, large molecule, such as a monoclonal antibody or a cell-signaling protein. A biosimilar is analogous but not the same as a generic of chemically derived drugs. While a generic is identical to the originator drug, a product designed to resemble an FDA-approved biologic can only be approved by the FDA as biologically similar to the reference product with no clinically meaningful differences, and, on further FDA approval, as interchangeable without the approval of a physician.

The day of the FDA announcement, Jay Siegel, J&J's chief biotechnology officer and head of scientific strategy and policy, pointed out in a statement that ''Celltrion's infliximab-dyyb is a biosimilar but not identical to Remicade.''

''It is important to note,'' he said, ''that the FDA has not approved Celltrion's infliximab-dyyb as being interchangeable with Remicade. For FDA to determine a biosimilar is interchangeable with its reference product, a manufacturer must demonstrate that the biosimilar is expected to produce the same clinical result as the reference product in any given patient. In addition, the manufacturer must demonstrate the risk of alternating or switching between the reference product and biosimilar is no greater than the risk of using the reference product,'' Siegel wrote.

Patients for Biologics Safety & Access (PBSA), a coalition of 23 national patient advocacy organizations dedicated to protecting patient access to safe and effective biologics, also expressed some concerns. In a statement, the group said, ''Regardless of the merits of the drug in question, patient advocates are concerned that the FDA now has approved a second biosimilar drug without having first put in place critical policies that safeguard patients. To date, and contrary to its own policy of transparency, FDA has not issued final guidance on a range of key issues that will impact patient safety including interchangeability, product labeling and naming and approval relying on indication extrapolation.''

The FDA last year released three final guidances on quality considerations, scientific considerations and questions and answers about biosimilars and the new law (13 PLIR 617, 5/1/15).

The PBSA said that while U.S. communities are eager for new and affordable treatments, patients with rare and chronic diseases are keenly aware of the possible risks associated with biosimilars.

''To date, we have not been satisfied with the extent FDA has included the patient voice in the formation of the biosimilars approval process,'' the PBSA said.

BY JOHN T. AQUINO

To contact the reporter on this story: John T. Aquino in Washington at jaquino@bna.com

To contact the editor responsible for this story: Lee Barnes at lbarnes@bna.com

Mergers and Acquisitions

Pfizer, Allergan End $160 Billion Merger Amid New Tax Rules

Pfizer Inc. and Allergan Plc have terminated their $160 billion merger in an abrupt end to the largest-ever health-care deal after the U.S. government cracked down on corporate tax inversions.

The U.S. Treasury Department's proposed new rules to deter companies from using acquisitions to shift their tax addresses overseas drove the decision, the companies said in an April 6 statement. New York-based Pfizer will pay Allergan $150 million in reimbursement for expenses associated with the failed transaction.

Both companies are now left looking for their next move—another deal, in Allergan's case.

''While this was not Plan A, we were prepared for this,'' Allergan Chief Executive Officer Brent Saunders said in an interview on Bloomberg TV April 6. ''We're going to go and look to find assets that complement and increase our growth profile.''

Pfizer, meanwhile, said it will decide whether to pursue a potential split of the company by no later than the end of this year. The split would probably involve two parts: one focused on new drug development, the other on selling older medications.

''The fact that the company is talking about the original split-up decision timeline of late 2016 almost seems to suggest they have given up on inversion,'' Timothy Anderson, an analyst at Sanford C. Bernstein & Co., said of Pfizer's decision.

Valeant Unit? Asked about whether he might be interested in buying Valeant Pharmaceuticals International Inc.'s eyecare unit, Bausch & Lomb, Saunders demurred, though did call it a premier asset. He declined to comment directly on what companies he might look at next.

The termination represents a victory for President Barack Obama, whose administration proposed tougher-than-expected new rules aimed at making inversions like the Pfizer-Allergan deal harder to achieve. In an inversion, a U.S. company shifts its tax address overseas, often through a merger.

Saunders said it wouldn't have been in the best interests of his shareholders or Pfizer's to fight the new rules.

''It would have been a long, protracted, expensive fight,'' he said during the interview. ''Perhaps we could

have won, but that's not a fair position to put our shareholders in, particularly when our stand-alone prospects, our growth prospects, our pipeline is so strong.''

Inversions Dead. With the Treasury rule, tax inversions—dozens of which were performed by U.S. companies seeking to escape the country's 35 percent corporate tax rate—appear to be largely over.

''Inversions are dead,'' said John Schroer, sector head of health care at Allianz Global Investors. Josh Earnest, a White House spokesman, said April 5 that the administration hoped its new proposals would stop the transactions.

Allergan, which is run from New Jersey but has a legal domicile in Dublin, last year agreed to merge with Pfizer in a deal that would have given the New York-based company an Irish address and a lower tax rate.

Pfizer still plans to report first-quarter earnings on May 3.

BY KRISTEN HALLAM, CYNTHIA KOONS AND ZACHARY TRACER

—With assistance from Ketaki Gokhale.

To contact the reporters on this story: Kristen Hallam in London at khallam@bloomberg.net; Cynthia Koons in New York at ckoons@bloomberg.net; Zachary Tracer in New York at ztracer1@bloomberg.net

To contact the editors responsible for this story: Chitra Somayaji at csomayaji@bloomberg.net; Drew Armstrong at darmstrong17@bloomberg.net, John Lauerman

The inversion rules are at http://src.bna.com/dTc and http://src.bna.com/dTd. More information on the Treasury Department rules is at https://www.treasury.gov/press-center/press-releases/Pages/jl0404.aspx.

Mergers and Acquisitions

Gilead to Pay $400 Million For Nimbus's Liver Disease Drug

Gilead Sciences Inc. will pay $400 million to buy a drug from closely held Nimbus Therapeutics LLC as the biotechnology company expands its development portfolio of treatments for the fatty liver disease known as NASH.

Nimbus will get $400 million up front and as much as $800 million in potential milestones for the acetyl-CoA carboxylase (ACC) inhibitor called NDI-010976. The drug is being developed for non-alcoholic steatohepatitis, or NASH, which affects 2 percent to 5 percent of Americans and is caused by fat buildup in the liver, according to the National Institutes of Health. It can eventually lead to scarring and damage of the organ. Analysts have estimated that the market for NASH drugs could eventually be worth $35 billion.

''These molecules will complement and further strengthen Gilead's pipeline and capabilities to advance a broad clinical program in NASH,'' Norbert Bischofberger, Gilead's chief scientific officer, said in a statement announcing the deal. Gilead will also acquire other similar drugs from Nimbus, which is based in Cambridge, Mass.

After its success with two blockbuster hepatitis C treatments, Gilead is sitting on $26.2 billion in cash and equivalents and is looking to diversify its portfolio. Gilead's website lists three compounds in development for NASH, including two in mid-stage trials.

NDI-010976 gained a fast track designation from the Food and Drug Administration in February, which can help speed submission and approval. Results from an early stage trial of the drug, which the company is also looking to use to treat liver cancer, will be presented next month, according to the statement.

BY DONI BLOOMFIELD

To contact the reporter on this story: Doni Bloomfield in Boston at mbloomfiel12@bloomberg.net

To contact the editors responsible for this story: Cecile Daurat at cdaurat@bloomberg.net, Drew Armstrong

Advertising and Marketing

FDA Warns Shionogi That Copay Assistance Voucher Misbrands Ulesfia

The FDA told Shionogi Inc. that its copayment assistance voucher for the head lice treatment Ulesfia is false or misleading because it omits important risk information.

The omission means that the voucher ''misbrands Ulesfia within the meaning of the Federal Food, Drug and Cosmetic Act (FD&C Act) and makes its distribution violative,'' the Food and Drug Administration's Office of Prescription Drug Promotion (OPDP) said in a late March warning letter. The company also failed to submit a copy of the voucher to the OPDP as required, the letter said.

John Kamp, consulting counsel to Wiley Rein LLP and executive director of the Coalition for Healthcare Communication in New York, told Bloomberg BNA April 5 that he doesn't ''find this letter too surprising.''

Kamp said the letter is consistent with what the FDA has done in the past, in that the agency has said that vouchers ''have to have fair balance.'' He noted that this is only the second warning letter that the OPDP has issued in 2016.

Omission of Risks. Ulesfia (benzyl alcohol) lotion is indicated for the topical treatment of head lice infestation in patients six months of age and older. The prescribing information contains warnings and precautions on neonatal toxicity, eye irritation, contact dermatitis and use in children.

The FDA said the voucher makes representations about the efficacy of Ulesfia, but doesn't communicate any of the risk information.

The voucher provides links to websites that contain the full prescribing information for the drug, but the agency said these statements don't ''mitigate the omission of risk information from the voucher.''

''By omitting the risks associated with Ulesfia, the voucher fails to provide material information about the consequences that may result from the use of the drug and creates a misleading impression of the drug's safety,'' the OPDP said.

  PLIR ISSN 1542-9547

Requested Action. The OPDP asked the company to stop misbranding Ulesfia and/or to stop introducing the misbranded drug into interstate commerce.

The company was asked to submit a response to the warning letter.

The warning letter was signed by Robert Dean, division director of the OPDP.

Concordia Involved, Too. While Shionogi holds the new drug application for the product, Ontario-based Concordia Healthcare Corp. has licensed the rights to distribute Ulesfia in the U.S.

Adam Peeler, vice president of investor relations and communications for Concordia, told Bloomberg BNA in an April 5 e-mail that the company is ''working with Ulesfia's NDA holder to address the FDA's correspondence.''

Shionogi Inc. is based in Florham Park, N.J., and is part of Japan-based Shionogi & Co.

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

The letter is at http://src.bna.com/dSo and the voucher is at http://src.bna.com/dSp.

Approvals

FDA Approves Gilead's Descovy For Treating HIV-1 Infection

Gilead Sciences Inc. April 4 said that the FDA has approved Descovy (emtricitabine 200 milligram (mg)/tenofovir alafenamide 25 mg, F/TAF), a fixed-dose combination for treating HIV.

Descovy is indicated in combination with other antiretroviral agents for treating HIV-1 infection in adults and pediatric patients 12 years of age and older, the Foster City, Calif.-based company said. Descovy isn't indicated for use as pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 in adults at high risk.

TAF, part of Descovy, is a novel targeted prodrug of tenofovir that has demonstrated high antiviral efficacy similar to and at a dose less than one-tenth that of Gilead's Viread (tenofovir disoproxil fumarate, TDF), Gilead said. A prodrug converts into active form once processed inside the body. TAF also has demonstrated improvement in surrogate laboratory markers of renal and bone safety as compared to TDF in clinical trials in combination with other antiretroviral agents, the company said.

Data show that because TAF enters cells, including HIV-infected cells, more efficiently than TDF, it can be given at a much lower dose and there is 90 percent less tenofovir in the bloodstream, Gilead said.

Ryan McKeel, a spokesman for Gilead, told Bloomberg BNA in an April 5 e-mail that Descovy will be available by April 8. He said the drug's annual wholesale acquisition cost is $17,842, which is ''at parity with'' Gilead's other HIV drug, Truvada.

Boxed Warning. Descovy has a boxed warning in its product label regarding the risks of lactic acidosis, severe hepatomegaly with steatosis and post treatment acute exacerbation of hepatitis B.

Lactic acidosis is a medical condition characterized by the buildup of lactate in the body and severe hepatomegaly with steatosis is a liver condition.

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

Drug Compounding

FDA Warns Two Pharmacies About Violations Involving Sterile Drug Production

The FDA told compounding pharmacies in Arkansas and Virginia that it found serious deficiencies in their practices for producing sterile drugs, according to warning letters posted April 5 on the FDA's website.

The Food and Drug Administration said that based on inspections, the pharmacies appear to be producing drugs that violate the Federal Food, Drug, and Cosmetic Act. The agency also said the pharmacies aren't receiving valid prescriptions for individually identified patients for a portion of their drug products as required for compounding pharmacies.

The compounding pharmacies are the Custom Compounding Center in Little Rock, Ark., and the Wellness Pharmacy LLC in Winchester, Va.

Arkansas Pharmacy. In a March 16 letter, the FDA's Dallas office told Custom Compounding Center that the facility isn't designed properly because rooms with different classifications aren't properly separated by a physical door.

The agency also said its investigators observed operators processing sterile drug products with exposed neck and facial skin.

''Therefore, your products may be produced in an environment that poses a significant contamination risk,'' the warning letter said.

The FDA also said its investigators found current good manufacturing practice (cGMP) violations at the facility, including, for example:

- failure to establish and follow appropriate written procedures designed to prevent microbiological contamination of sterile drug products;

- failure to ensure that manufacturing personnel wear clothing appropriate to protect drug products from contamination;

- failure to establish an adequate system for monitoring environmental conditions in aseptic processing areas; and

- failure to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use the results of that testing to determine appropriate storage conditions and expiration dates.

The FDA said it issued a Form 483 (inspectional observations) to the facility on April 9, 2015. The agency said it acknowledges the pharmacy's responses to the Form 483.

Custom Compounding Centers was asked to correct the violations and submit a response to the warning letter. The letter was signed by Reynaldo R. Rodriguez, Jr., director of the FDA's Dallas District.

Virginia Pharmacy. In a March 23 letter, the FDA's Baltimore office told the Wellness Pharmacy that its investigators found that the pharmacy uses non-sterile gloves when producing sterile products.

The agency also said its investigators found cGMP violations at the facility, including, for example:

- failure to establish an adequate system for maintaining equipment used to control the aseptic conditions;
- failure to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes;
- failure to establish an adequate system for cleaning and disinfecting the room and equipment to procedure aseptic conditions; and
- failure to ensure that manufacturing personnel wear clothing appropriate to protect drug products from contamination.

The FDA said it issued a Form 483 to the facility on March 12, 2015. The agency said it acknowledges the pharmacy's response to the Form 483.

The Wellness Pharmacy was asked to correct the violations and submit a response to the warning letter. The letter was signed by Evelyn Bonnin, director of the FDA's Baltimore District.

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

The letter to Custom Compounding Center is at http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2016/ucm492685.htm and the letter to the Wellness Pharmacy is at http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2016/ucm492676.htm.

New Products

Janssen Biotech Obtains Rights to Tesaro's Cancer Drug Niraparib for Prostate Cancer

Janssen Biotech Inc. April 6 said it has obtained from Tesaro Inc. the exclusive rights to the investigational compound niraparib for prostate cancer.

Niraparib is an orally administered poly polymerase (PARP) inhibitor that's in late-stage development for patients with metastatic breast cancer and ovarian cancer, the companies said.

Under the agreement, Janssen will develop and commercialize niraparib for patients with prostate cancer worldwide, except in Japan. Tesaro will receive an upfront payment of $35 million and is eligible to receive additional milestone payments of up to $415 million, contingent on Janssen reaching development, regulatory and commercial milestones, in addition to tiered, double-digit royalty payments.

Janssen will be responsible for funding all development and commercialization activities related to niraparib in prostate cancer.

Janssen Biotech is one of the Janssen Pharmaceutical Cos. of Johnson & Johnson. Separate from the exclusive license and collaboration agreement for niraparib, Johnson & Johnson Innovation will make a $50 million equity investment in Tesaro, the companies said.

''PARP inhibitors are an exciting, emerging class of medicines in prostate cancer, and we believe niraparib will perfectly complement our existing portfolio,'' Peter F. Lebowitz, oncology therapeutic area head, Janssen Research & Development LLC, said in a statement. ''Our team is eager to apply its prostate cancer expertise to niraparib, and enthusiastic about its potential to expand our impact on the lives of men with this disease.''

Tesaro is based in Waltham, Mass., and Janssen is based in Raritan, N.J.

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Lee Barnes at lbarnes@bna.com

Drug Safety

Diabetes Drugs Saxagliptin, Alogliptin Linked to Heart Failure, FDA Says

Type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure, particularly in patients who already have heart or kidney disease, the FDA said April 5.

The agency said that as a result of these findings, it's adding new warnings to the labels of these drugs. These medicines include AstraZeneca's Onglyza (saxagliptin) and Kombiglyze XR (saxagliptin and metformin extended release), and Takeda's Nesina (alogliptin), Kazano (alogliptin and metformin) and Oseni (alogliptin and pioglitazone).

The FDA said it evaluated two large clinical trails conducted in heart disease patients. The FDA's Endocrinologic and Metabolic Drugs Advisory Committee also discussed these clinical trials in April 2015. Each trial showed that more patients who received medicines containing saxagliptin or alogliptin were hospitalized for heart failure compared to patients who received a placebo, the agency said.

Label Changes. The FDA said it has added new warnings and precautions to the labels of these medicines to inform patients and health-care providers of the potential increased risk of heart failure.

Patients taking these medicines should contact their health-care professionals right away if they develop signs and symptoms of heart failure such as unusual shortness of breath, the agency said. Patients shouldn't stop taking their medicine without first talking to their health-care professionals.

  PLIR ISSN 1542-9547

Health-care professionals should consider discontinuing the medicine in patients who develop heart failure and monitor their diabetes control, the FDA said. If a patient's blood sugar level isn't well-controlled with their current treatment, other diabetes medicines may be required.

Health-care professionals and patients should report side effects involving saxagliptin, alogliptin or other medicines to the FDA's MedWatch Adverse Event Reporting Program.

Company Response. Michele L. Meixell, head of external and executive communications for AstraZeneca's U.S. corporate affairs, told Bloomberg BNA in an April 6 e-mail that ''the prescribing information and medication guides for Onglyza and Kombiglyze XR now include additional data and safety information based on the results of'' the clinical trial, called the SAVOR trial.

''Efficacy and safety information from the SAVOR study has been included in the Clinical studies, Warnings and Precautions, Adverse Reactions and other sections of the label,'' Meixell said. ''AstraZeneca is committed to patient safety, and we believe the results of the SAVOR trial provide prescribers and patients with important additional information about the benefit-risk profile of Onglyza and Kombiglyze XR.''

According to the SAVOR clinical trial, ''caution is warranted if saxagliptin is used in patients who have known risk factors for heart failure, such as a history of heart failure or moderate to severe renal impairment'' and ''patients should be advised of the characteristic symptoms of heart failure, and to immediately report such symptoms,'' Meixell said.

Takeda Response. Elissa Johnson, a spokeswoman for Takeda, told Bloomberg BNA in an April 7 e-mail that Takeda ''has discussed this topic with the FDA and the U.S. label will be updated to include this information.''

''Takeda remains confident in the clinical profile of alogliptin and alogliptin-containing products as important treatment options for patients living with type 2 diabetes,'' Johnson said. ''It is important to note that the outcome of the EXAMINE (Examination of Cardiovascular Outcomes: Alogliptin vs. Standard of Care in patients with type 2 diabetes mellitus and recent acute coronary syndrome) trial showed that there was no statistically significant signal for heart failure.''

BY BRONWYN MIXTER

To contact the reporter on this story: Bronwyn Mixter in Washington at bmixter@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

More information is available at http://www.fda.gov/Drugs/DrugSafety/ucm486096.htm.

International News

Canada

Health Canada to Publish Regulatory Decisions on New Drugs and Devices

Health Canada is moving forward with an initiative to increase public disclosure of its regulatory decisions on new pharmaceuticals and medical devices, but medical device manufacturers remain concerned that Canada is going beyond international regulatory norms.

The federal health department is implementing, effective May 1, the second phase of two initiatives launched in 2015 that are intended to enhance the transparency of Canada's pharmaceutical, biologic and medical device regulatory review processes. The measures are part of the department's broader Regulatory Transparency and Openness Framework.

The second phase was originally scheduled to take effect April 1, but was postponed for a month to provide more time to notify affected parties, Health Canada spokesman Andre Gagnon said March 31.

The delay responded to consultations with the industry earlier in 2016, with a report on the consultation's results expected in late spring or early summer, Gagnon told Bloomberg BNA in an e-mail.

Under the new disclosure provisions, Health Canada will publish final negative decisions on all new drug submissions, supplemental new drug submissions for new indications and applications for approval of new Class IV medical devices received after May 1, the department said March 18 in a notice.

Health Canada classifies medical devices as Class I, II, III or IV, based on risk. Class IV medical devices are the highest risk, including cardiac pacemakers, angiography catheters and cranial shunts.

The department also will publish details of the medicinal ingredient and therapeutic class for all new drug submissions and supplemental new drug submissions for new indications, whether pharmaceuticals or biologics, that are accepted for review on or after May 1.

''Greater transparency and openness with Canadians strengthens the trust in our regulatory decisions,'' it said. ''This will ultimately support Canadians in making better decisions about their health.''

The decision to proceed with the second phase of implementing the Regulatory Decision Summary (RDS) and Submissions under Review (SUR) List initiatives followed consultations with stakeholders in January and February 2016, the department said. Further analysis of the consultation's results will inform a potential third phase of the initiatives, it said.

Industry Reacts. Canada's medical devices sector is ''very supportive'' of the government's Regulatory Transparency and Openness Framework but remains concerned that the planned disclosures go beyond what other jurisdictions are doing, Gerry Frenette, executive director of public and member relations with Canada's Medical Technology Companies (MEDEC), said March 31.

Device companies are concerned that Health Canada's decision to post negative decisions for all new Class IV device applications could cause manufacturers to delay submissions in Canada until they receive approval in other regions to avoid the potential global implications of a ''negative decision perception'' from Canada, Frenette told Bloomberg BNA in an e-mail.

The U.S. Food and Drug Administration doesn't post negative decisions for 510(k) pre-market notification clearances or pre-market approval (PMA) applications, nor does the European Union make public its negative decisions for CE marked devices, he said.

''It was MEDEC's position that the rejection of a new application for a license should remain a process between the applicant and Health Canada,'' he said.

Industry supports Health Canada's participation in multijurisdictional initiatives such as the International Medical Device Regulators Forum, which demonstrates the department's efforts to align Canadian regulations with those in other jurisdictions, but the new initiatives go beyond that, Frenette said.

''MEDEC supports this goal and believes that great care should be taken to ensure Health Canada is in line with international partners and does not go significantly beyond the transparency initiatives in other jurisdictions in order to avoid unintended consequences,'' he said.

The Canadian pharmaceutical industry could not comment on the regulatory initiative at this time, Sarah Douglas, director of media and government relations with Innovative Medicines Canada, which represents Canada's brand-name pharmaceutical companies, said March 29. ''We're still taking the time to review the announcement internally,'' Douglas told Bloomberg BNA in an e-mail.

First Phases. The first phase of the RDS initiative involved posting of positive decisions issued after April 1, 2015, for new drug submissions, supplemental new drug submissions for new indications and positive decisions for new Class IV medical devices, as well as final negative decisions and withdrawals on new drug submissions for new active substances accepted for review on or after April 1, 2015.

The first phase of the SUR initiative involved inclusion on the SUR List of the medicinal ingredient and therapeutic class for new drug submissions for new active substances, both pharmaceuticals and biologics, accepted for review on or after April 1, 2015.

The department's initial notice in March 2015 announcing the transparency initiatives indicated that the increased publication of information would initially only apply to medical devices and prescription drugs, noting that work on a Consumer Health Products Framework was also underway.

  PLIR ISSN 1542-9547

''Initiatives related to transparency and communicating rationales for decisions for consumer health products (including non-prescription drugs and natural health products) will be developed in conjunction with the new framework,'' the department said.

The SUR List is updated nightly and is searchable, and once a final decision on a drug or medical device is issued, the submission is removed from the list because it is no longer under review. Information provided in Regulatory Decision Summaries is intended to capture the rationale for the department's decisions, including the purpose for the submission and the department's reasons for its decision.

BY PETER MENYASZ

To contact the reporter on this story: Peter Menyasz in Ottawa at correspondents@bna.com

To contact the editor responsible for this story: Allison Gatrone at agatrone@bna.com

The Health Canada notice is available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/rds-sdr/drug-med/rds-sur-notice-phaseii-avis-sdr-pce-eng.php.

Additional details on the initiatives are available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/rds-sdr/drug-med/rds-sur-notice-phasei-avis-sdr-pce-eng.php.

Patents

Glaxo Pledges Not to Seek Drug Patents in Poor Countries

GlaxoSmithKline Plc will refrain from seeking patent protection for its products in the world's poorest countries, one of several steps to make all its medicines more widely available from Afghanistan to Haiti.

The U.K.'s biggest drugmaker also pledged to pursue partnerships with generic drug companies to make low-cost versions of Glaxo products accessible in lower middle-income countries, the company said in an e-mailed statement March 31. The new patent strategy applies to all Glaxo drugs, ranging from respiratory treatments to cancer therapies.

Clarity for Generics. The approach will ''give clarity and confidence to generic companies seeking to manufacture and supply generic versions of GSK medicines in those countries,'' Glaxo said.

Rising demand for the newest life-saving medicines in developing countries has led nations including India, Thailand and Brazil to issue compulsory licenses, enabling local production without the patent-holder's consent. Gilead Sciences Inc., Glaxo's rival in HIV drugs, has been cutting deals with generic drug makers that give it a small share of sales in poor countries and win the goodwill of governments.

Gilead has licensed rights to make copies of its medicines to generic-drug makers in India, South Africa and China, including licenses to 11 drugmakers in India for its blockbuster hepatitis C treatment Sovaldi, and agreements with 19 companies to produce and sell generic versions of the company's HIV and hepatitis B therapies.

Will Offer Licenses. London-based Glaxo also generally will apply for patents for its medicines in lower middle-income countries, and then offer generic drug makers licenses to allow production of its medicines for 10 years, it said in the statement. Glaxo intends to seek a royalty on sales in those countries and will continue to seek patent protection in high income countries and upper middle income countries.

Glaxo also said it would commit to making generic versions of its future cancer treatments available through the Medicines Patent Pool, a United Nations-backed initiative set up to facilitate licensing of therapies for HIV, hepatitis C and cancer in low-income and middle-income countries.

BY KETAKI GOKHALE

To contact the reporter on this story: Ketaki Gokhale in London at kgokhale@bloomberg.net

To contact the editor responsible for this story: Chitra Somayaji at csomayaji@bloomberg.net

India

India Focuses on Pharmacovigilance In New Biosimilar Draft Guidelines

India's drug regulator has announced updated draft guidelines on biosimilar drugs that would set specific requirements for efficacy and safety testing of the products in clinical trials both before and after they're approved for marketing.

The new draft guidelines also would require that when the original or reference biologic product isn't approved for marketing in India, it should be licensed by a member country of the International Conference on Harmonisation (ICH), which includes the U.S. and Japan.

Prepared by the Central Drugs Standard Control Organization (CDSCO) and the Department of Biotechnology in consultation with industry and academia, the ''Guidelines on Similar Biologic: Regulatory Requirements for Marketing Authorization in India'' would speed up permits while making drugmakers generate more data on Indian patients.

This would reduce the current time to develop an investigational new biologic drug in India from an estimated 990 days to one year, Guljit Chaudhri, senior adviser with the Association of Biotechnology Led Enterprises (ABLE), which worked closely with the government on formulating the guidelines, told Bloomberg BNA in an e-mail April 4.

Raising the Bar. The emphasis in the draft, which is an updated version of guidelines first issued in 2012, is on post-approval pharmacovigilance. It proposes that after a biosimilar drug is approved for marketing in India, safety data might have to be generated for at least 200 patients under a phase IV study protocol approved by the CDSCO.

''[A]dditional safety data may need to be collected after market approval through a predefined single arm study of generally, more than 200 evaluable patients and compared to historical data of the Reference prod-

uct,'' the draft said. ''The study should be completed preferably within 2 years of the marketing permission/manufacturing license unless otherwise justified.''

The draft guidelines also said the proposed biosimilar drug should be tested for safety and efficacy in at least 100 patents in a phase III study before it's approved, to establish that it's comparable to the reference biologic.

This is the first time that the CDSCO has defined the minimum number of patients that need to be tested in a clinical trial before the product is approved for marketing, P.M. Murali, honorary president of ABLE, told Bloomberg BNA in a March 31 e-mail. ''This increases the bar for the Indian companies. So far different companies were getting approval for biosimilar drugs in India with much lower patient data and post marketing data collection was not objectively defined,'' he said.

This also would raise the bar for all biologic drug companies, as earlier, drugmakers could win approval to make and sell the follow-on version of a biologic drug in India by securing approval based on clinical data for the original reference product, Murali said. ''Now all will need to carry out clinical studies (pre and post registration) for their follow-on version of the drug,'' he said.

Significant Proposals. Significant changes in the new draft compared to the 2012 version include:

- A new Annexure 2 lists in detail the critical attributes for proving similarity to the reference biologic at the preclinical stage, based on physicochemical and in vitro functional characteristics.

- The reference product could be registered in India or any ICH country (the U.S., Japan, any country in the EU, etc.). Before, only biologic drugs permitted to be sold in India could be used as reference drugs.

- A minimum of 100 patients must be studied in comparative phase III clinical trials for the proposed biosimilar.

- New and mandatory phase IV postmarketing studies must be conducted on at least 200 subjects in a single test arm. If a company conducts pre-approval phase III studies on more than 100 patients on the proposed biosimilar drug, the number of patients in the post-approval phase IV study could be reduced accordingly so that the safety data from the phase III and IV studies combined are derived from a minimum of 300 patients treated with the drug.

- The regulatory pathway would remain unchanged, although it would be possible to apply for permissions from the two relevant government agencies—the Review Committee on Genetic Manipulation, which oversees the development and preclinical evaluation of recombinant biologics, and the Drugs Controller General of India, which is responsible for granting import/export licenses, clinical trial approval and permission for marketing and manufacturing. A CDSCO question-and-answer document details the regulatory pathway.

Like the 2012 guidelines, the draft specifies the regulatory pathway for local manufacture, premarketing regulatory requirements and the quality aspect, including comparability exercises, pre-clinical and clinical studies and postmarketing regulatory requirements.

Global Efforts. Dozens of drugs based on biosimilar active substances are being sold in India, including the breast cancer drug trastuzumab, a copy of Roche/Genentech's Herceptin, and a range of diabetes, rheumatoid arthritis, osteoporosis and other drugs.

The Indian agency's draft comes as other nations, including the U.S., are implementing biosimilars policies. According to the U.S. Food and Drug Administration, a biosimilar product is a biological product that is approved based on a showing that it is highly similar to an already-approved biological product, known as a reference product.

The U.S. agency also said that a biosimilar must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference product. So far, only one U.S. biosimilar has been approved under a 2010 law.

The Indian agency's draft is open for stakeholder comment until April 30.

BY MADHUR SINGH

To contact the reporter on this story: Madhur Singh in Chandigarh, India, at correspondents@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

The draft guidelines are available at http://www.cdsco.nic.in/writereaddata/Proposed%20Guidelines%20for%20Similar%20Biologic%202016.pdf.

Canada

Health Canada Drops Proposal To Require Tamper-Resistant Oxycodone

The Canadian government withdrew its proposal to require pharmaceutical manufacturers to incorporate tamper-resistant properties in therapeutic drugs containing controlled-released oxycodone, at the same time providing guidance to manufacturers seeking approval of new drugs containing oxycodone.

Consultations on the proposed Tamper-Resistant Properties of Drugs Regulations, together with a comprehensive review of the latest scientific evidence, confirmed that the regulations as proposed wouldn't have produced the intended health and safety impact, Health Canada said April 4.

''Requiring tamper-resistant properties on all legitimate preparations of controlled-release oxycodone would have served to eliminate certain lower cost drugs from the market, increasing costs for patients and the health system, while having little to no effect in the fight against problematic opioid use,'' the department said in a statement.

''While the proposed regulations will not move ahead at this time, Health Canada supports efforts to develop strategies that can address problematic opioid use, including industry efforts to develop tamper-resistant formulations of drugs.''

Pointing to Guidance Instead. The department pointed to its recent guidance for the pharmaceutical industry on the evidence required under Canada's Food and Drugs Act to demonstrate tamper-resistant properties for prescription drugs considered to pose a high risk of abuse.

  PLIR ISSN 1542-9547

It also noted that it will continue other measures to address abuse of oxycodone-containing drugs, including educating prescribers on abuse risks, increasing inspections to minimize diversion of prescription drugs from pharmacies and improving surveillance data on problematic opioid use.

The Health Canada guidance document, titled Tamper-Resistance Formulations of Opioid Drug Products and which took effect March 30, indicates that it is intended to guide sponsors of new drug submissions seeking approval for controlled-release opioid drugs who wish to include scientific statements and claims related to tamper resistance in their product overviews, or monographs.

Still Awaiting Final Standards. Standards haven't been developed for criteria and data requirements for the various potential approaches to abuse deterrence, but demonstration of tamper resistance should be based on scientific methods and studies that provide evidence of sufficient quality, said the document, which had been issued in June 2014 in draft form alongside the draft regulations.

Sponsors of proposed opioid products with tamper-resistance properties should seek dialogue with Health Canada in the presubmission stage to discuss labeling plans and language, as well as readiness of the application, risk management plans and risk monitoring and mitigation measures, including the design of supportive studies, it said.

Health Canada will consider the ''totality of the evidence'' provided by the manufacturer in evaluating tamper-resistance claims for new products, and as data become available on the impact of tamper-resistance formulations in deterring abuse, the department may amend its current position and practices, it said.

Health Canada published in June 2015 the draft regulations to impose tamper-resistance requirements on prescription opioids, starting with controlled-release oxycodone tablets (13 PLIR 954, 7/3/15).

It had announced in June 2014 development of the regulations as part of a broader plan to address prescription drug abuse.

The regulations would have required tamper-resistant properties for controlled-release solid oral dosage products in which oxycodone was the only medicinal ingredient. They would have required a statement in the product's monograph that the product has tamper-resistant properties and would have required drug companies to submit evidence to support the claim, including in vitro and clinical studies.

BY PETER MENYASZ

To contact the reporter on this story: Peter Menyasz in Ottawa at correspondents@bna.com

To contact the editor responsible for this story: Brian Broderick at bbroderick@bna.com

The recent Canadian guidance document is available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/guid-opioid-ld-eng.php.

BNA Insights

LITIGATION

Attorneys from Sterne Kessler examine a recent Federal Circuit decision on where abbreviated new drug application (ANDA) cases can be heard. They say that, for the time being, ANDA plaintiffs can rest easy on their choice of forum. In the meantime, ANDA defendants should prepare to face litigation anywhere in the United States.

Acorda Therapeutics v. Mylan Pharmaceuticals: A New Kind of Jurisdiction for ANDA Cases

BY PAUL A. AINSWORTH AND JOSHUA I. MILLER

The Supreme Court's decision in Daimler AG v. Bauman[1] looked as if it had stripped the Hatch-Waxman plaintiff's favored jurisdictional weapon from its armament: the doctrine of general personal jurisdiction. Daimler was written broadly enough that at least one court read it to vitiate the question of consent to general jurisdiction. Another court in the same jurisdiction came to the opposite conclusion—in a case against the same defendant.

[1] 134 S. Ct. 746 (2014).

Paul A. Ainsworth is a Director at Sterne, Kessler, Goldstein & Fox P.L.L.C. He focuses his practice on representing patent owners in enforcement proceedings and in representing pharmaceutical industry clients in patent litigation arising under the Hatch-Waxman Act. Joshua I. Miller is an Associate at the firm whose work involves complex intellectual property disputes in the U.S. District Courts and in the ITC.

That defendant—Mylan—appealed both district court rulings to the Federal Circuit, and the Federal Circuit has clarified the relevance of Daimler to abbreviated new drug application (ANDA) cases—in a rather unexpected way. The Federal Circuit majority, like both district court judges, determined that specific personal jurisdiction attached due to Mylan's activities in Delaware [2]. This was expected.

The sweeping scope of the Federal Circuit's decision, however, was not expected. The majority's reasoning is hardly limited to the facts of the Mylan cases; in fact, much of the Court's analysis revolves around Mylan's (or any ANDA filer's) obligations under federal law. As we explain below, the result is effectively national jurisdiction over any ANDA filer.

The District Court Decisions

In two ANDA cases over different patents filed against Mylan Pharmaceuticals in Delaware, Judge Sleet and Chief Judge Stark addressed three potential grounds for personal jurisdiction.[3] The judges decided

[2] *Acorda Therapeutics, Inc. v. Mylan Pharm., Inc.*, 2016 BL 83256 (Fed. Cir., Mar. 18, 2016).

[3] *See AstraZeneca AB v. Mylan Pharms. Inc.* (D. Del. Nov. 5, 2015) (Sleet, J.); *Acorda Therapeutics Inc. v. Mylan Pharm. Inc.* (D. Del. Jan. 14, 2015).

  PLIR ISSN 1542-9547

these issues—(1) general jurisdiction, (2) consent to jurisdiction, and (3) specific jurisdiction—in different ways, but the result was the same: Delaware had personal jurisdiction over Mylan. The two judges largely agreed on the questions of general and specific jurisdiction: they each found that Daimler prohibited the exercise of general jurisdiction on the facts of their cases, but found that Mylan's actions gave rise to specific jurisdiction in Delaware.

The judges disagreed on whether Daimler left untouched the question of consent to jurisdiction. The key fact on consent, in both decisions, was that Mylan was registered to do business in Delaware. Under Delaware law that predated Daimler, registering to do business in the state equates to consent to jurisdiction. In Judge Sleet's estimation, through Daimler's broad language regarding jurisdiction, the Supreme Court had vitiated the doctrine of consent— and therefore Mylan had not consented to jurisdiction in Delaware. Chief Judge Stark, on the other hand, observed that Daimler was not about consent. In his view, a party could still consent to jurisdiction—and Mylan had done so.

The Majority Decision

Mylan filed interlocutory appeals on both decisions. The majority decision, penned by Judge Taranto, sidestepped the consent issue—it only addressed the question of specific jurisdiction and found that Mylan was subject to specific jurisdiction in Delaware. Judge O'Malley, in concurrence, agreed that Delaware had specific jurisdiction but argued that the question of consent was the simpler analysis. In her view, Daimler did not change the law of consent and Mylan had consented to jurisdiction in Delaware.

The curious part of the majority opinion is not that it found specific jurisdiction. Rather, it is how the majority arrived at that conclusion. Most of the analysis is dedicated not to the facts of the case but to generally applicable ANDA filing requirements. For example, the majority highlighted: the fact that Mylan had filed an ANDA; the fee for filing an ANDA; the potential costs for bioequivalence studies to satisfy the FDA's requirements; and the fact that an ANDA filer seeks approval to market a generic drug throughout the nation. Every ANDA filer does these things.

The majority did discuss some of the case-specific facts as well. For example, it emphasized that Mylan has distribution channels that will either directly or indirectly lead to sales in Delaware. It also noted that Mylan has litigated ANDA cases before in Delaware, and that Mylan is registered to do business in Delaware. Again, nearly every ANDA filer will mirror these facts, with the possible exception of registration to do business in Delaware.

In any event, the majority's analysis is notable for its focus on the actions of the defendant and the relationship of those actions to the litigation, rather than specifically on the harm to the plaintiff. The distinction is a fine one, but important for the reasons discussed below.

As a final point, the majority recognized that a defendant may defeat specific jurisdiction by showing that other considerations render jurisdiction unreasonable. These factors include the burden on the defendant, the forum state's interest in adjudicating the dispute, the plaintiff's interest in obtaining convenient and effective relief, and the interstate judicial system's interest in obtaining the most efficient resolution of controversies.

These considerations are given short shrift in the majority opinion, and the analysis is once again quite broad. For example, the majority observed that Delaware has an interest in adjudicating the case because it involves the pricing and sales of drugs that will wind up in Delaware and because it involves harm to firms doing business in Delaware. The nature of ANDA litigation makes these statements true in any state, not just Delaware. The majority also noted that judicial efficiency is furthered because other cases over the same patents had already been filed in Delaware. But under the majority's analysis, a brand company could just as easily bring suit against multiple defendants in Tennessee, shifting the improved efficiency to that forum. These considerations, like the factors considered in the initial jurisdictional inquiry, are generally true across the board.

Practical Takeaways

There is really only one practical takeaway from this case: ANDA plaintiffs' lives are much easier. The majority opinion focuses its analysis on the defendant's actions outside the State, and expected actions within the State that. But, as explained above, each of these ''actions'' is national in scope. An ANDA seeks approval to market a generic drug *nationally*. Every ANDA filer must pay the filing fee and satisfy the bioequivalence requirement. Most, if not all, ANDA filers will have distribution channels that reach every state. These actions have a national reach and, under the Federal Circuit's analysis, they give rise to specific jurisdiction in every state. The corollary is that generic manufacturers are now at risk of being haled into federal court in virtually every jurisdiction in the country.

Is en banc or certiorari coming?

At this time, no petition for *en banc* rehearing or *certiorari* has been filed, but the sheer scope of this decision opens the door for both. Even if these appeals are not taken further, ANDA defendants in particular should be aware of these issues in their own cases.

First, the majority opinion creates a special kind of jurisdiction that is (for now) specific to ANDA patent cases. As explained above, the Federal Circuit's analysis centered on the defendant's actions, not the harm to the plaintiff. And many of the actions the majority relied upon are national in scope: an ANDA filer seeks *national* approval, and many generics will distribute their drugs throughout the country. The logical result is a prospective nationwide jurisdiction over any ANDA filer. This national jurisdiction is unique to ANDA litigants. This unique rule runs contrary to the Supreme Court's recent emphasis that the Federal Circuit should not deviate from the general body of law to create specialized rules for patent cases. The Court has rejected patent-specific rules in cases like eBay[4] and Teva[5], and it may do so again here. Like the injunctions and standards of review addressed in those cases, jurisdiction is a fundamental legal principle that applies to all cases, not just patent litigations.

Second, the opinion effectively shifts the burdens in the specific jurisdiction inquiry. Until Acorda, the plain-

[4] *eBay Inc. v. MercExchange, L.L.C.*, 126 S. Ct. 1837 (2006).
[5] *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831 (2015).

tiff had the burden of proving jurisdiction.[6] Upon adequate showing, the burden shifted to the defendant to show that other considerations defeat jurisdiction. But here, based strictly on the legal requirements attendant to an ANDA filing, an ANDA plaintiff may establish jurisdiction. Thus, the ''old'' *prima facie* showing is gone and the burden falls immediately upon the defendant to show other considerations. Given that the Daimer decision—the case that precipitated the Federal Circuit's ruling here—was intended to narrow the scope of jurisdiction, it seems likely that the Supreme Court may also curtail this unprecedented expansion of specific jurisdiction.

[6] *See, e.g., Grayson v. Anderson*, —- F.3d —— (4th Cir. Mar. 7, 2016); *IMO Indus., Inc. v. Kiekert AG*, 155 F.3d 254 (3d Cir. 1998); *Northern Laminate Sales, Inc. v. Davis*, 403 F.3d 14 (1st Cir. 2005); *Grober v. Mako Products, Inc.*, 686 F.3d 1335 (Fed. Cir. 2012).

Final Thoughts

The Mylan decision, as it stands, creates a new type of personal jurisdiction—one that will be very hard for ANDA defendants to defeat. For the time being, ANDA plaintiffs can rest easy on their choice of forum. In the meantime, ANDA defendants should prepare to face litigation anywhere in the United States. They may also consider challenging personal jurisdiction in order to bring these issues before the full Federal Circuit or even the Supreme Court.

  PLIR ISSN 1542-9547

Litigation Table

Patents

Hatch-Waxman Litigation Update

The Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act, amended the Federal Food, Drug, and Cosmetic Act and the Patent Act in order to speed the introduction of lower-cost generic drugs into the marketplace, while at the same time preserving the rights of pharmaceutical patentees and compensating them for market time lost satisfying the U.S. Food and Drug Administration's (FDA) safety and efficacy requirements.

The Hatch-Waxman Act establishes a mechanism for prospective manufacturers of a generic drug to challenge an extant patent covering an FDA-approved drug by filing an Abbreviated New Drug Application (ANDA) with a so-called ''Paragraph IV'' certification setting forth the basis for challenging the patent. See 21 U.S.C. § § 355(j), 355(j)(2)(A)(vii)(IV). A Paragraph IV certification constitutes technical infringement of the patent (see 35 U.S.C. § 271(e)(2)), triggering a 45-day period during which the patentee can, by filing suit against the generic manufacturer, invoke a statutory 30-month stay of approval of the ANDA drug. 21 U.S.C. § 355(j)(5)(B)(iii).

Following are court complaints collected during the period of March 25 - 31, 2016.

Recent Hatch-Waxman Filings

Matter	NDA Holder / Licensee(s)	ANDA Filer	Patent(s)	Brand Name
Gilead Scis., Inc., Mylan Pharms. Inc., No. 1:16-cv-00053, Complaint (N.D. W.Va. Mar. 30, 2016)	Gilead Sciences, Inc.	Mylan Pharmaceuticals Inc.	U.S. Patent No. 8,148,374 (cobicistat)	TYBOST (HIV)
Boehringer Ingelheim Pharms. Inc. v. Sun Pharm. Indus. Ltd., No. 3:16-cv-01727, Complaint (D.N.J. Mar. 29, 2016)	Boehringer Ingelheim Corp.; Boehringer Ingelheim International GmbH; Boehringer Ingelheim Pharma GmbH & Co. KG; Boehringer Ingelheim Pharmaceuticals Inc.	Sun Pharma Global FZE; Sun Pharmaceutical Industries Ltd.; Sun Pharmaceutical Industries, Inc.	U.S. Patent No. 9,173,859 (linagliptin; metformin hydrochloride)	TRADJENTA; JENTADUETO (diabetes)
Alcon Research, Ltd. v. Lupin Ltd., No. 1:16-cv-00195, Complaint (D. Del. Mar. 28, 2016)	Alcon Research, Ltd.	Lupin Ltd.; Lupin Pharmaceuticals, Inc	U.S. Patent No. 8,791,154 (olopatadine hydrochloride)	PAZEO (ocular itching)
Rhodes Pharms. L.P. v. Actavis, Inc., No. 2:16-cv-01668, Complaint (D.N.J. Mar. 25, 2016)	Rhodes Pharmaceuticals L.P.	Actavis Elizabeth LLC; Actavis LLC; Actavis, Inc.; Allergan plc;	U.S. Patent Nos. 6,419,960; 7,083,808; 7,247,318; 7,438,930; 8,580,310; 9,066,869 (methylphenidate hydrochloride)	APTENSIO XR (ADHD)
Gilead Scis. Inc. v. Mylan	Gilead Sciences Inc.	Mylan	U.S. Patent No.	TYBOST

Recent Hatch-Waxman Filings – Continued

Matter	NDA Holder / Licensee(s)	ANDA Filer	Patent(s)	Brand Name
Pharms. Inc., **No. 1:16-cv-00192, Complaint (D. Del. Mar. 25, 2016)**		Pharmaceuticals Inc.	8,148,374 (cobicistat)	(HIV)
Genzyme Corp. v. Sun Pharma Global FZE, No. 2:16-cv-01635, Complaint (D.N.J. Mar. 24, 2016)	Genzyme Corp.; sanofi-aventis U.S. LLC; Southern Research Institute	Sun Pharma Global FZE; Sun Pharma Global Inc.; Sun Pharmaceutical Industries, Inc.; Sun Pharmaceutical Industries, Ltd.	U.S. Patent No. 5,661,136 (clofarabine)	CLOLAR (leukemia)
AstraZeneca AB v. Macleods Pharms. Ltd., No. 3:16-cv-01682, Complaint (D.N.J. Mar. 24, 2016)	AstraZeneca AB; Aktiebolaget Hassle; AstraZeneca LP; Zeneca Inc.	Macleods Pharmaceuticals Ltd.; Macleods Pharma USA, Inc.	U.S. Patent Nos. 6,369,085; 7,411,070; 8,466,175 (esomeprazole)	NEXIUM (heartburn)
Helsinn Healthcare S.A. v. Actavis LLC, No. 3:16-cv-01683, Complaint (D.N.J. Mar. 24, 2016)	Helsinn Healthcare S.A.; Roche Palo Alto LLC	Actavis LLC	U.S. Patent Nos. 7,947,724; 9,066,980 (palonosetron)	ALOXI (nausea)

   ISSN 1542-9547