Bloomberg BNA

Pharmaceutical Law & Industry Report®

VOL. 13, NO. 5 PAGES 125–162 JANUARY 30, 2015

HIGHLIGHTS

Supreme Court Denies Attempt to Expedite Remand in Copaxone Case
Mylan Pharmaceuticals and Sandoz likely will have to wait until mid-February to resume their quest at the Federal Circuit to invalidate Teva Pharmaceutical's patent on the multiple sclerosis drug Copaxone. Supreme Court Justice Stephen G. Breyer denies the generic companies' application requesting transmission of the high court's Jan. 20 opinion to the appeals court immediately so as to avoid any delay. **Page 129**

FDA Says Ranbaxy Forfeited Its 180-Day Exclusivity for Generic Nexium
In a notice of administrative action filed in a federal district court, the FDA says Ranbaxy forfeited its eligibility for 180-day exclusivity for a generic version of the heartburn treatment Nexium because it didn't obtain tentative approval of its ANDA within 30 months of submitting the application. Ranbaxy files a motion seeking to expedite the court's decision in the company's ongoing dispute with the FDA over the agency's withdrawal of tentative approvals of two Ranbaxy ANDAs. **Page 129**

Takeda, Colcrys Investors Appeal Ruling Over Approval of Competing Drug
Takeda Pharmaceutical, which makes the gout drug Colcrys, and Elliott Associates, which has a right to royalties from Takeda's Colcrys sales, appeal a federal district court's ruling that upheld the FDA's approval of Mitigare, a competing gout treatment. **Page 130**

Supreme Court Remands Three Cases to Federal Circuit in Light of *Teva*
The Supreme Court remands three cases, including a pharmaceutical case, where the petitions for writ of certiorari were held up pending its *Teva v. Sandoz* decision modifying the Federal Circuit's standards for review of district court claim construction judgments. The drug case involves litigation over Shire's patent underlying its Lialda colitis treatment. **Page 132**

House Committee Releases Draft Language on 21st Century Cures Initiative
The House Energy and Commerce Committee releases a draft discussion document and white paper under its 21st Century Cures initiative designed to accelerate the pace of discovery, development and delivery of promising new medical treatments. **Page 137**

Branded Industry Cites Importance of Abuse Deterrence in Opioid Generics
The FDA shouldn't approve generic opioid pain drugs without abuse-deterrent properties if the brand version has abuse-deterrent properties, branded pharmaceutical industry groups say in comments to the agency. **Page 137**

FDA Imposes Import Ban on Indian Drug Manufacturer IPCA Laboratories
Indian generic drugmaker IPCA Laboratories is placed on an FDA import alert after it was found not to have conformed to good manufacturing practices. The company says it's working to resolve the issue. **Page 147**

ALSO IN THE NEWS

PERSONALIZED MEDICINE: Twenty percent of CDER-approved drugs in 2014 were personalized medicines, an industry group says. **Page 147**

COMBINATION PRODUCTS: The FDA asks for input on a draft guidance for combination product manufacturing. **Page 140**

GENERICS: Teva will sell the first generic version of heartburn drug Nexium. **Page 148**

DRUG SAFETY: Rep. Pitts says he will reintroduce a House bill on timely DEA scheduling of new drugs. **Page 139**

PATENTS: A petition to the Supreme Court cites a ''deeply fractured'' Federal Circuit obviousness ruling on BMS's hepatitis drug. **Page 133**

DRUG COMPOUNDING: The FDA will hold the first meeting of the drug compounding advisory panel in February. **Page 142**

MEDICARE: The HHS announces plans to tie Medicare payments to quality. **Page 141**

LITIGATION TABLE

PATENTS: A table lists recent Hatch-Waxman case filings against generic companies. **Page 158**

 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 $2,474 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.

In This Issue

COURT PROCEEDINGS

FEDERAL NEWS

STATE NEWS

INDUSTRY NEWS

INDUSTRY NEWS

Continued from previous page

INTERNATIONAL NEWS

LITIGATION TABLE

JOURNAL

TABLE OF CASES

COMPANY NAMES INDEX

  PLIR ISSN 1542-9547

Court Proceedings

Patents

High Court Denies Mylan, Sandoz Attempt To Expedite Remand in Copaxone Case

Mylan Pharmaceuticals and Sandoz likely will have to wait until mid-February to resume their quest at the Federal Circuit to invalidate Teva Pharmaceutical's patent on the multiple sclerosis drug Copaxone.

Supreme Court Justice Stephen G. Breyer Jan. 27 denied the generic companies' application requesting transmission of the court's Jan. 20 opinion (13 PLIR 99, 1/23/15) to the appeals court immediately so as to avoid any delay, a Supreme Court spokesperson said.

The patent expires Sept. 1, and the generic companies could only benefit from a quick transmission if the Federal Circuit rules that the patent is invalid for indefiniteness before then—a decision the Supreme Court vacated but didn't reverse—and the Food and Drug Administration approves one or both generic versions immediately thereafter.

As to the latter possibility, ''Teva cannot speculate regarding if or when any generic ANDA filer(s) will gain approval by FDA,'' a spokesman told Bloomberg BNA in an e-mail Jan. 27, referring to abbreviated new drug applications for generic approval.

Mylan didn't respond to Bloomberg BNA's request for comment seeking information on whether either of the generics has tentative approval from the FDA that would allow a quick turnaround.

Breyer's rejection was without prejudice and, according to Supreme Court Rule 22.4, the generic companies can resubmit the application for review by another justice.

But the normal, 25-day transmission clock is ticking and, assuming Teva opposes the resubmitted application, any advantage to be gained is quickly evaporating.

BY TONY DUTRA

To contact the reporter on this story: Tony Dutra in Washington at adutra@bna.com

To contact the editor responsible for this story: Tom P. Taylor at ttaylor@bna.com

Exclusivity Periods

FDA Says Ranbaxy Gave Up Generic Nexium Exclusivity; Ranbaxy Seeks Quick Ruling

The Food and Drug Administration Jan. 26 decided that generic drugmaker Ranbaxy forfeited its 180-day exclusivity for the generic version of the blockbuster heartburn treatment Nexium (esomeprazole magnesium delayed release capsule).

In a notice of administrative action filed in the U.S. District Court for the District of Columbia, the FDA said Ranbaxy forfeited its eligibility for 180-day exclusivity for esomeprazole because it didn't obtain tentative approval of abbreviated new drug application (ANDA) within 30 months after the date on which the ANDA was submitted (*Ranbaxy Laboratories, Ltd. v. Burwell*, D.D.C., No. 1:14-cv-1923-BAH, *notice of administrative action filed* 1/26/15).

The agency filed the notice in ongoing litigation in which Ranbaxy sued the agency over its 2014 decisions to withdraw its tentative approvals of Ranbaxy's ANDAs to make generic versions of both Nexium and the anti-viral drug Valcyte (valganciclovir) because of problems at some of the company's manufacturing facilities (12 PLIR 1575, 11/14/14).

''[T]hat failure was not caused by a change in or a review of the requirements for approval,'' the agency added. The agency added that because of its forfeiture determination, it was withdrawing its arguments that Ranbaxy's claims regarding the FDA's decisions on generic Nexium weren't yet ripe for decision.

Ranbaxy Jan. 26 filed a motion with the court seeking to expedite its decision in its litigation against the FDA over the approval withdrawals.

In a Jan. 27 statement, Ranbaxy said it was ''disappointed with the result and is pursuing all available legal options to preserve its rights.''

In the case, Ranbaxy is seeking a preliminary injunction to block the FDA's actions on both generic Nexium and Valcyte. In November 2014, the agency gave final approval to Valcyte ANDAs submitted by Dr. Reddy's Laboratories and Endo Pharmaceuticals (12 PLIR 1582, 11/14/14).

Teva Gets FDA Nexium Nod. Meanwhile, in a related development, the agency Jan. 26 approved another company, Teva Pharmaceuticals USA, to market the first-ever generic version of Nexium (*see related item in the Industry News section*).

The FDA also said in its court filing that it denied a 2012 citizen petition (docket FDA-2012-P-0661) submitted by Sandoz Inc. related to how the FDA should calculate the 30-month period in which an applicant must obtain tentative approval for a generic drug.

But Ranbaxy says it's legally entitled to 180-day marketing exclusivity for both generic Nexium and Valcyte and that the FDA is legally prohibited from approving any other company's ANDA for either of those products while the company's exclusivity rights remain in force.

Need for Prompt Action Cited. In its motion to expedite the court's decision in the litigation, Ranbaxy says that the FDA's latest actions illustrate ''the need for a prompt decision'' in the case.

''FDA's notice concedes that its action removes any jurisdictional impediment to this Court's resolution of Ranbaxy's claims regarding either of the products at issue in this litigation,'' Ranbaxy says. ''And FDA's approval of yet another competing ANDA product—this

time for generic Nexium—renders prompt action essential,'' its court filing says.

Ranbaxy's loss of its exclusivity rights ''threatens to impose literally hundreds of millions of dollars in damages for which Ranbaxy has no remedy at law,'' the company says.

''[T]ime is of the essence,'' Ranbaxy says in its request for preliminary injunctive relief and a prompt disposition of the matter.

The notice of administrative action was filed by Roger Gural, trial attorney, Department of Justice, Consumer Protection Branch, Portland, Ore., and Joyce R. Branda, acting assistant attorney general, Department of Justice, Jonathan F. Olin, deputy assistant attorney general, Department of Justice, Michael S. Blume, director, Consumer Protection Branch, Department of Justice, and Andrew Clark, assistant director, Consumer Protection Branch, Department of Justice, all in Washington.

Michael D. Shumsky, John K. Crisham, Stephen S. Schwartz and Robert A. Gretch, of Kirkland & Ellis LLP, in Washington, represent Ranbaxy Laboratories Ltd. and Ranbaxy Inc. Ranbaxy Laboratories is based in India, and Ranbaxy Inc. is based in Princeton, N.J.

Douglas B. Farquhar, of Hyman, Phelps & McNamara PC, in Washington, represents intervenor-defendant Dr. Reddy's Laboratories Inc.

Chad A. Landmon, of Axinn, Veltrop & Harkrider LLP, Washington, represents intervenor-defendant Endo Pharmaceuticals Inc.

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

The FDA's notice of administrative action is at http://www.bloomberglaw.com/public/document/RANBAXY_LABORATORIES_LTD_et_al_v_BURWELL_et_al_Docket_No_114cv019/1.

A copy of Ranbaxy's Jan. 26 memorandum in support of its motion for an expedited ruling on pending motions is at http://www.bloomberglaw.com/public/document/RANBAXY_LABORATORIES_LTD_et_al_v_BURWELL_et_al_Docket_No_114cv019/2.

The FDA's citizen petition denial is at http://op.bna.com/hl.nsf/r?Open=bbrk-9t6str.

Approvals

Takeda, Colcrys Investors Appeal Ruling Upholding FDA's Approval of Competing Drug

Japanese drugmaker Takeda Pharmaceutical Co., which makes the gout drug Colcrys (colchicine), and Elliott Associates LP, which has a right to royalties from Takeda's Colcrys sales, are appealing a district court's ruling that upheld the Food and Drug Administration's approval of a competing gout treatment (*Takeda Pharm. U.S.A., Inc. v. Burwell,* D.C. Cir., Nos. 15-5021, 15-5022, *appeal docketed* 1/26/15; *Elliott Associates LP v. Burwell,* D.C. Cir., Nos. 15-5022, *appeal docketed* 1/26/15).

Both Takeda and Elliott Associates are appealing a Jan. 12 ruling from Judge Ketanji Brown Jackson of the U.S. District Court for the District of Columbia, unsealed Jan. 20, in which Jackson denied Takeda's request to overturn the agency's approval of West-Ward Pharmaceutical Corp. and Hikma Pharmaceuticals' (collectively Hikma) Mitigare 0.6 mg capsules for prophylaxis of gout flares in adults. The judge also granted summary judgment to the FDA in a related case against the agency filed by Elliott (D.D.C., No. 1:14-cv-01850-KBJ, 1/12/15).

While Mitigare is a capsule, Colcrys is in tablet form.

Takeda and Elliott each sued the FDA separately in federal district court, with each alleging that the FDA's September 2014 approval of Mitigare ''was unlawful, arbitrary and capricious'' partly because the agency didn't require Hikma/West-Ward to reference Takeda's own colchicine drug, Colcrys, in violation of agency procedure and, according to Elliott, in violation of the Federal Food, Drug, and Cosmetic Act (13 PLIR 61, 1/16/15).

But Jackson disagreed.

''Based on the court's opinion, it is now clear that 505(b)(2) NDA filers can avoid the need to submit a Paragraph IV certification on Orange Book patents for another drug product so long as they do not need to identify the other product as a reference listed drug to support approval.''

—STEVEN H. SKLAR, LEYDIG, VOIT & MAYER

''[T]his Court discerns no basis in law or fact for Plaintiffs' insistence that FDA was legally required to force West-Ward to reference Colcrys and to certify to the Colcrys patents under the circumstances presented here,'' she said.

Decision Could Affect Future 505(b)(2) Applications. Some experts told Bloomberg BNA that the district court's decision, if it stands, may affect drug companies' willingness to engage in the 505(b)(2) drug approval process when dealing with older, grandfathered drugs like colchicine. Indeed, attorneys said the district court's decision that a patent certification to a previously approved application isn't necessarily required in the 505(b)(2) process could discourage companies from engaging in the drug approval process in the first place.

Takeda's notice of appeal to the U.S. Court of Appeals for the District of Columbia Circuit was docketed Jan. 26, as was Elliott'sappeal.

Judge Rules for FDA. In her 80-page opinion, unsealed Jan. 20, Jackson rejected arguments made by Takeda and Elliott.

''Plaintiffs are wrong to characterize FDA's actions with respect to Mitigare as unauthorized, unsafe, or unreasoned; to the contrary, it is clear on the record presented that FDA's approval of Mitigare was consistent with the FDCA, the regulations the agency has promulgated pursuant to the FDCA, the Citizen Petition Responses FDA has issued, and the policies and practices under which the agency operates,'' she wrote.

  PLIR ISSN 1542-9547

''Furthermore,'' the judge said, ''the record clearly reveals the reasonableness of FDA's expert determination that Mitigare is safe and effective as labeled, and it supports the agency's conclusion that Mitigare's labeling best reflects current scientific information regarding the risks and benefits of Mitigare—a conclusion that, in any event, is entitled to a high degree of deference.''

Accordingly, Jackson ruled against the plaintiffs and entered summary judgment as a matter of law in favor of the agency.

505(b)(2) Pathway. The new drug application for Mitigare was approved under Section 505(b)(2) of the FDCA. The 505(b)(2) process is an abbreviated pathway that allows the FDA to rely on data not developed by the applicant for approval of a new drug application.

''Based on the court's opinion, it is now clear that 505(b)(2) NDA filers can avoid the need to submit a Paragraph IV certification on Orange Book patents for another drug product so long as they do not need to identify the other product as a reference listed drug to support approval,'' attorney Steven H. Sklar, of Leydig, Voit & Mayer Ltd. in Chicago, told Bloomberg BNA Jan. 29. ''In other words, so long as a 505(b)(2) filer provides sufficient safety and efficacy data in its own application to support FDA approval, then the fact that FDA itself may go look to and even consider information on another drug product as part of the review does not create a requirement to submit a Paragraph IV certification.''

The Orange Book, formally titled Approved Drug Products with Therapeutic Equivalence Evaluations, lists patents submitted to the agency by branded drug companies as covering a branded drug or its use.

Judge Jackson, he said, ''clearly rejected Takeda's argument that the patent certification process is mandatory if FDA merely considers safety and efficacy information in its possession on another drug product. Because the 505(b)(2) NDA filer, Hikma/West-Ward, did not identify the other drug product as a reference listed drug, FDA did not violate any statutory or procedural requirement relating to patent certifications in approving Mitigare.''

Sklar added, ''Because Hikma/West-Ward were able to provide FDA sufficient data and other information to support approval of Mitigare without needing to identify Colcrys as a reference listed drug, then a certification to the Colcrys Orange Book patents was not necessary.''

But attorney Terry G. Mahn, with Fish & Richardson in Washington, told Bloomberg BNA Jan. 28 that Jackson's holding ''threatens to gut the patent certification provisions in the 505(b)(2) application approval process for certain drugs.''

''The whole idea behind the Hatch-Waxman 'right of reference' was to 'compensate' the brand in some way for the use of its proprietary information for the benefit of a third party. That compensation arrangement was the patent certification process,'' Mahn said.

''If FDA can use brand data 'already in its head' for the benefit of a third party without regard to the patent certification process, Hatch-Waxman's statutory balance starts to fall apart,'' he added.

Patent Litigation Continuing. Meanwhile, Takeda also is continuing with its patent infringement litigation against Hikma, which was filed in the U.S. District Court for the District of Delaware in 2014. On Jan. 9, the U.S. Court of Appeals for the Federal Circuit upheld a decision by the District of Delaware that affirmed the denial of Takeda's request for a preliminary injunction that would have prohibited the sale of Hikma's colchicine for gout ''during the pendency of Takeda's patent infringement litigation against Hikma.''

''If FDA can use brand data 'already in its head' for the benefit of a third party without regard to the patent certification process, Hatch-Waxman's statutory balance starts to fall apart.''

—TERRY G. MAHN, FISH & RICHARDSON

Takeda said its Colcrys (colchicine, USP) is protected by patents that extend through 2028 and 2029. Meanwhile, London-based Hikma Jan. 12 said that it's preparing to distribute Mitigare.

In a separate announcement, Takeda Jan. 12 said that it reached an agreement with Prasco Laboratories, an Ohio-based company, for distribution of an authorized generic of Colcrys. The two companies said Colchicine Tablets, USP will be marketed under the Prasco label and will be widely available in U.S. pharmacies beginning in mid-January.

According to figures from IMS Health, sales of colchicine in the U.S. totaled about $688 million for the 12 months ended August 2014.

Susan M. Cook, Catherine E. Stetson and Jessica L. Ellsworth, of Hogan Lovells, in Washington, submitted the appeal on behalf of Takeda.

Matthew D. McGill, Lucas C. Townsend and Mithun Mansinghani, of Gibson Dunn & Crutcher LLP, in Washington, and Michael A. Sitzman, of Gibson Dunn & Crutcher LLP, in San Francisco, submitted the appeal on behalf of the Elliott plaintiffs.

Intervenor-defendant Hikma is represented by Winston & Strawn LLP and Goodwin Procter LLP.

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

---

The Jan. 12 opinion is at http://www.bloomberglaw.com/public/document/TAKEDA_PHARMACEUTICALS_USA_INC_TPUSA_v_BURWELL_et_al_Docket_No_11/2.

Takeda's notice of appeal is at http://www.bloomberglaw.com/public/document/Takeda_Pharmaceuticals_USA_et_al_v_Sylvia_Burwell_et_al_Docket_No.

The Elliott plaintiffs' notice of appeal is at http://www.bloomberglaw.com/public/document/Takeda_Pharmaceuticals_USA_et_al_v_Sylvia_Burwell_et_al_Docket_No/1.

Patents

Supreme Court Sends Three Cases Back To Federal Circuit in Light of *Teva v. Sandoz*

The Supreme Court Jan. 26 remanded three cases, including a pharmaceutical case, where the petitions for writ of certiorari were held up pending its *Teva v. Sandoz* decision modifying the Federal Circuit's standards for review of district court claim construction judgments (*Lighting Ballast Control LLC v. Universal Lighting Techs., Inc.*, U.S., No. 13-1536, *judgment vacated* 1/26/15; *Gevo, Inc. v. Butamax Advanced Biofuels LLC*, U.S., No. 13-1286, *judgment vacated* 1/26/15; and *Shire Dev., LLC v. Watson Pharm., Inc.*, U.S., No. 14-206, *judgment vacated* 1/26/15).

Each of the three petitions asked the same question presented in *Teva*:

> Whether a district court's factual findings in support of its construction of a patent claim term may be reviewed *de novo*, as the Federal Circuit currently requires, or only for clear error, as Federal Rule of Civil Procedure 52(a) requires.

***Teva* Changes Rules.** On Jan. 20, the high court held that the Federal Circuit must review the ''subsidiary factual findings'' underlying a district court's claim construction judgments using a clear error review standard (*Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 2015 BL 12182 (U.S. 2015) (13 PLIR 99, 1/23/15).

The court's decision allows the Federal Circuit to continue with its no-deference review ''when the district court reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent's prosecution history).''

The court continued:

> The district judge, after deciding the factual dispute, will then interpret the patent claim in light of the facts as he has found them. This ultimate interpretation is a legal conclusion. The appellate court can still review the district court's ultimate construction of the claim *de novo*. But, to overturn the judge's resolution of an underlying factual dispute, the Court of Appeals must find that the judge, in respect to those factual findings, has made a clear error.

Conceivably, the high court could have determined that one or more of the cases didn't feature factual findings that would justify a grant-vacate-and-remand (GVR) decision and deny certiorari outright. But the decisions give the Federal Circuit a variety of situations that will test the new standards.

GVR in all three cases is a slight surprise given that the court denied several other cert. petitions—each filed after the three at issue here but presenting the same question—after the court heard oral argument in the *Teva* case .

Lighting Ballast v. Universal Lighting. As in *Teva*, Lighting Ballast's loss at the appeals court was based on indefiniteness, as to asserted claims of a patent (U.S. Patent No. 5,436,529) relating to control and protection circuits for electronic lighting ballasts commonly used in fluorescent lighting.

The question involved whether ''voltage source means'' implicated means-plus-function analysis under 35 U.S.C. § 112, para. 6. Treating the term as functional, the court concluded that the specification lacked corresponding structure and thus, the asserted claims were invalid for indefiniteness, overturning the lower court's opposite determination.

This was actually the case that the Federal Circuit took en banc. In a 6-4 decision, the court, invoking stare decisis, said it ''should retain plenary review of claim construction, thereby providing national uniformity, consistency, and finality to the meaning and scope of patent claims'' (*Lighting Ballast Control LLC v. Philips Elecs. N. Amer. Corp.*, 744 F.3d 1272, 109 U.S.P.Q.2d 1969 (Fed. Cir. 2014).

Lighting Ballast filed its cert. petition in June 2014 and said that the high court ''should hold the petition in this case pending its disposition of *Teva*.'' (12 PLIR 941, 7/4/14)

Paul D. Clement, of Bancroft PLLC, Washington, represented Lighting Ballast. Steven J. Routh, of Orrick, Herrington & Sutcliffe LLP, Washington, represented Universal Lighting Technologies Inc.

Gevo. v. Butamax. Butamax Advanced Biofuels LLC is a joint venture between BP Plc—British Petroleum—and E. I. du Pont de Nemours and Co. and is assignee of patents (U.S. Patent Nos. 7,851,188 and 7,993,889) related to isobutanol, which is useful as a solvent and a gasoline blendstock. A district court granted summary judgments of noninfringement and invalidity for lack of adequate written description in favor of the alleged infringer Gevo Inc.

The Federal Circuit reversed following a revised claim construction. The court held that the patentee's definition of a key term was not as narrow as the lower court found because evidence about the knowledge of the person of ordinary skill at the time showed that a broader interpretation was more reasonable (*Butamax Advanced Biofuels LLC v. Gevo, Inc.*, 746 F.3d 1302, 109 U.S.P.Q.2d 1701 (Fed. Cir. 2014).

Gevo's cert. petition was filed in April 2014.

Michelle S. Rhyu, of Cooley LLP, Palo Alto, Calif., represented Gevo. Leora Ben-Ami, of Kirkland & Ellis LLP, New York, represented Butamax.

Shire v. Watson. The Federal Circuit ruled in March 2014 that a district court overly broadened the scope of Shire Development LLC's patent (U.S. Patent No. 6,773,720) underlying its Lialda colitis drug (*Shire Dev., LLC v. Watson Pharm., Inc.*, 746 F.3d 1326, 110 U.S.P.Q.2d 1244 (Fed. Cir. 2014) (12 PLIR 455, 4/4/14).

The court's opinion focused on statements Shire made during prosecution history and its use of Markush groups in separate claim limitations. However, the decision ultimately rested on logical conclusions from the structure and terminology of the patent claims themselves.

Shire filed its petition in August 2014 (12 PLIR 1229, 9/5/14).

Edgar H. Haug, of Frommer Lawrence & Haug LLP, New York, represented Shire. Steven A. Maddox, of Knobbe, Martens, Olson & Bear LLP, Washington, represented Watson Labs, which is seeking to market generic Lialda.

BY TONY DUTRA

To contact the reporter on this story: Tony Dutra in Washington at adutra@bna.com

To contact the editor responsible for this story: Tom P. Taylor at ttaylor@bna.com

  PLIR ISSN 1542-9547

Patents

Petition Cites Splintered Federal Circuit Obviousness Ruling on BMS's Hepatitis Drug

A Jan. 20 petition for writ of certiorari described the Federal Circuit as ''internally divided,'' ''fragmented'' and ''deeply fractured'' on how to apply post-filing evidence to the patent obviousness analysis (*Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, U.S., No. 14-886, *review sought* 1/20/15).

The appeals court's decision was on an aspect of pharmaceutical patent obviousness, where the later learned discovery was on the toxicity of a compound in the prior art. The Federal Circuit, after denying en banc rehearing in the case, now has five separate opinions on whether that information should be considered.

The question presented in the petition for review is simply:

> Should courts consider post-filing evidence showing the actual differences between a patented invention and the prior art?

Should the high court decide to address that question, however, it conceivably could expand review to what ''unexpected results'' in general mean in the obviousness review, which presented a conflict at the Federal Circuit.

What BMS Didn't Know at Invention Time. Claim 8 of Bristol-Myers Squibb's patent (U.S. Patent No. 5,206,244) is directed to the compound entecavir, a compound that is sold to treat Hepatitis B under the brand name Baraclude. BMS sued Teva Pharmaceuticals USA Inc. when Teva filed an abbreviated new drug application with the Food and Drug Administration to make a generic version.

Most relevant to the panel's decision and the four opinions in the en banc review is that the compound 2'-CDG was available to researchers at the time BMS developed entecavir, but its toxicity was not yet known.

The obviousness analysis requires choosing a lead compound and determining whether modifications to create the patented new compound would have been obvious. In Federal Circuit jurisprudence, an ''unexpected result'' may be relevant, but it usually relates to a property of the patented compound that was a surprise even to the inventor.

The unexpected result in this case, though, was that the nontoxic entecavir would result from testing and product development based on the toxic 2'-CDG, with all other properties except nontoxicity arguably predictable.

Five Opinions From Federal Circuit. The Federal Circuit panel affirmed a district court's obviousness judgment (*Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, (Fed. Cir. 2014) (12 PLIR 873, 6/20/14).

The court held that a person of ordinary skill in the art would have selected 2'-CDG as a lead compound for further development before BMS filed its patent application, and, from that point, a ''minor modification'' was all it took to arrive at entecavir from 2'-CDG.

The panel said that ''unexpected results do not *per se* defeat, or prevent, the finding that a modification to a lead compound will yield expected, beneficial properties.''

Judge Raymond T. Chen wrote the opinion, which was joined by Chief Judge Sharon Prost and Senior Judge S. Jay Plager.

Eleven active members of the court—not including Plager—voted on the petition for rehearing en banc (*Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 769 F.3d 1339 (Fed. Cir. 2014) (12 PLIR 1477, 10/24/14).

Two separate dissents to the denial contended that the panel decision—left intact by the decision to forgo rehearing—might be read as changing the court's jurisprudence as to how events occurring after the patent application is filed affect the analysis.

Judge Kathleen M. O'Malley wrote one opinion concurring with the denial ''to assuage the fears'' raised by BMS and seven amicus briefs ''that this panel decision has rewritten the test for obviousness for pharmaceutical patents.''

Notably, though, a second concurrence presented a different defense of the panel's opinion, and the two members of the original panel with a vote on the en banc petition didn't join either concurrence, suggesting differences of opinion in multiple corners.

What Is Improper Hindsight? In prior obviousness decisions, certain members of the Federal Circuit have cautioned against ''hindsight bias'' in the sense of assuming an invention was obvious based on what is later discovered. The added wrinkle to this case was that the second concurrence, written by Judge Timothy B. Dyk and joined by Judge Evan J. Wallach, characterized later-discovered unexpected results as potentially being hindsight bias as well.

''The patent applicant's discovery of unexpected results at the time of the invention can help to establish that the invention would not have been obvious to another skilled person,'' Dyk wrote, putting an end date—the application filing—on the applicability of unexpected results to obviousness. ''But hindsight bias must be avoided in determining obviousness,'' he added.

BMS's petition directly addressed that comment:

> Post-filing evidence of unexpected results can show that the situation was less predictable and more complicated than it may have at first appeared with the benefit of hindsight. This is not the replacement of one form of hindsight with another. Instead, it is reliance on scientific truth and the actual differences between an invention and the prior art, even if belatedly realized, to check the natural tendency to underestimate the inventiveness of a new invention after it has been disclosed.

Seth P. Waxman, of Wilmer Cutler Pickering Hale and Dorr, Washington, filed the petition. A response is due Feb. 23.

Teva was represented by George C. Lombardi, of Winston & Strawn LLP, Chicago, before the Federal Circuit.

BY TONY DUTRA

To contact the reporter on this story: Tony Dutra in Washington at adutra@bna.com

To contact the editor responsible for this story: Tom P. Taylor at ttaylor@bna.com

The petition is at http://pub.bna.com/ptcj/140886petition.pdf.

Antitrust

End-Payer Class Certification in Nexium 'Pay for Delay' Litigation Survives Appeal

A district court didn't abuse its discretion in certifying a class of Nexium purchasers asserting Sherman Act claims against drugmakers despite the likely presence in the class of a small, unidentified number of uninjured class members, according to a Jan. 21 decision by the U.S. Court of Appeals for the First Circuit (*In re Nexium Antitrust Litigation,* 1st Cir., No. 14-1521, 1/21/15).

Judge Timothy B. Dyk, sitting by designation from the Federal Circuit, joined Judges Juan R. Torruella and William J. Kayatta, Jr., in upholding the district court's class certification.

While the class might contain some purchasers who weren't injured by generic foreclosure under the alleged ''pay for delay'' deal—''for example, individual consumers who would have continued to purchase branded Nexium for the same price after generic entry''—that possibility didn't foreclose a conclusion that common issues of law and fact predominate among class members, the First Circuit held.

The plaintiffs, union health and welfare funds that reimburse plan members for prescription drugs including Nexium, alleged that AstraZeneca entered into illegal reverse payment agreements with generic manufacturers to exclude generic versions of its heartburn medication Nexium from the market in violation of the Sherman Act.

The district court certified the end-payer class. On appeal, however, the drugmakers contended that the presence of any uninjured class members (even a de minimis number) defeats the Fed. R. Civ. P. 23(b)(3) predominance requirement because the existence of uninjured class members precludes the use of common proof at trial. They further argued that the number of uninjured class members here isn't de minimis.

Court: Class Appropriately Definite. The court disagreed. The class is appropriately definite, and the damages method likewise is calculated to charge the defendants only for aggregate damages equivalent to the injury that the defendants caused, the court said. The question at issue, therefore, is whether a method exists for determining at the liability and damages stage of the litigation which class members are in fact injured.

''[W]e have confidence that a mechanism would exist for establishing injury at the liability stage of this case, compliant with the requirements of the Seventh Amendment and due process,'' the court concluded. ''Defendants have merely speculated that a mechanism for exclusion cannot be developed later. This is not enough to overcome plaintiffs' case for having met the requirements of Rule 23.''

Therefore, the court said, ''[w]e do not think the need for individual determinations or inquiry for a de minimis number of uninjured members at later stages of the litigation defeats class certification.''

The court concluded: ''Ultimately, the defendants will not pay, and the class members will not recover, amounts attributable to uninjured class members, and judgment will not be entered in favor of such members.''

On Jan. 26, the Food and Drug Administration announced its approval of the first generic version of Nexium (esomeprazole magnesium delayed-release capsules) to treat gastroesophageal reflux disease in adults and children ages 1 and older. The approval is for a version made by Ivax Pharmaceuticals Inc., a subsidiary of Teva Pharmaceuticals USA.

Kannon K. Shanmugam, Dane H. Butswinkas, Paul B. Gaffney, and John E. Schmidtlein, of Williams & Connolly LLP; Laurence A. Schoen, of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC; Jay P. Lefkowitz and Karen N. Walker, of Kirkland & Ellis LLP; Kevin D. McDonald and Jonathan Berman, of Jones Day; Timothy C. Hester, of Covington & Burling LLP; Michael P. Kelly and William A. Zucker, of McCarter & English, LLP; Leslie F. Su, of Minerva Law PC; and J. Douglas Baldridge, Lisa Jose Fales, Danielle R. Foley, and Sarah Choi, of Venable LLP, represented the appellants.

Kenneth A. Wexler, of Wexler Wallace LLP; Steve D. Shadowen, of Hillard & Shadowen LLC; J. Douglas Richards, of Cohen Milstein Sellers & Toll PLLC; Jayne A. Goldstein, of Pomerantz Grossman Hufford, Dahlstrom & Gross LLP; and Glen DeValerio, of Berman DeValerio, represented the appellees.

The court's decision is at http://www.bloomberglaw.com/public/document/ASTRAZENECA_AB_et_al_DefendantsAppellants_v_UNITED_FOOD_AND_COMME.

Patents

Boehringer, Amneal Agree to End Aggrenox Dispute, Begin Confidential Licensing Pact

Boehringer Ingelheim and Amneal Pharmaceuticals Jan. 27 ended patent litigation over Amneal's application to market a generic copy of Boehringer's stroke treatment Aggrenox (*Boehringer Ingelheim Pharma GmbH & Co. v. Amneal Pharm., LLC,* D.N.J., No. 1:14-cv-04726, *stipulation and order of dismissal filed*1/27/15).

In a stipulation and order of dismissal filed in the U.S. District Court for the District of New Jersey, the companies told the court they had entered into a confidential settlement and licensing agreement over the drug.

The patent at issue, U.S. Patent No. 6,015,577 (the '577 patent) doesn't expire until Jan. 18, 2017.

Aggrenox, a combination of aspirin and extended-release dipyridamole, is designed to reduce the risk of stroke in patients who have had transient ischemia of the brain or completed ischemic stroke due to thrombosis.

Representing German drug company Boehringer were Bruce M. Wexler, Joseph M. O'Malley Jr., Eric W. Dittman, Jason T. Christiansen and Angela C. Ni, of Paul Hastings LLP, in New York, and Charles M. Lizza and William C. Baton, of Saul Ewing LLP, Newark, N.J.

Co-plaintiff Boehringer Ingelheim Pharmaceuticals Inc. is based in Ridgefield, Conn.

Representing Amneal, which is based in Bridgewater, N.J., were H. Keeto Sabharwal, Dennies Varughese and Sana F. Hussain, of Sterne Kessler Goldstein & Fox

  PLIR ISSN 1542-9547

PLLC, in Washington, and Paul H. Kochanski, of Lerner, David, Littenberg, Krumholz & Mentlik LLP, in Westfield, N.J.

The stipulation and order of dismissal is available at http://www.bloomberglaw.com/public/document/BOEHRINGER_INGELHEIM_PHARMA_GMBH__CO_KG_et_al_v_AMNEAL_PHARMACEUT/2.

Fraud and Abuse

Court Shrinks FCA Claims Against Drug Company, Allows Off-Label Theory to Proceed

A federal district court in Texas partially granted a motion for summary judgment Jan. 23 that narrowed the scope of allegations against a pharmaceutical company accused of illegally promoting three drugs to state Medicaid programs through off-label promotion and kickbacks (*United States ex rel. King v. Solvay, SA*, S.D. Tex., No 4:06-cv-02662, 1/23/15).

The U.S. District Court for the Southern District of Texas granted Solvay Pharmaceuticals Inc.'s motion to dismiss some claims that it sought to ''woo'' members of state Medicaid pharmaceutical and therapeutics committees (P&T committees) to place three of its drugs on preferred drug lists (PDLs) or formularies.

The court dismissed these claims for states that didn't have P&T committees during the relevant time period, but denied Solvay's motion to dismiss without prejudice for claims relating to states in which P&T committees existed but the drugs weren't placed on PDLs.

Solvay, which is now part of AbbVie Products LLC, was unsuccessful in arguing that even those drugs placed on state Medicaid PDLs didn't constitute false claims because reimbursement would still only be available for medically accepted uses. The court said the relator's evidence of increased utilization for drugs on PDLs was sufficient to show the possibility of false claims submissions, and denied summary judgment on that issue.

10-Year Scheme Alleged. Relators John King and Tammy Drummond alleged in their complaint that Solvay sought to increase Medicaid prescriptions of its drugs Aceon, Luvox and AndroGel through the alleged kickbacks and promoting off-label uses for the drugs to physicians who sat on P&T committees. The relators said the scheme ran from 1997 through 2007, and included allegations of false claim submissions to Medicare and other federal health-care programs, but the instant motion concerned only Medicaid claims.

The relators said that Solvay's off-label promotion efforts to get the three drugs on PDL and Medicaid formularies resulted in Medicaid prescriptions that were ''medically unnecessary or inappropriate.'' The relators said placement of drugs on a PDL or formulary results in fewer administrative controls for reimbursements, therefore allowing false claims for medically unnecessary drug claims to be paid by Medicaid agencies.

In 2011, the court allowed the off-label promotion allegations, along with allegations of physician kickbacks in the form of speaker and research fees and other perks, to proceed following a partial denial of Solvay's motion to dismiss (09 PLIR 1313, 10/21/11).

State-Specific Distinctions. Judge Gray H. Miller also dismissed claims that Solvay allegedly influenced drug utilization review boards (DUR boards) because the relator only plead facts supporting allegations of improper influence over P&T committee members. Miller said it was inappropriate to equate DUR board members with P&T committee members under the pleading specificity required under the FCA, and noted that the relators had already amended their complaint five times.

The court was more forgiving towards the relators in allowing claims alleging preferential Medicaid treatment of drugs on ''preferred lists,'' ''preferred status'' or ''formularies'' that weren't formally codified as PDLs. Solvay argued that there couldn't be any false claims associated with a ''Medicaid formulary'' because none existed, but Miller said ''formulary'' was a generic term for a drug list that even Solvay used in internal communications.

Berg & Androphy represented the relators. Hogan Lovells US LLP represented Solvay.

BY ERIC TOPOR

To contact the reporter on this story: Eric Topor in Washington at etopor@bna.com

To contact the editor responsible for this story: Ward Pimley at wpimley@bna.com

The opinion is at http://www.bloomberglaw.com/public/document/King_et_al_vs_Solvay_SA_et_al_Docket_No_406cv02662_SD_Tex_Aug_15_/2.

Drug Safety

Owner of Turkish Wholesaler Sentenced To Prison Term in Missouri Imports Case

The owner and manager of a Turkish drug wholesaler was sentenced Jan. 23 to 30 months imprisonment and ordered to pay a $150,000 fine for smuggling misbranded and adulterated cancer drugs into the U.S., the office of the U.S. Attorney for the Eastern District of Missouri said (*United States v. Semizoglu,* E.D. Mo., No. 4:14-CR-00003, 1/23/15).

Sabahaddin Akman had pleaded guilty to making multiple shipments of Altuzan, the Turkish version of Avastin, from Turkey to Chesterfield, Mo. At least some of the shipments were suspected of containing drugs with no active ingredients (12 PLIR 1169, 8/15/14).

In addition to the prison sentence and fine, Akman paid a forfeiture of $150,000 before sentencing.

According to a statement from the U.S. Attorney's Office, Akman admitted his company used shipping labels that concealed the illegal nature of its prescription-drug shipments, including customs declarations falsely describing the contents as items with no or low declared monetary value, such as gifts, documents or product samples. Akman's company also ensured that large drug shipments were broken into several smaller packages, to reduce the likelihood of seizures by U.S. Customs authorities.

The statement also said that Akman and his company shipped drugs to the U.S. that required constant cold temperatures to maintain their stability and integrity, but did so without making adequate efforts to maintain proper temperatures during shipping. He also admitted

that some chemotherapy drugs he shipped to the U.S. had different lot numbers on the exterior packaging than the lot numbers on the drug vials inside the packages.

In addition, the statement said that Akman was a source of Altuzan for a drug wholesaler in the U.K., Richard Taylor, who had shipped drugs to physicians and customers in the U.S. in 2012. An investigation by the Office of Criminal Investigations (OCI) in the Food and Drug Administration determined that the Altuzan from Taylor had no active ingredients, and that the vials contained mold and water rather than medicine.

The FDA issued several public safety alerts in connection with Taylor's shipments, and its investigation led to a number of related prosecutions, including those of Ozkan Semizoglu, Abid Nisar, Sandra Behe, James Newcomb, Taylor, Erick Falconer (12 PLIR 1100, 8/1/14) and Greg Martin, as well as prosecutions in the Southern District of California, the statement said (10 PLIR 836, 6/29/12;10 PLIR 1149, 9/7/12; 12 PLIR 1100, 8/1/14).

''Patients receiving cancer treatment drugs should be assured that the medications meet FDA's standards for safety and quality,'' said Catherine Hermsen, special agent in charge, FDA Kansas City field office. ''OCI will continue its vigilance over the prescription drug supply chain to ensure that the drugs reaching patients comply with federal law, and that those who attempt to circumvent the agency's oversight will be brought to justice.''

The case was prosecuted by the Health Care Fraud Unit of the U.S. Attorney's Office for the Eastern District of Missouri.

In Brief

Drugmaker Wants Permission to Deny Samples

BioMarin Pharmaceutical Inc., maker of the drug Kuvan, Jan. 16 filed a declaratory action in the U.S. District Court for the Southern District of New York seeking a ruling that it doesn't have to provide its drug to competitor Dr. Reddy's Laboratories for use in bioequivalence tests (*BioMarin Pharmaceutical, Inc. v. Dr. Reddy's Laboratories, Ltd.*, S.D.N.Y., No. 15-cv-00362, *filed* 1/16/15).

BioMarin doesn't want to supply its drug Kuvan, which isn't available through wholesalers, to Dr. Reddy's, a generic drugmaker. According to the complaint, Dr. Reddy's alleged in correspondence that BioMarin's refusal to deal is an anticompetitive attempt to prevent Dr. Reddy's from developing a generic form of the drug, which is approved by the Food and Drug Administration to treat patients who have phenylketonuria, or PKU. Accordingly, BioMarin wants a determination under the Declaratory Judgment Act that it is within its rights to refuse to deal with Dr. Reddy's.

BioMarin also has sued Dr. Reddy's for patent infringement (12 PLIR 1674, 12/5/14).

  PLIR ISSN 1542-9547

Federal News

Generics

Branded Industry Cites Importance Of Abuse Deterrence in Approving Generics

The Food and Drug Administration shouldn't approve generic opioid pain drugs without abuse-deterrent properties if the brand version has abuse-deterrent properties, branded pharmaceutical industry groups said in recent comments to the agency.

In a joint letter, the Biotechnology Industry Organization (BIO) and the Pharmaceutical Research and Manufacturers of America (PhRMA) said they ''believe that permitting the approval of generic products that lack comparable abuse deterrence not only undermines the incentive for innovative biopharmaceutical companies to invest in important new abuse deterrent technologies, but more importantly, fails to mitigate a public and societal health risk.''

The industry groups also encouraged the FDA to remove non-abuse deterrent generic formulations of a drug from the market when an abuse-deterrent formulation of the drug has been approved.

''Payors are often narrowly focused on cost, and continued use of generic formulations that lack abuse deterrent characteristics is likely to continue, despite the usefulness of abuse deterrent formulations in reducing overall healthcare costs due to abuse of medications,'' PhRMA and BIO said. ''FDA has the ability to remove generic formulations that lack abuse deterrent characteristics from the market, when the additional relative safety of a new formulation of a medication with abuse deterrent properties is available.''

PhRMA and BIO said that FDA should provide incentives for the development of abuse-deterrent formulations, ''which is in the best interest of patients.''

Background. In a Sept. 23, 2014, Federal Register notice (79 Fed. Reg. 56,810)(12 PLIR 1347, 9/26/14), the FDA announced that it would hold a public meeting in late October to discuss abuse-deterrent formulations of opioids and also said it would be accepting comments on this topic until Jan. 9 under Docket No. FDA-2014-N-1359.

During the public meeting on Oct. 30, 2014, Douglas C. Throckmorton, deputy director of regulatory programs at the FDA's Center for Drug Evaluation and Research (CDER), said incentives are needed for the development of abuse-deterrent formulations of opioids (12 PLIR 1548, 11/7/14). Also, Robert Lionberger, acting director of the Office of Research and Standards in the FDA's Office of Generic Drugs, said the goal for generic products is to be no less abuse-deterrent than their reference listed drug.

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://op.bna.com/hl.nsf/r?Open=bdmr-9sznx6.

Research and Development

House Panel Releases Draft Language on 21st Century Cures

A House panel Jan. 27 offered a first look at its legislation to accelerate the discovery, development and delivery of promising new treatments and cures.

The legislation has proposals for new advisory bodies and approval pathways but doesn't mention funding increases, according to the discussion document from the House Energy and Commerce Committee.

The discussion document and accompanying summary and white paper culminate a year of hearings, roundtables and white papers under the 21st Century Cures initiative that is designed to transform the clinical trials process and ultimately speed the pace of new medical cures and treatments. Energy and Commerce Committee Chairman Rep. Fred Upton (R-Mich.), who launched the initiative last April with Rep. Diana DeGette (D-Colo.), called the draft a critical first step in the legislation process.

''Our solutions to boost cures and jobs are starting to take shape as we move from broad principles to legislative language. However, this document is far from the final product. Some things may be dropped, some items may be added, but everything is on the table as we hope to trigger a thoughtful discussion toward a more polished product,'' Upton said.

DeGette said in a Jan. 27 statement she appreciates Upton's efforts but stopped short of endorsing the legislative draft: ''While I don't endorse the draft document, I know that with continued engagement, we can reach a bipartisan consensus to help advance biomedical research and cures.''

Last year, Upton, DeGette and other members of the committee said they wanted to introduce legislation by the end of January (12 PLIR 1604, 11/21/14). In releasing the draft document a few days before that deadline, the Energy and Commerce Committee said it will ''continue on an aggressive schedule to introduce 21st Century Cures legislation and ultimately send a bill to President Obama's desk for signature by the end of the year.''

The discussion document covers a wide range of topics from the regulation of drugs and devices and modernizing the clinical trials process to data sharing, Medicare coverage of new technologies and health information technology interoperability.

All provisions of the legislation, according to the discussion document, would fall under five titles:

■ putting patients first by incorporating their perspectives into the regulatory process and addressing unmet needs;

■ building the foundation for 21st century medicine, including helping young scientists;

■ modernizing clinical trials;

■ accelerating the discovery, development and delivery cycle and continuing 21st century innovation at the National Institutes of Health, the Food and Drug Administration, Centers for Disease Control and Prevention and the Centers for Medicare & Medicaid Services; and

■ modernizing medical product regulation.

Some Criticism. Rep. Frank Pallone Jr. (D-N.J.), the top Democrat on the Energy and Commerce Committee, said he was disappointed because the discussion document didn't reflect true bipartisanship.

''In its current form, I am concerned that the nearly 400 page draft could create more problems for our health care system than it solves. Further, the draft does not include any real dollars to fund additional basic research at the National Institutes of Health. Increased funding was a common theme during last year's public engagement, from both sides of the aisle, and is fundamental to truly advancing 21st century cures,'' Pallone said.

''Moving forward, I stand ready to work with Chairman Upton, and all Members of the Energy and Commerce Committee, to find bipartisan consensus legislation that would pass the House and the Senate and ultimately be signed by the President,'' Pallone said.

MedPAC-Like Body for Discovery, Development. The draft would require the FDA to establish a structured framework ''for the meaningful incorporation of patient experience data into the regulatory decision-making process, including the assessment of desired benefits and tolerable risks associated with new treatments.''

There also is a proposal to create an advisory body similar to the Medicare Payment Advisory Commission that would advise Congress on issues related to the discovery-development-delivery cycle. The bill also would establish an accelerated approval pathway for medical devices similar to the breakthrough pathway that already is in place for drugs at the FDA, and allow the FDA to accept and review data summaries rather than full data packages.

The committee said in the discussion draft that it is working on language to clarify what information can be shared about experimental drugs and devices to physicians, insurers and researchers.

''The FDA's current rules and policies governing what drug and device developers may say about their own products were designed decades ago. Since then, the way that medicine is practiced and delivered and the way that information is communicated have fundamentally changed,'' the discussion document said.

Combo Products, Health IT. The bill also would require FDA to issue a guidance document within a year of enacting the legislation on the review process for combination products, which have components of both drugs and devices. The proposal in the discussion document states that the agency center with primary jurisdiction for reviewing a combination product be the sole point of contact for the sponsor.

The discussion document language also includes several health information technology-related provisions, including a section to provide ''regulatory certainty'' for those who are developing apps and other health information technologies, along with another section to work toward national interoperable health information infrastructure.

While the discussion draft doesn't address funding at the NIH—which has experienced a nearly 25 percent decrease in its purchasing power over the past decade, a point that has been voiced by both research advocates and NIH Director Francis S. Collins—the discussion document includes language to require the medical research agency to issue a NIH research strategic investment plan, in which Congress would require the NIH to ensure at least 55 percent of the agency's budget supports extramural research, which occurs at universities and other research institutions. It is currently about 83 percent, according to figures from the NIH Office of Extramural Research . There also is a proposal to require data sharing by any NIH grantees, issue policies that help promote the careers of young scientists and foster high-risk, high-reward science, which typically doesn't get funded amid budget constraints.

There also is a proposal to require a single institutional review board to review multisite studies, and another proposal to allow clinical data registries to comply with Health Insurance Portability and Accountability Act ''privacy and security law'' in lieu of complying with the privacy and security provisions of the Common Rule governing human subject protection.

Drug Approvals. Attorney James Czaban, with Wiley Rein LLP, told Bloomberg BNA that the legislative draft has two key proposals that would change exclusivity rights under the Hatch-Waxman Act. First, he pointed to Section 1241, which the summary from the committee said would extend exclusivity for two years for significant improvements to ''existing molecules'' or drugs. The summary said, ''These improvements could include developing new delivery systems, new drug combinations, and new formulations that lead to less adverse events and increase patient benefits and adherence.''

He also noted that Section 5001 would grant an extension of the 180-day exclusivity period for generic drugs manufactured in the U.S.

Czaban said, ''These provisions would be controversial under any circumstances given the highly competitive landscape in the pharmaceutical industry, but they promise to be especially challenging for many companies to address given that more and more companies now have mixed branded/generic business models, and many generic companies manufacture products both in the U.S. and abroad. Thus, both of these provisions may be simultaneously beneficial and detrimental to the same company.''

The head of a generic drug trade group also criticized some provisions of the bill Jan. 27. Ralph G. Neas, the president and chief executive officer of the Generic Pharmaceutical Association (GPhA), said the ''bill would upset the important balance between creating competition and encouraging innovation in the pharmaceutical marketplace, putting savings at risk and limit-

  PLIR ISSN 1542-9547

ing access to affordable medicines for millions of American patients.''

For example, he said the ''dormant therapies'' part of the measure (Sections 1221-1223), which has incentives for treating unmet medical needs, ''would potentially grant brand drug companies an unprecedented increase in exclusivity for a curiously broad category of new drugs, delaying the competition from generic drugs and biosimilars that promotes beneficial innovations in treatments.'' Neas also said an ''overdependence on market exclusivity as an incentive for innovation threatens to turn back the clock more than 30 years,'' referring to the Hatch–Waxman law that made it easier for generics to reach the market.

Groups Praise Initial Effort. Stephen J. Ubl, president and chief executive officer of the Advanced Medical Technology Association (AdvaMed), a devices industry group, applauded Upton and DeGette's leadership.

''The medical technology industry is central to the development of technologies and diagnostics that will provide the life-saving and life-enhancing treatments of the future. But the innovation ecosystem that supports our industry is severely stressed. Policy improvements are essential if America is to retain its world leadership and the potential for medical progress in this century of the life sciences is to be fulfilled,'' Ubl said. ''We look forward to reviewing the discussion draft in detail and continuing to work with Chairman Upton, Congresswoman DeGette, and other policy makers towards this important goal.''

Carrie Wolinetz, president of United for Medical Research, a coalition of nearly 30 patient groups, universities and private industry companies, said in a Jan. 27 statement that the draft represents a promising opportunity for passing meaningful legislation on National Institutes of Health funding and policy.

The 21st Century Cures initiative will help the NIH ''restart its engine and ensure the U.S. keeps its title of world leader in medical innovation,'' she said.

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

The discussion draft is available at http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/114/Analysis/Cures/20150127-Cures-Discussion-Document.pdf. A summary is available at http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/114/Analysis/Cures/20150127-Cures-Discussion-Document-Section-by-Section.pdf.

The white paper is at http://1.usa.gov/1tmepsb.

Drug Safety

Pitts Will Reintroduce House Bill On Timely DEA Scheduling of New Drugs

Rep. Joe Pitts (R-Pa.), chairman of the House Energy and Commerce Health Subcommittee, said during a Jan. 27 hearing he will soon reintroduce a bill designed to expedite Drug Enforcement Administration actions to allow marketing of drugs already approved by the Food and Drug Administration.

Pitts said the bill ''seeks to improve the transparency and consistency of the Drug Enforcement Agency's scheduling of new FDA-approved drugs under the Controlled Substances Act (CSA).''

Currently, for a new drug that could be abused, there is no deadline for the DEA to make a scheduling decision after receiving the FDA's recommendation.

The bill was authored in the previous Congress by Pitts and Rep. Frank Pallone Jr. (D-N.J.) and was approved by the House Energy and Commerce Committee in June 2014 (12 PLIR 844, 6/13/14). It would require the DEA to issue an interim final rule on the scheduling of a new drug no later than 45 days after it receives the FDA's scheduling recommendation.

Support for Bill. Nathan B. Fountain, chairman of the Epilepsy Foundation of America's Professional Advisory Board, said during the hearing that when the FDA approves a new treatment, ''the epilepsy community is filled with hope.''

''This hope can be short lived when consumers learn that the product will not reach them or their loved one immediately due to the scheduling process at'' the DEA, Fountain said. ''It is further troubling as a patient advocacy organization that we cannot offer a timeline or explanation of why there is no timeline; nor can we offer a clear explanation of why this delay occurs since DEA review has never changed the drug schedule recommendation.''

Fountain said in his written testimony that the time period between initial drug approval by the FDA and final scheduling by the DEA has been increasing. Between 1997-1999 and 2009-2013, the average time between the FDA's approval and the DEA's final scheduling increased from an average of 49.3 days to an average of 237.6 days, an almost fivefold increase, he said.

''Due to the unpredictable delay caused by the lack of a timeline for the DEA, companies cannot accurately predict the amount of time they will have left on their patent once the drug goes to market, or the amount of time for which they will have data exclusivity,'' Fountain said. ''They cannot accurately predict or plan for their product reaching consumers and physicians. This is a disincentive to innovation in an already challenging area of neurological development.''

Fountain said the bill ''is a simple solution to the problem and would ensure that drugs will not sit around waiting to be scheduled and patients won't be forced to wait on potentially lifesaving drugs.''

Other Bills Discussed. The subcommittee also discussed the Ensuring Patient Access to Effective Drug Enforcement Act (H.R. 471), which was introduced Jan. 22 by Reps. Marsha Blackburn (R-Tenn.), Tom Marino (R-Pa.), Peter Welch (D-Vt.) and Judy Chu (D-Calif.).

The bill is intended to facilitate greater collaboration between industry stakeholders and regulators in an effort to combat prescription drug abuse. Identical legislation (H.R. 4709) introduced in the previous Congress was passed by the full House in July 2014 (12 PLIR 1107, 8/1/14).

Pitts said the bill ''would improve law enforcement efforts regarding prescription drug diversion and abuse.''

It has been referred to the House Energy and Commerce Committee and the House Judiciary Committee for consideration.

In addition, the subcommittee discussed bills that would streamline state licensing requirements for military veteran emergency medical technicians; reauthorize the trauma care systems planning grants; reauthorize language from the Public Health Service Act to fund trauma care centers; and reauthorize the National All Schedules Prescription Electronic Reporting (NASPER) Reauthorization Act to support state prescription drug monitoring programs.

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 on the hearing is available at http://energycommerce.house.gov/hearing/examining-public-health-legislation-help-patients-and-local-communities.

Drug Development

More Combination Drugs Would Receive Market Exclusivity Under Proposed House Bill

Rep. Jason Chaffetz (R-Utah) Jan. 22 introduced a bill (H.R. 406) that would give five years of market exclusivity to new combination drugs containing molecules already approved by the Food and Drug Administration.

The Hatch-Waxman Act gives new drugs five years of market exclusivity to help companies defray the cost of undergoing the FDA new drug approval process, Chaffetz said in a press release. Therefore, regardless of the patent situation of a new drug, a company can count on having five years as the exclusive seller of the product.

When the Hatch-Waxman Act was enacted 30 years ago, all new drugs were ''new chemical entities,'' or new molecules that had never before been approved, Chaffetz said. No one at the time considered the possibility that a new drug might be created by combining existing molecules (that is, molecules that had already been approved).

''As the law is currently written, virtually all combination new drugs are excluded from the five years of market exclusivity and therefore are not being developed,'' Chaffetz said in a statement. ''A new drug that has been created using one or more existing molecules should not be required to go through the same rigorous, lengthy and expensive FDA new drug approval process.''

The bill was referred to the House Energy and Commerce Committee for consideration. In August 2013, Chaffetz introduced similar legislation (H.R. 2985) but the bill didn't go anywhere.

FDA Guidance. In October 2014, the FDA issued a guidance that extended the five-year new chemical entity (NCE) exclusivity to new combination drugs that contain previously-approved drug substances as long as they also contain a drug substance that hasn't been approved (12 PLIR 1445, 10/17/14). However, the FDA said its new interpretation doesn't apply to combination drugs that were approved before the guidance was published. Therefore, combination drugs approved before October 2014 aren't eligible for five years of exclusivity.

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 bill is at http://op.bna.com/hl.nsf/r?Open=bdmr-9t6s9a.

Combination Products

FDA Asks for Input on Draft Guidance For Combination Product Manufacturing

The Food and Drug Administration is asking for input on a draft guidance on the manufacturing practice requirements for combination products, according to a Jan. 27 Federal Register notice (80 Fed. Reg. 4,280).

The agency asked for comments by March 30, and the docket is FDA-2015-D-0198. Already, the guidance spurred a positive reaction from a health-care attorney for including examples of how to comply with the FDA's manufacturing rules.

The draft guidance, which the agency posted online Jan. 23, presents what the FDA calls general considerations for current good manufacturing practice compliance ''as well as analysis of hypothetical scenarios.'' The name of the guidance is ''Current Good Manufacturing Practice Requirements for Combination Products.'' The document builds on a final rule (FDA-2009-N-0435) from 2013 (78 Fed. Reg. 4,307, Jan. 22, 2013) (11 PLIR 109, 1/25/13) on manufacturing requirements for combination products, which include drug-device combinations.

The scenarios in the draft guidance examine applying manufacturing requirements to three specific types of combination products: a prefilled syringe, a drug-coated mesh and a drug-eluting stent.

The agency pointed out in the draft that a combination product can include a product comprising two or more regulated components, such as a drug with a device, or a drug with a device and biologic product that are produced as a single entity (what the agency calls a ''single entity'' combination product). A combination product also can include two or more separate products packaged together (or co-packaged, in the FDA's term) in a single package. In addition, a combination product can include a drug or device or biologic packaged separately but ''cross-labeled'' for use with another product, where both are required to achieve the intended use or indication, the draft said.

Reaction. Attorney Bradley Merrill Thompson, who represents combination product makers and is with the firm Epstein Becker & Green, told Bloomberg BNA Jan. 26 that the examples in the draft ''were in direct response to our begging and pleading for examples. These things are so complex that we really felt until we got to the level of examples there was too much ambiguity.''

Thompson said, ''From well before FDA's publication in January 2013 of its final rule on combination product

  PLIR ISSN 1542-9547

GMPs, the Combination Products Coalition has been asking for—indeed begging for—the agency to produce a companion guidance document that dives into the details around how the GMPs are to be implemented.'' The Combination Products Coalition is an industry group.

''We knew even before the final rule was written that the devil would be in the detail,'' he said, adding that after the rule was published in January 2013, ''we immediately began pressing FDA to publish the companion guidance document. Sprinkled throughout the preamble to the final rule was an express promise to provide additional detail in guidance. Now, two years after the final rule, it is here. And it is good.''

Thompson said the guidance document ''addresses many of the questions that we have been asking. We don't necessarily like all of the answers, but we deeply appreciate FDA's publishing the guidance document in which the agency shares its views. Further, we had asked that not only the agency clarify the rules generally, but the agency provide illustrative examples to help make its views more concrete and clear.''

Among the issues that FDA clarified, he said, is the distinction between drug containers and closures, on the one hand, and drug delivery devices on the other. Thompson said, ''It is a frequent practice in the pharmaceutical industry to provide certain containers that also facilitate delivery of the drug. Likewise, companies sometimes provide convenience kits, and the agency addressed the regulatory status of such kits.''

However, Thompson said, ''there are a few areas that have not yet been addressed and we are disappointed at their omission. Probably one of the biggest is the relatively little discussion of how the new rule should be applied to legacy products. For years the application of the medical device GMPs to container closure systems that also served to aid the delivery of the drug was unclear.''

Thompson said it's one thing for the agency to clarify that the ''device GMPs–contrary to general understanding and also contrary to FDA's historical enforcement practice—applied to such container closure systems. But what do companies do that have been making these products for quite some time?'' He said that design controls, for example, aren't something ''that's easy to address 10 years after the product has been on the market. In one brief paragraph, FDA suggests that the design controls will indeed apply to these legacy products, but that industry will not be expected to prepare a development plan or conduct design review meetings for the product. Instead, industry will be expected to gather up and analyze the evidence of safety and effectiveness, and perhaps do additional testing. For products that have been around for 20 years, that seems like overkill. We will be studying the guidance document over the coming two months and indeed commenting on it.''

Thompson also said the Combination Products Coalition is collaborating with the Regulatory Affairs Professionals Society to host a public meeting to collect additional thoughts and suggestions. The date of that meeting hasn't yet been set, he said, ''but we hope to do it within the comment period.''

The Federal Register notice is at http://www.gpo.gov/fdsys/pkg/FR-2015-01-27/pdf/2015-01410.pdf. http://www.fda.gov/RegulatoryInformation/Guidances/ucm126198.htm.

Medicare

HHS Announces Plans to Tie Medicare Payments to Quality

HHS Secretary Sylvia Mathews Burwell Jan. 26 announced goals and a timeline to move the Medicare program, and the health-care system at large, toward paying providers based on the quality, rather than the quantity, of care they provide.

Many stakeholders greeted the announcement with praise, although some asked the Department of Health and Human Services to move carefully.

This is ''the first time in the history of the Medicare program that HHS has set explicit goals for alternative payment models and value-based payments,'' the department said in a statement. The HHS has set a goal of tying 30 percent of traditional, fee-for-service Medicare payments to quality or value through alternative payment models, such as accountable care organizations or bundled payment arrangements, by the end of 2016, and tying 50 percent of payments to these models by the end of 2018, the statement said.

In addition, the HHS also set a goal of tying 85 percent of all traditional Medicare payments to quality or value by 2016 and 90 percent by 2018 through programs such as the Hospital Value-Based Purchasing and the Hospital Readmissions Reduction programs, the statement said. The HHS designed the new Medicare payment goals to deliver better patient care and to make Medicare spending ''smarter,'' a fact sheet released by the Centers for Medicare & Medicaid Services said.

Medicare fee-for-service payments totaled $362 billion in 2014, the HHS statement said.

Currently, the CMS makes about 20 percent of its Medicare payments through alternative payment models, the HHS statement said. ''The goals announced today represent a 50 percent increase by 2016,'' it said.

Burwell announced the Medicare payment goals at a meeting with nearly two dozen leaders from groups that represent consumers, insurers, providers and businesses. In addition, she announced the creation of a network to help stakeholders expand alternative payment models into their programs.

Hospitals: Don't Cut Funding. Provider groups and other stakeholders generally praised the HHS announcement. However, some stakeholders said they wanted protections for covering the cost of new technology and wanted changes to be geared toward the specific needs of different communities.

In a Jan. 26 blog post, Charles Kahn, president and chief executive officer of the Federation of American Hospitals, said his group welcomed the HHS announcement. However, he noted that since 2010, hospitals have faced spending cuts that equal $122 billion and further cuts ''would undermine our ability to invest in delivery system innovations.''

The Association of American Medical Colleges (AAMC) also said it backs the new Medicare payment goals. In a statement e-mailed to Bloomberg BNA Jan. 26, the AAMC's Chief Health Care Officer Janis Orlowski said, ''We look forward to continuing to work with CMS to develop payment methodologies that ensure high-quality, high-value care for the medically

complex and underserved patients that depend on medical schools and teaching hospitals.''

Likewise, Rick Pollack, executive vice president for advocacy and public policy at the American Hospital Association, praised the HHS Medicare payment goals. ''We welcome continued efforts of the Administration and others to promote innovative approaches that enhance these ambitious objectives,'' he said in a Jan. 26 e-mail to Bloomberg BNA.

Pollack also called on the HHS to phase in changes in a ''thoughtful manner'' tailored to individual communities' specific needs.

Other Providers Supportive. Nonhospital groups supported the HHS announcement, as well. ''We strongly support reform of the Medicare payment system, including elimination of Medicare's flawed sustainable growth rate formula, which provides a pathway for physicians to innovate and develop new models of health care delivery for our patients,'' Robert Wah, president of the American Medical Association, said in a Jan. 26 statement.

The AMA looks forward ''to hearing more details behind the percentages HHS put forward as well as their plans to reach these percentage targets,'' Wah said.

Mark Parkinson, president and CEO of the American Health Care Association and National Center for Assisted Living, said in a statement, ''We are encouraged the Administration has also made this a priority, and we hope we can continue working with the White House, CMS and other stakeholders to determine the best path forward for achieving the administration's aggressive goals without sacrificing access to high-quality skilled nursing care for our nation's seniors.'' The AHCA/NCAL represents more than 12,000 nonprofit and proprietary skilled nursing centers, assisted living communities, sub-acute centers and homes for individuals with intellectual and developmental disabilities.

Pharmaceutical Industry. Also in a Jan. 26 statement, Pharmaceutical Research and Manufacturers of America (PhRMA) President and CEO John Castellani said his group supports the department's goals.

However, Castellani urged the HHS to incorporate clear mechanisms for recognizing the value of new treatment advances, such as precision medicine and other new tests and treatments. Moreover PhRMA supports shared decision making between providers and patients that is informed by high-quality evidence about the full range of available treatment options, as the HHS develops and expands alternative payment models for Medicare, Castellani said.

Any new payment and health-care delivery models that the HHS develops should be grounded in strong quality measures and incentives, with emphasis on outcomes that matter to patients and transparency so that drug manufacturers and other stakeholders can work collaboratively, Castellani said.

Payment Cuts? Dan Mendelson, CEO of consultant Avalere Health, said the HHS announcement may lead to lower payments for doctors if they don't meet quality standards.

''Real wages for physicians have been decreasing for years,'' Mendelson said Jan. 26 in an e-mail to Bloomberg BNA. ''The significance of this announcement is the resolve of the federal government to link payments to quality and to hold providers accountable for integration of services.

''Over time, physicians will need to perform on quality metrics—just as hospitals and health plans do—to see favorable compensation,'' he said.

Information Sharing. Implementing electronic health records (EHRs) at more facilities may be part of how the HHS meets its new Medicare payment goals. In the HHS fact sheet, the agency said it will focus on better sharing of information, through increased EHR adoption, to achieve its goal of better care, smarter spending and healthier people.

''While we have made great strides in encouraging and supporting the adoption of electronic health records, there are many areas where important information is missing,'' the fact sheet said. ''For example, many important providers in the health system such as nursing homes do not have electronic health records to be able to store and share health information electronically with their patients or other providers, and some providers find that their electronic health records do not share information (i.e. are not 'interoperable') with other systems as easily as they would have hoped,'' the agency fact sheet said.

March Meeting. Burwell also announced the creation of a Health Care Payment Learning and Action Network to help make the department's goals ''scalable beyond Medicare,'' the HHS statement said. ''Through the Learning and Action Network, HHS will work with private payers, employers, consumers, providers, states and state Medicaid programs, and other partners to expand alternative payment models into their programs,'' the statement said.

In addition, the network ''will hold its first meeting in March 2015, and more details will be announced in the near future,'' according to the statement.

BY MICHAEL D. WILLIAMSON

To contact the reporter on this story: Michael D. Williamson in Washington at mwilliamson@bna.com

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

A blog post on the HHS announcement is at http://www.hhs.gov/blog/2015/01/26/progress-towards-better-care-smarter-spending-healthier-people.html. The CMS fact sheet is at http://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2015-Fact-sheets-items/2015-01-26-2.html. The FAH blog is at http://fahpolicy.org/the-fah-responds-to-hhs-announcement-of-better-care-smarter-spending-and-healthier-people-initiative/.

Drug Compounding

FDA to Hold First Meeting Of Drug Compounding Advisory Panel

The Food and Drug Administration will hold the first meeting of the Pharmacy Compounding Advisory Committee in February, according to a Jan. 26 Federal Register notice (80 Fed. Reg. 3,967).

The Drug Quality and Security Act (Pub. L. No. 113-54), which was signed into law in November 2013 (11 PLIR 1438, 12/6/13)), distinguishes between compound-

   ISSN 1542-9547

ers engaged in the traditional pharmacy practice of making customized drugs for specific patient needs from those making large volumes of compounded drugs without individual prescriptions. Compounders outside the scope of traditional pharmacy practice can voluntarily register with the FDA as ''outsourcing facilities'' and become subject to federal oversight like traditional drug manufacturers. The law responds to a deadly outbreak of meningitis from compounded, or custom-made, drugs from a pharmacy in Massachusetts in the fall of 2012.

The advisory committee will provide advice on scientific, technical and medical issues concerning drug compounding under sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the agency said. Section 503A governs traditional compounding facilities, and Section 503B governs outsourcing facilities.

Bulk Drug Substances. During the meeting, the committee will discuss the list of bulk drug substances that may not be compounded under the exemptions provided by sections 503A and 503B of the FD&C Act. Those drug products or their components have been withdrawn or removed from the market because they were found to be unsafe or not effective, the agency said.

On Dec. 4, 2013 (11 PLIR 1437, 12/6/13) and July 2, 2014 (12 PLIR 950, 7/4/14), the FDA published notices in the Federal Register soliciting nominations for the list of bulk drug substances. The FDA said the committee will discuss six of the nominated substances and the nominators are invited to make a short presentation supporting each drug substance nomination.

The meeting will be held Feb. 23 from 8:30 a.m. to 5 p.m. and Feb. 24. from 8:15 a.m. to 3 p.m. at the FDA's White Oak campus in Silver Spring, Md. Interested persons may present data, information or views, orally or in writing, on issues pending before the committee. Written submissions may be made on or before Feb. 9.

In December 2014, the FDA announced the membership of the advisory committee (12 PLIR 1732, 12/19/14).

The Federal Register notice is at http://www.gpo.gov/fdsys/pkg/FR-2015-01-26/pdf/2015-01267.pdf.

Drug Safety

Oversight Lacking in Hospital Use Of Compounded Drugs, OIG Report Says

The entities that oversee Medicare-participating hospitals may not be effectively evaluating hospital use of compounded sterile preparations (CSP) due to a lack of personnel and training, according to a report from the Department of Health and Human Services Office of Inspector General released Jan. 22.

The report, ''Medicare's Oversight of Compounded Pharmaceuticals Used in Hospitals'' (OEI-01-13-00400), said that due to a limited time frame to review a hospital's overall operations, ''oversight entities may address some of the recommended practices for oversight of CSPs on a case-by-case basis.''

Compounded drugs come in two forms, sterile and nonsterile, and refer to drugs that are made for an individual patient. While compounded drugs have traditionally been made by a pharmacist upon receiving a prescription, hospitals have lately begun contracting with stand-alone compounding pharmacies for their supply of compounded drugs.

In 2012, contaminated steroid injections that were compounded by the New England Compounding Pharmacy led to an outbreak of fungal meningitis that killed 64 patients .

The OIG examined CSP oversight efforts at the Centers for Medicare & Medicaid Services and the four entities that accredit hospitals for participation in Medicare—the Joint Commission, the American Osteopathic Association, Det Norske Veritas Healthcare and the Center for Improvement in Healthcare Quality.

Contract Oversight. The report found that only one of the five oversight entities always reviewed hospital contracts with stand-alone compounding pharmacies.

''This review could include whether the terms of the contracts address CSP recall procedures, proper storage of CSPs while in transit, and quality assurance related to CSP sterility and potency, among others,'' the report said.

The OIG said that hospitals generally contract with stand-alone compounding pharmacies to supply the highest-risk CSPs.

Additionally, three of the oversight entities said they don't review whether stand-alone compounding pharmacies have voluntarily registered with the Food and Drug Administration.

The OIG report also said that while reviewing a hospital's use of CSPs can be highly technical, only two of the oversight entities employed pharmacists as hospital surveyors, and both didn't include pharmacists on every survey team.

Furthermore, two of the oversight entities said they didn't provide any training on compounded drugs to their hospital surveyors and the remaining three said their training on compounded drugs ranged from observing drugs being compounded to online educational classes.

Three of the oversight entities told the OIG they are considering changing the way they evaluate CSP use in hospitals, such as providing increased training for hospital surveyors. The other two entities said they have no plans to change their procedures.

None of the oversight entities said they plan on changing procedures regarding the review of hospital contracts with stand-alone compounding pharmacies.

OIG Recommendations. The OIG recommended that the CMS ensure that hospital surveyors have effective training on compounded drugs, and suggested the agency work with professional organizations to develop new standards.

The OIG also said that the CMS should amend the guidelines for hospital surveys and tell surveyors to review hospital contracts with stand-alone compounding pharmacies.

The CMS agreed with both of the recommendations, and said ''surveyors could benefit from more training to ensure their basic competencies in assessing compounding practices in hospitals.''

The OIG report is at http://oig.hhs.gov/oei/reports/oei-01-13-00400.pdf.

Counterfeit Drugs

Counterfeit Versions of Cialis Found In Mail on Way to U.S. Consumer, FDA Says

The Food and Drug Administration Jan. 21 said that counterfeit versions of Cialis 20 mg tablets were found in the mail on the way to a U.S. consumer.

The FDA said that while the shipment was stopped, it is concerned about other possible mail shipments to consumers. An FDA laboratory analysis showed the counterfeit versions of the erectile dysfunction drug contain multiple ingredients, which if used could result in adverse effects or harm, the agency said.

Consumers should only buy prescription medicines from state-licensed pharmacies located in the U.S., the agency said. The FDA said it cannot confirm that the manufacturing, quality, storage and handling of these products follow U.S. standards because these products are from an unknown source. Therefore, these products are considered unsafe and shouldn't be used, the agency said.

The FDA also said it recommends consumers talk to their health-care professional about their condition and options for treatment if they received a counterfeit product.

FDA-approved Cialis tablets made by Eli Lilly & Co. contain the active ingredient tadalafil and are used for the treatment of erectile dysfunction and other approved indications, the agency said. Currently, Eli Lilly's authentic product is considered safe and effective for its intended uses.

There is no indication that the legitimate supply chain is at risk, therefore consumers can be confident that prescription medicines received through legitimate state-licensed pharmacies located in the U.S. are safe and effective, the agency said.

Identifying Bogus Versions. The FDA said counterfeit versions of Cialis can be identified by the following differences on the label of the bottle when compared to the authentic product:

- the label lists ''AUSTR81137'' on the front of the bottle;
- the label doesn't include an NDC number on the front of the bottle, such as ''NDC 0002-4462-30'' for the 20 mg tablets;
- the label doesn't include the tablet strength in a colored box;
- the label has yellow and darker green designs on the front;
- the label has misspellings;
- the label lists the manufacturer location as ''112 Warf Road, West Ryde, NSW 2114'' in Australia on the side of the bottle; and
- the label lists ''Lot: AC 066018, Exp: 01SEP17'' on the side of the bottle.

Consumers shouldn't use products that match one or more of the descriptions above, the agency said. For additional information about these products, contact the FDA at DrugSupplyChainIntegrity@fda.hhs.gov.

The FDA said it isn't aware of consumer adverse events related to the use of these counterfeit versions of Cialis. Health-care professionals and consumers are encouraged to report adverse events related to the use of any suspect medication to the FDA's MedWatch Adverse Event Reporting program.

More information is available at http://www.fda.gov/Drugs/DrugSafety/ucm431071.htm.

FDA

FDA Appoints Deputy Commissioner For Medical Products, Tobacco

The Food and Drug Administration Jan. 26 announced that Robert Califf has been appointed the deputy commissioner for medical products and tobacco.

Califf will fill an FDA job that has been vacant since mid-2013.

In his position, Califf will provide executive leadership to the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, the Center for Devices and Radiological Health and the Center for Tobacco Products, the agency said. Califf also will oversee the Office of Special Medical Programs in the Office of the Commissioner.

Califf will provide high-level advice and policy direction and will manage cross-cutting clinical, scientific and regulatory initiatives in several key areas, including personalized medicine, orphan drugs, pediatric science and the advisory committee system, the agency said.

The FDA said Califf will join the agency in late February.

Filling Vacant Position. The FDA confirmed to Bloomberg BNA that the deputy commissioner's position was created in 2011.

Stephen Spielberg held the position from September 2011 to February 2013. He left the agency to edit Therapeutic Innovation and Regulatory Science, a journal launched by the Drug Information Association (11 PLIR 112, 1/25/13).

After that, Leona Brenner-Gati, acting deputy commissioner, left the agency in May 2013 due to what the agency called unexpected personal circumstances (11 PLIR 601, 5/10/13).

The position has been vacant since May 2013, the agency press office confirmed.

Knowledge, Experience Cited. ''I am delighted to announce this important addition to FDA's senior leadership team,'' FDA Commissioner Margaret A. Hamburg said in a statement. ''Dr. Califf's deep knowledge and experience in the areas of medicine and clinical research will enable the agency to capitalize on, and improve upon, the significant advances we've made in medical product development and regulation over the last few years.''

Califf is vice chancellor of clinical and translational research at Duke University, the agency said. Other prominent roles during his tenure at Duke include director of the Duke Translational Medicine Institute (DTMI) and professor of medicine in the cardiology division at the Duke University Medical Center in Durham, N.C.

  PLIR ISSN 1542-9547

Before serving as director of DTMI, Califf was the founding director of the Duke Clinical Research Institute, the world's largest academic research organization, the agency said. Califf has led many landmark clinical studies and is a nationally and internationally recognized expert in cardiovascular medicine, health outcomes research, health-care quality and clinical research.

Califf was a member of the Institute of Medicine (IOM) committees that recommended Medicare coverage of clinical trials and the removal of ephedra from the market and of the IOM's Committee on Identifying and Preventing Medication Errors. In addition, Califf served as a member of the FDA Cardiorenal Advisory Panel and the FDA Science Board's Subcommittee on Science and Technology. He is a member of the IOM Policy Committee and liaison to the Forum on Drug Discovery, Development, and Translation, the agency said.

State News

New York

Doctors Urge Health Commissioner To Delay E-Prescribing Requirements

The Medical Society of the State of New York (MSSNY) and 17 other health care groups released a letter Jan. 22 urging New York to delay implementation of its electronic prescribing requirements, saying electronic health records systems won't be ready in time.

Under the 2012 law known as I-STOP (Internet System for Tracking Over-Prescribing Act), prescriptions for all controlled and noncontrolled substances must be made electronically by March 27.

Lack of Certification. Many electronic health records vendors, however, haven't yet been certified by the U.S. Drug Enforcement Administration to e-prescribe controlled substances, according to MSSNY. Moreover, at least half of the state's nursing homes and assisted living facilities don't have EHR systems in place, according to MSSNY.

''While we recognize the important efficiencies and patient safety enhancements which can be achieved through electronic prescribing, it is quite concerning that many EHR vendors, including several with significant market share in New York State, are not yet certified for electronic prescribing of controlled substances (EPCS) and will not be certified in most cases until sometime in the first quarter of 2015,'' MSSNY and the 17 groups said in a Jan. 8 letter to acting state Health Commissioner Howard Zucker.

''This is quite concerning for all prescribers, particularly large group and institutional prescribers whose systems must be tested and re-tested to remove operational flaws before the installation and implementation of software updates.''

MSSNY urged the state Department of Health (DOH) or the Legislature to delay implementation of the law for one year. If that could not be accomplished, MSSNY asked Zucker to use his authority to suspend enforcement of the law until adequate systems are in place.

The letter also asked Zucker to consider approving a waiver for physicians who prescribe fewer than 25 prescriptions per year.

''For those who cannot reasonably comply, the law allows for DOH to issue a waiver from the electronic prescribing of controlled substances requirement upon showing technological limitation, undue economic burden or other exceptional circumstance,'' said a spokesperson for the Health Department who asked to remain anonymous.

''Since the e-prescribing legislation took effect in August 2012, the New York State Department of Health has conducted outreach to providers, pharmacists and other interested stakeholders about the e-prescribing requirements,'' the spokesperson said in a Jan. 23 e-mail to Bloomberg BNA. ''Outreach efforts included webinars, live presentations, and e-mail notifications.''

The letter also asked the state health commissioner to consider approving a waiver for physicians who prescribe fewer than 25 prescriptions per year.

The I-STOP law was enacted to control the abuse of drugs such as the painkiller hydrocodone by creating a statewide registry and requiring the use of e-prescriptions (11 PLIR 1069, 9/6/13).

The groups that signed the letter are: American Academy of Pediatrics, District II; American Congress of Obstetricians & Gynecologists; Continuing Care Leadership Coalition; Leading Age New York; New York Chapter, American College of Physicians; New York State Academy of Family Physicians; New York State Dental Association; New York State Health Facilities Association; New York State Ophthalmological Society; New York State Psychiatric Association; New York State Society of Otolaryngology-Head and Neck Surgery; New York State Society of Orthopedic Surgery; New York State Podiatric Medical Association; New York State Radiological Society; New York State Society of Physician Assistants; Nurse Practitioner Association of New York State; and the NYS Society of Plastic Surgeons Inc.

By Gerald B. Silverman

To contact the reporter on this story: Gerald B. Silverman in Albany, N.Y., at gsilverman@bna.com

To contact the editor responsible for this story: Patty Logan at plogan@bna.com

The letter is available at http://www.mssny.org/MSSNY/Public_Health/E-Perscribing/Howard-A-Zucker_Letter.aspx.

  PLIR ISSN 1542-9547

Industry News

Drug Importation

U.S. FDA Imposes Ban on Indian Drug Manufacturer IPCA Laboratories

Indian generic drugmaker IPCA Laboratories Ltd., which Jan. 22 was placed on a U.S. Food and Drug Administration import alert, says it is working to resolve the issue as soon as possible.

IPCA's Joint Managing Director A.K Jain told Bloomberg BNA via telephone Jan. 28 that the company already was aware of the problems, and had stopped shipments to the U.S. in July 2014 after the FDA had pointed out violations.

He said there were no new issues, and his company was working to resolve them at the earliest, but refused to speak further, citing a ''silent period'' during which company executives aren't entertaining media inquiries.

In an import alert posted online Jan. 22, the FDA added IPCA to the listed pharmaceutical manufacturers found to have not conformed to good manufacturing practices. The agency authorized district authorities to detain their products—included in a ''Red List''—without physical examination.

Products manufactured at IPCA's plant in Ratlam in central India are included in the alert, although five products–sulfamethoxazole, trimethoprim, ondansetron, hydroxychloroquine sulfate and propranolol hydrochloride—are excluded.

India is the second-largest supplier of generic drugs to the U.S., after Canada. However, a number of Indian drugmakers have faced FDA-imposed import bans in recent years, including big names such as Ranbaxy Laboratories Ltd., RPG Life Sciences Ltd. and Sun Pharmaceutical Industries Ltd., for failure to comply with the good manufacturing practices mandated by U.S. authorities.

On Jan. 27, a House committee in the U.S. released draft legislation under its 21st Century Cures initiative that would provide, under Section 5001 of the draft, ''incentives for manufacturing generic drugs here in the U.S'' (*see related item in the Federal News section*).

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 import alert is available at http://www.accessdata.fda.gov/cms_ia/importalert_189.html.

Personalized Medicine

20 Percent of CDER-Approved Drugs in 2014 Were Personalized Medicines, Group Says

The Personalized Medicine Coalition (PMC) Jan. 28 announced that more than 20 percent of the novel new drugs approved by the Food and Drug Administration's Center for Drug Evaluation and Research (CDER) in 2014 were personalized medicines.

The announcement, which reported the results of the PMC's first full assessment of CDER's novel drug approvals, indicated that CDER approved 41 novel new drugs (NNDs), either new molecular entities or new therapeutic biologics, in 2014, and of these, nine were personalized medicines as defined by the PMC.

PMC's definition of personalized medicines is: those therapeutic products for which the label includes reference to specific biological markers, identified by diagnostic tools, that help guide decisions and/or procedures for the product's use in individual patients.

PMC President Edward Abrahams said in a press statement, ''We applaud FDA's commitment to ensure that patients have access to novel personalized medicines that improve health and can also lower overall costs.''

The coalition describes itself as representing innovators, scientists, patients, providers and payers.

Includes Cancer, Hepatitis Drugs. The nine personalized medicines that CDER approved include treatments for certain cancers and hepatitis.

The nine drugs are:

- Lynparza (olaparib) for treating advanced ovarian cancer—the decision to treat with this product is affected by the BRCA biomarker status in patients;
- Vimizim (elosulfase alfa) for treating Mucopolysaccharidosis Type IV (Morquio Syndrome)—the decision to treat with this product is affected by the type A or B biomarker status in patients;
- Cyrazma (ramucirumab) for treating advanced gastric or gastro-esophageal junction adenocarcinoma or non-small cell lung cancer (NSCLC)—treatment procedures are influenced by the EGFR or ALK biomarker status in patients;
- Zykadia (ceritinib) for treating non–small cell lung cancer (NSCLC)—the decision to treat with this product is affected by the ALK biomarker status in patients;
- Beleodaq (belinostat) for treating peripheral T-cell lymphoma—treatment procedures are influenced by the UGT1A1 biomarker status in patients;
- Cerdelga (eliglustat) for the long-term treatment of Gaucher disease type 1—treatment procedures are influenced by the CYP2D6 biomarker status in patients;

■ Harvoni (ledipasvir and sofosbuvir) for treating chronic hepatitis C infection—the decision to treat with this product is affected by the genotype 1 biomarker status of the viral infection in patients;

■ Viekira Pak (ombitasvir, paritaprevir and ritonavir; dasabuvir) for treating chronic hepatitis C infection—the decision to treat with this product is affected by the genotype 1 biomarker status of the viral infection in patients; and

■ Blincyto (blinatumomab) for treating B-cell precursor acute lymphoblastic leukemia (ALL)—the decision to treat with this product is affected by the Philadelphia chromosome biomarker status in patients.

Integral Part of Clinical Care. Daryl Pritchard, PMC's vice president for science policy, said, ''We have gone from one or two targeted drugs approved each year to a significant amount in 2014. It is clear that personalized medicine is increasingly becoming an integral part of clinical care, and we expect this trend to continue along with greater recognition of the value of personalized medicine by payers and providers.''

The PMC added that, despite these successes, there remain many challenges to advancing personalized medicine, particularly in the areas of scientific discovery, regulatory policy, reimbursement and integration of new technologies into clinical practice.

''The biomedical community continues to address these challenges. With an environment that supports progress in personalized medicine, the approvals we have seen in 2014 will be just the beginning of many advances for years to come,'' the coalition said.

Follows State of the Union. The PMC's announcement followed by eight days President Barack Obama's State of the Union address, in which he urged Congress to spend U.S. taxpayers' money for research in ''precision medicine'' (13 PLIR 107, 1/23/15), a term that the FDA in its October 2013 report ''Paving the Way for Personalized Medicine'' defined as a synonym for personalized medicine.

Some have preferred the term ''precision medicine'' to acknowledge those who insist that the best medicine always is personalized and also because ''precision'' reflects the precise targeting of the molecular underpinnings of a specific disease in each patient.

The PMC applauded the president's focus on personalized medicine in his address and his announcement of a new ''Precision Medicine Initiative.''

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 PMC's announcement is at http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/2014-fda-approvals-personalized-medicine2.pdf. The complete list of CDER's 2014 novel new drug approvals is at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm429247.htm.

Generics

FDA Approves First Generic Version of GERD Drug Esomeprazole

The Food and Drug Administration Jan. 26 said it approved the first generic version of AstraZeneca's heartburn drug Nexium (esomeprazole magnesium delayed-release capsules).

Ivax Pharmaceuticals Inc., a subsidiary of Teva Pharmaceuticals USA, has gained approval to market esomeprazole in 20 mg and 40 mg capsules, the FDA said. Nexium, which is made by AstraZeneca, is a proton pump inhibitor that reduces the amount of acid in the stomach.

Esomeprazole capsules are approved to treat gastroesophageal reflux disease (GERD) in adults and children ages one and older, to reduce the risk of gastric ulcers associated with use of nonsteroidal anti-inflammatory drugs (NSAIDs), to treat the stomach infection Helicobacter pylori along with certain antibiotics and to treat conditions where the stomach makes too much acid, including Zollinger-Ellison syndrome, the agency said.

''Health care professionals and consumers can be assured that these FDA-approved generic drugs have met our rigorous standards,'' Kathleen Uhl, director of the Office of Generic Drugs in the FDA's Center for Drug Evaluation and Research, said in a statement. ''It is important for patients to have access to treatment options for chronic conditions.''

Medication Guide. Generic esomeprazole capsules will be dispensed with a patient medication guide that provides important information about the medication's use and risks, the agency said. The most serious risks are stomach problems, including severe diarrhea, and a warning that people who take multiple daily doses of PPIs for a long period of time may have an increased risk of bone fractures.

The most common side effects reported by those taking Nexium in clinical trials include headache, diarrhea, nausea, flatulence, abdominal pain, sleepiness, constipation and dry mouth, the agency said.

Teva said in a separate statement it's ''preparing to launch the product in the near future.'' The generic drugmaker said Nexium Delayed-Release Capsules, marketed by AstraZeneca, had annual sales of approximately $6 billion in the United States, according to IMS data as of November 2014.

Litigation. The effort to put a generic version of Nexium on the market has been the subject of patent litigation and antitrust litigation.

In 2010, Israel-based Teva Pharmaceutical Industries Ltd. and British drugmaker AstraZeneca announced that they had agreed to settle patent litigation regarding Teva's effort to enter the market with a generic version of Nexium (*AstraZeneca AB v. Ivax Corp.*, D.N.J., No. 05-cv-05553-JAP-TJB, consent judgment filed 1/7/10) (8 PLIR 59, 1/15/10).

Under the parties' agreement on Nexium, Teva received a license from AstraZeneca to enter the U.S. market with its generic esomeprazole delayed-release capsules. According to information in the FDA's Orange Book, this allowed Teva to sell its product before the last of the listed patents on the drug expires.

  PLIR ISSN 1542-9547

According to the Orange Book, the last of the patents expiring on Nexium runs out in May 2020. The Orange Book, formally titled Approved Drug Products with Therapeutic Equivalence Evaluations, lists patents submitted to the agency by branded drug companies as covering a branded drug or its use.

India's Ranbaxy Pharmaceuticals Inc. reached a similar settlement with AstraZeneca over Nexium in 2008 (6 PLIR 474, 4/25/08).

In recent antitrust litigation, AstraZeneca avoided a damages award that might have reached $10 billion after a jury in Massachusetts federal court found the drugmaker's deal with Ranbaxy to delay a generic version of the top-selling heartburn tablet Nexium wasn't unreasonably anticompetitive. That verdict, handed down Dec. 5, 2014, in the U.S. District Court for the District of Massachusetts, followed a six-week trial in which dozens of wholesalers, drugstore chains and a class of possibly hundreds of thousands of individual consumers claimed they were overcharged for the drug for years as a result of the ''pay-for-delay'' deal (12 PLIR 1684, 12/12/14).

Effectiveness Research

Board of Patient Outcomes Group Approves Developing Funding Call for Obesity Studies

The board of a patient outcomes research group Jan. 27 voted to provide funding for two obesity studies.

The Patient-Centered Outcomes Research Institute's (PCORI) board of governors unanimously approved a motion to allow the organization to develop a funding announcement for two obesity studies.

One study will examine the comparative effectiveness with respect to weight loss and weight regain of different bariatric surgical procedures, such as Roux-en-Y gastric bypass, sleeve gastrectomy and adjustable gastric banding.

The other study will examine the comparative effects of alternative antibiotics used during the first two years of life on body mass index and risk of overweight and obesity during the third to fifth years of life.

A single funding announcement will be developed for the two study topics. Total costs for both studies isn't to exceed $9 million over a two-year period, according to a presentation made to the board by Rachael Fleurence, PCORI's program director for science.

PCORI's funding announcement for the obesity studies is expected in February and applications will be due in the spring, Fleurence said in her presentation. Final selection of the award will take place this summer, she said.

Next Meeting. The decision to approve the funding announcement for the obesity studies occurred during a previously scheduled web conference meeting of the PCORI board. The next meeting of the board is scheduled for Feb. 24 and will be held via webinar and teleconference.

PCORI is an independent, nonprofit organization created under the Affordable Care Act to conduct research for patients and caregivers on the best health-care outcomes.

Design of Studies. Both studies are demonstration projects for PCORI's PCORnet, Fleurence said. PCORI created PCORnet to serve as a large, highly representative, national network for conducting clinical outcomes research. The network seeks to transform clinical research by engaging patients, care providers and health systems in collaborative partnerships to improve health care and advance medical knowledge.

Fleurence told the board that a significant objective of demonstration projects is to report on the testing of the emergent PCORnet data infrastructure.

In addition, the studies will employ an observational design and will test the technical and operational aspects of PCORnet's distributed research network, Fleurence said.

Separate Action. In a separate action, the board also approved the charter for a communication and dissemination research (CDR) advisory panel.

In a presentation to the board, Jean Slutsky, PCORI's chief engagement and dissemination officer, said the advisory panel on CDR will:

- identify and prioritize critical research questions for possible funding initiatives under PCORI's Communication and Dissemination Research program; and
- provide ongoing feedback and advice on evaluating and disseminating the research conducted under this program.

The Communication and Dissemination Program at PCORI seeks to fund studies that investigate the comparative effectiveness of communication and dissemination strategies to promote the use of health and health-care comparative effectiveness research evidence by patients, caregivers and clinicians, Slutsky said.

BY MICHAEL D. WILLIAMSON

To contact the reporter on this story: Michael D. Williamson in Washington at mwilliamson@bna.com

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

Information about the PCORI board of governors meeting is at http://www.pcori.org/events/2015/board-governors-meeting-1.

Materials presented to the board are at http://www.pcori.org/sites/default/files/PCORI-Board-Meeting-Slide-Presentation-012715.pdf.

The charter for the CDR advisory panel is at http://www.pcori.org/sites/default/files/PCORI-Advisory-Panel-CDR-Charter.pdf.

E-Prescribing

Standards Group Approved to Certify Apps For e-Prescribing of Controlled Substances

The Electronic Healthcare Network Accreditation Commission (EHNAC), a nonprofit health IT standards development group, has been approved by the Drug Enforcement Administration to certify applications used to electronically prescribe controlled substances.

Physicians increasingly are using electronic health records enabled to electronically prescribe and are fuel-

ing demand for e-prescribing networks and applications that are DEA-approved for transmitting prescriptions for controlled substances, Lee Barrett, executive director of EHNAC, told Bloomberg BNA Jan. 28. He said EHNAC hopes to offer its certification services to health information exchange organizations and EHR vendor networks offering products that are capable of e-prescribing controlled substances.

''E-prescribing is very much part of the meaningful use program and many states are legislating the use of e-prescribing to reduce error rates and get patients their prescriptions faster,'' Barrett said. ''The capability is there and I think more and more we're going to see physicians and physician practices using it and demanding it.''

EHNAC offers two certification programs for technology developers handling e-prescribing of controlled substances, the group said in a release. The programs evaluate pharmacy and prescribing companies that offer applications supporting electronic prescription of controlled substances.

The DEA requires that any e-prescribing or pharmacy application used to transmit prescriptions for controlled substances be certified by a DEA-approved certification body, the agency said in its database of certification bodies. These certification bodies audit the applications for compliance with federal privacy and security requirements for e-prescribing of controlled substances.

Five organizations other than EHNAC have been approved to certify e-prescribing applications: InfoGard Labs of San Luis Obispo, Calif.; the Drummond Group of Austin, Texas; iBeta of Aurora, Colo.; Global Sage Group of Salem, N.H.; and ComplySmart of Scottsdale, Ariz.

While Barrett said he is optimistic about growing demand for e-prescribing of controlled substances from physicians, a November 2014 study found that federal and state regulatory barriers have kept health-care providers from adopting electronic prescribing technologies for controlled substances at the same rate as pharmacists.

In New York, health-care groups urged the state Jan. 22 to delay implementation e-prescribing requirements because of worries that EHRs aren't yet certified as meeting DEA requirements for e-prescribing controlled substances (*see related item in the State News section*).

BY ALEX RUOFF

To contact the reporter on this story: Alex Ruoff in Washington at aruoff@bna.com

To contact the editor responsible for this story: Kendra Casey Plank at kcasey@bna.com

New Products

Basilea CEO Sees Blockbuster Potential for Antifungal Drug

Basilea Pharmaceutica AG, an antibiotic producer with a market value exceeding $1 billion, says it sees a chance for its drug isavuconazole to reach sales of about $1 billion if it gets regulatory approval in the U.S. and Europe.

''There is a significant medical need for isavuconazole due to limited treatment options,'' Chief Executive Officer Ronald Scott said in an interview Jan. 23. ''We don't provide forecasts for our drug sales,'' he said, adding that he sees Pfizer Inc.'s voriconazole as a benchmark.

''We will need to see what's achievable, certainly it has the potential for Basilea to become a significant asset.'' When asked if $1 billion in sales was achievable, he said it could be more than that or less than that.

Pfizer's voriconazole is an antifungal treatment that generated $775 million in sales in 2013 and received initial Food and Drug Administration approval in 2002.

Scott said Basilea won't become profitable before 2016.

The remarks by Basilea's CEO come after an advisory committee to the Food and Drug Administration recommended the treatment for approval to treat two fungal infections—aspergillosis and mucormycosis—that predominately occur in patients with a weak immune system. A final FDA decision will be made in March.

''Usually the FDA follows those recommendations,'' Bob Pooler, an independent analyst at valuationLAB, said by phone.

He doesn't have a rating on the stock and said that $1 billion in annual sales could be a possible target.

Astellas Pharma. Basilea's partner Astellas Pharma Inc. presented the data to the FDA and intends to market the drug in the U.S.

Basilea, which is based in Basel, Switzerland, may receive up to 374 million Swiss francs ($426 million) depending on regulatory approvals in the U.S. and future sales, Scott said. So far it has received 12 million Swiss francs in milestone payments.

The company also is seeking approval for the drug in Europe; it expects a final decision in the fourth quarter.

Basilea received approval for an antibiotic called ceftobiprole in Europe in 2013. Scott didn't provide sales figures, saying it is too early yet as hospitals need six to 12 months to test resistance strains.

BY JAN-HENRIK FORSTER

To contact the reporter on this story: Jan-Henrik Förster in Zurich at jforster20@bloomberg.net

To contact the editors responsible for this story: Mariajose Vera at mvera1@bloomberg.net, James Kraus, Jim Silver

More information about the Jan. 22 meeting of the FDA's Anti-Infective Drugs Advisory Committee is at http://www.fda.gov/AdvisoryCommittees/Calendar/ucm424436.htm.

New Products

FDA Panel Set to Meet in March On Treatment for Double Chins

People who suffer from an unsightly double chin may not need to contort their head, neck and face into funny positions to try to work off the extra roll if U.S. regulators sign off on a new drug.

Kythera Biopharmaceuticals Inc.'s experimental drug is injected into fat under the chin. The drug is a version

of deoxycholic acid, a molecule that occurs naturally in the body to help destroy fat.

The injection still isn't approved by the Food and Drug Administration. A panel of outside advisers and academics will discuss whether the FDA should approve the first-of-its-kind treatment on March 9. The agency doesn't have to follow the panel's recommendation.

The FDA's Dermatologic and Ophthalmic Drugs Advisory Committee will consider the new drug application March 9, according to a notice set for Jan. 26 Federal Register publication.

Kythera, based in Westlake Village, Calif., says the drug, ATX-101, contours the chin without affecting surrounding tissue. Injectable drugs like Allergan Inc.'s Botox and dermal fillers aren't approved to fix fat and loose skin under the chin, making ATX-101 potentially the first injection for the area to hit the market if approved.

Chin augmentations were the fastest-growing category of plastic surgery in the U.S. in 2011, according to an analysis by the American Society of Plastic Surgeons. There were 20,680 chin procedures in 2011, and they grew more than breast augmentation, Botox and liposuction treatments combined, according to the society.

The FDA is scheduled to rule on the drug by May 13. It would be Kythera's first product for sale, and could generate $505 million in sales in 2020, according to data compiled by Bloomberg.

The drug has been tested on 1,600 patients in clinical trials, more than 90 percent of whom maintained a meaningful reduction of fat after two years, Kythera said on its website.

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: Crayton Harrison at tharrison5@bloomberg.net, Drew Armstrong, John Lear

Generics

FDA Approves Generic Version Of Lamictal Orally Disintegrating Tablets

Impax Laboratories Inc. Jan. 26 said the Food and Drug Administration has approved its generic version of GlaxoSmithKline's Lamictal (lamotrigine) orally disintegrating 25 mg, 50 mg, 100 mg and 200 mg tablets in blister packaging.

Lamictal ODT is indicated for treating epilepsy and bipolar disorder.

Impax, which is based in Hayward, Calif., said it will commercialize this product promptly through Global Pharmaceuticals, its generic division.

In July 2014, Impax acquired from Actavis the approved abbreviated new drug application (ANDA) for generic lamotrigine ODT packaged in bottles under an asset purchase agreement with Actavis (12 PLIR 964, 7/4/14).

Impax said it believes its ANDA was the first substantially complete ANDA with a paragraph IV certification and expects to be entitled to 180 days of market exclusivity. Under the Hatch-Waxman Act, the first company to file an ANDA with a paragraph IV certification challenging the branded drug's patent is eligible for 180 days of exclusivity.

According to the consulting firm IMS Health, the U.S. sales of Lamictal ODT were about $56 million for the 12 months ended November 2014.

Approvals

FDA Approves New Strength Of Novo Nordisk's Norditropin FlexPro

Novo Nordisk Jan. 26 said the Food and Drug Administration has approved Norditropin (somatropin [rDNA origin] injection) FlexPro 30 mg/3.0 mL, a prefilled injection pen for patients with growth hormone-related disorders.

The company said it plans to make Norditropin FlexPro 30 mg/3.0 mL available by April.

The FlexPro 30 mg/3.0 milliliter device complements the Norditropin FlexPro products available in 5 mg/1.5 mL, 10 mg/1.5 mL and 15 mg/1.5 mL pens, the company said.

Having four strengths of Norditropin FlexPro enhances physicians' ability to better address the unique needs of appropriate patients, Novo Nordisk said. Each Norditropin FlexPro pen is prefilled with Norditropin, and is color coded to differentiate the various strengths.

''Novo Nordisk is committed to advancing growth hormone delivery devices with patients in mind,'' Eddie Williams, Novo Nordisk senior vice president of biopharmaceuticals, said in a statement. ''This approval marks another option for patients who may need higher doses of treatment.''

Novo Nordisk is based in Denmark.

Orphan Drugs

FDA Grants Orphan Status To Drugs for Pancreatic, Lung Cancer

The Food and Drug Administration recently announced on its website that it has granted orphan drug designation to three products, two of which treat pancreatic cancer and one that treats small cell lung cancer.

The orphan designation gives special incentives to sponsors, including tax credits, research and development grant funding, reduced user fees and seven years of marketing exclusivity upon approval.

On Jan. 21, the FDA granted orphan status to Golden Biotechnology Corp.'s antroquinonol for the treatment of pancreatic cancer. Golden Biotechnology is based in Taiwan.

Also, on Jan. 26, the agency granted orphan designations to OncoMed Pharmaceuticals Inc.'s tarextumab for the treatment of small cell lung cancer and Incyte Corp.'s pancreatic cancer drug. The generic name of Incyte Corp.'s product is 2-(3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-l-yl)-1-(1-(3-fluoro-2-

(trifluoromethyl)isonicotinoyl)piperidin-4-yl)azetidin-3-yl)acetonitrile adipate.

OncoMed is based in Redwood City, Calif., and Incyte is based in Wilmington, Del.

Pharmacy Benefits

Another Insurer Limits Patients' Expenses for HIV/AIDS Drugs in Florida

A fourth health insurer has agreed to limit the out-of-pocket expenses Florida consumers pay for HIV and AIDS prescriptions, joining three other insurers who are named in a federal complaint alleging discriminatory coverage policies.

Meanwhile, health-care advocates are pushing for federal guidelines and enforcement of nondiscrimination rules in the Affordable Care Act, rather than leaving the job to state regulators.

Preferred Medical Plan Inc. agreed in a two-paragraph letter to the Florida Office of Insurance Regulation that it will limit monthly out-of-pocket costs to $200 for each of the drugs Atripla, Complera, Stribild and Fuzeon. The letter, dated Jan. 14, also notes that the Florida OIR hasn't found that Preferred is guilty of discriminatory practices related to its coverage offerings through the federal insurance exchange.

Preferred is one of four insurers—along with Cigna, Coventry Health Care and Humana—that were named in a May 29, 2014, complaint to the U.S. Department of Health and Human Services. The organizations that filed the complaint, the National Health Law Program and the AIDS Institute, asked the HHS to investigate whether the insurers' coverage practices for HIV and AIDS drugs in Florida were discriminatory.

According to the complaint, the companies placed all HIV and AIDS drugs, including generic versions, on a tier 5 or specialty tier of prescription drugs, which resulted in consumers having to pay coinsurance of 40 percent to 50 percent, in some cases after meeting a deductible as high as $2,750.

Federal Complaint Still Pending. The HHS hasn't publicly responded to the complaint, but each of the four insurers has reached an agreement with the Florida OIR to adjust the pricing of these drugs, at least temporarily.

Preferred's letter to the state OIR doesn't specify the time period for which it is committing to the $200-a-month limit. The other three insurers committed to steps that would limit consumers' out-of-pocket costs during the 2015 plan year and said they would work with the Florida OIR to devise a viable long-term coverage scheme.

Urging Federal Standards, Enforcement. Wayne Turner, staff attorney at the National Health Law Program, told Bloomberg BNA Jan. 22 the agreements don't resolve the federal complaint, and his organization still is advocating for strong federal enforcement of the Affordable Care Act's nondiscrimination provisions.

Concerns about discrimination stretch beyond HIV drugs to other types of expensive therapies such as those for cancer and multiple sclerosis, Turner previously told Bloomberg BNA.

The National Health Law Program sent a follow-up letter to HHS Jan. 8, urging the department to take action without delay on its May 2014 complaint.

''We want to see clear standards articulated by the feds on what constitutes a discriminatory plan design, and we want to see ongoing monitoring and enforcement,'' Turner said.

HHS has made some ''steps in the right direction,'' he said, by including language regarding discriminatory policies in its Draft 2016 Letter to Issuers and in the preamble of a proposed federal rule, called the Notice of Benefits and Payment Parameters for 2016 (CMS–9944–P, RIN 0938–AS19), published in the Federal Register Nov. 26, 2014 (79 Fed. Reg. 70,674).

BY CHRIS MARR

To contact the reporter on this story: Chris Marr in Atlanta at cmarr@bna.com

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

---

Preferred Medical's letter is at http://op.bna.com/hl.nsf/r?Open=bbrk-9szty8.

The National Health Law Program's Jan. 8 letter is at http://www.healthlaw.org/publications/browse-all-publications/Letter-to-HHSOfficeofCivilRights#.VMFg_vkRJps.

The HHS's Draft Letter to Issuers for 2016 is at http://www.cms.gov/CCIIO/Resources/Regulations-and-Guidance/Downloads/2016DraftLettertoIssuers12-19-2014.pdf.

The HHS's proposed rule from November 2014 is at http://www.gpo.gov/fdsys/pkg/FR-2014-11-26/pdf/2014-27858.pdf.

sNDAs

Amgen, Onyx Submit sNDA For Multiple Myeloma Drug Kyprolis

Amgen Inc. and its subsidiary Onyx Pharmaceuticals Inc. Jan. 27 announced the submission of a supplemental new drug application (sNDA) to the Food and Drug Administration for Kyprolis (carfilzomib) for injection.

The companies are seeking approval of the drug for the treatment of patients with relapsed multiple myeloma who have received at least one prior therapy. Multiple myeloma is a hematologic cancer and results from an abnormality of plasma cells.

The sNDA is designed to support the conversion of the drug's accelerated approval to full approval and expand the current approved indication, the companies said. In July 2012, the FDA granted accelerated approval to Kyprolis for treating multiple myeloma patients who have receive at least two prior therapies (10 PLIR 978, 7/27/12).

The FDA's accelerated approval program allows the agency to approve a drug to treat a serious disease based on clinical data showing the drug has an effect on an endpoint that is reasonably likely to predict a clinical benefit for patients.

Amgen is based in Thousand Oaks, Calif. and Onyx is based in South San Francisco.

   ISSN 1542-9547

Approvals

FDA Approves NPS's Natpara For Treating Hypoparathyroidism

The Food and Drug Administration Jan. 23 approved Natpara (parathyroid horomone) to control hypocalcemia (low blood calcium levels) in patients with hypoparathyroidism.

Hypoparathyroidism occurs when the body secretes abnormally low levels of parathyroid hormone, which helps regulate calcium and phosphorus levels in the body, the agency said. Patients with hypoparathyroidism can experience numbness, tingling, muscle twitching, spasms or cramps, abnormal heart rhythm and seizures as a consequence of low blood calcium levels.

Natpara, a hormonal injection administered once daily, helps to regulate the body's calcium levels, the agency said.

Natpara is manufactured by Bedminster, N.J.-based NPS Pharmaceuticals Inc. The company said in a statement that Natpara is expected to be available in the second quarter of 2015.

The FDA has granted orphan drug status for Natpara for the treatment of hypoparathyroidism. The orphan designation is granted to products intended for treating a rare disease or condition, affecting fewer than 200,000 patients in the U.S. It gives special incentives to sponsors, including tax credits, research and development grant funding, reduced user fees and seven years of marketing exclusivity upon approval.

''People with hypoparathyroidism have limited treatment options and face challenging symptoms that can severely impact their quality of life,'' said Jean-Marc Guettier, director of the Division of Metabolism and Endocrinology Products in the FDA's Center for Drug Evaluation and Research. ''This product offers an alternative to patients whose calcium levels cannot be controlled on calcium supplementation and active forms of vitamin D.''

Boxed Warning. Natpara carries a boxed warning that bone cancer (osteosarcoma) has been observed in rat studies with Natpara, the FDA said. It is unknown whether Natpara causes osteosarcoma in humans, but because of a potential risk of osteosarcoma, Natpara is only recommended for use in patients whose hypocalcemia can't be controlled on calcium supplementation and active forms of vitamin D, and for whom the potential benefits are considered to outweigh this potential risk.

Natpara is only available through a restricted program under a risk evaluation and mitigation strategy (REMS), the agency said.

The most common side effects observed in Natpara-treated participants were sensations of tingling, tickling, pricking or burning of the skin (paraesthesia); low blood calcium; headache; high blood calcium; and nausea, the FDA said.

In September 2014, an FDA advisory panel voted to recommend approval of Natpara (12 PLIR 1321, 9/19/14). The company submitted the biologics license application in October 2013 (11 PLIR 1322, 11/1/13), and the FDA accepted the BLA in January 2014 (12 PLIR 51, 1/10/14).

Drug Safety

Hospira Recalls One Lot of Sodium Chloride Injection Due to Human Hair

The Food and Drug Administration Jan. 23 announced on its website that Hospira Inc. has voluntarily recalled one lot of 0.9 percent sodium chloride injection, 250 milliliter, due to one confirmed customer report of particulate matter in a single unit.

Sodium chloride injection is intravenously administered and indicated as a source of water and electrolytes.

The company has identified the particulate as a human hair, sealed in the bag at the additive port area, the agency said. To date, Hospira hasn't received any reports of any adverse events associated with this issue for this lot.

Injected particulate material may result in local inflammation, phlebitis and/or low-level allergic response, the agency said. Capillaries may become occluded. Patients with preexisting condition of trauma or other medical condition that adversely affects the microvascular blood supply are at an increased risk.

Affected Lot. The affected lot was distributed nationwide from September 2014 through November 2014, the agency said. Anyone with an existing inventory of the recalled lot should stop use and distribution and quarantine the product immediately.

Hospira has notified its direct customers via a recall letter and is arranging for impacted product to be returned, the FDA said. Health-care professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Adverse Event Reporting Program.

In September 2014, Hospira also recalled one lot of heparin sodium chloride injection due to a confirmed customer report of human hair in the product (12 PLIR 1322, 9/19/14). Hospira has recalled several products over the past several years. For instance, on April 17, 2014, the company recalled seven lots of propofol injectable emulsion, an anesthetic, due to a glass defect on the interior neck of the vial (12 PLIR 608, 4/25/14). And on Dec. 24, 2013, the company recalled one lot of lidocaine HCl injection, USP, 2 percent, 5-milliliter single-dose vial due to particulate matter (12 PLIR 26, 1/3/14).

Hospira is based in Lake Forest, Ill.

More information is available at http://www.fda.gov/Safety/Recalls/ucm430929.htm.

Approvals

FDA Approves Second Manufacturing Facility for Octagam 10 Percent

Octapharma USA Jan. 26 announced that the Food and Drug Administration has approved its manufacturing facility in Vienna, Austria, for the production of Octagam 10 percent [Immune Globulin Intravenous (Human) 10 percent (100 mg/mL) Liquid Preparation].

Octagam 10 percent became available in the U.S. during October 2014, the company said. The FDA approved Octagam 10 percent for treating adults with chronic immune thrombocytopenic purpura (ITP) in July 2014 (12 PLIR 1039, 7/18/14).

The company said Octagam 10 percent for the U.S. market can now be manufactured at FDA-licensed facilities in both Stockholm and Vienna.

''The FDA approval of Octapharma's Vienna manufacturing site for Octagam 10% is great news for patients, as it will help facilitate product availability and enhances production flexibility,'' Flemming Nielsen, president of Octapharma USA, said in a statement. ''Octapharma owns six manufacturing facilities internationally, which all utilize the latest technology and strict quality control processes. Octapharma is committed to providing access to life-saving products, while continuing to focus on patient tolerability and safety.''

Octapharma USA, of Hoboken, N.J., is the U.S. division of Octapharma AG, a Swiss-based manufacturer of plasma products.

  PLIR ISSN 1542-9547

International News

India

Gilead Expands Generic Sovaldi Pact To Add Investigational Combination Pill

Gilead Sciences Inc. said it aims to launch Sovaldi, its blockbuster hepatitis C drug, in India by June while expanding the reach of a generic licensing agreement with Indian drugmakers to include an investigational combination pill.

The pill, which combines sofosbuvir, the chemical name for Sovaldi, with GS-5816, a compound in advanced clinical trials in the U.S., could treat six genotypes of hepatitis C if approved by regulators. Gilead will ask India's health ministry to waive clinical trials and expedite approval for the compound, which eliminates the need for costly genotype tests, Gregg Alton, an executive vice president at the Foster City, Calif.-based company, said in a phone interview.

''In many of the resource limited environments around the world, it's very difficult, and not feasible to do genotyping,'' Alton said. ''It's an expensive diagnostic that's simply not available many places.''

Gilead's Sovaldi, which will launch at $900 for a 12-week regimen in India, has drawn criticism from patient advocates in developing countries, who say that its generic licensing agreement doesn't cover enough of the middle-income countries with high hepatitis C burdens. The investigational fixed dose combination pill that's been added to the licenses could be a more cost effective way of treating hepatitis C in poor countries, Alton said.

Gilead Sciences has licensed eight India-based generic drugmakers to bring cheaper versions of Sovaldi to 91 mainly low-income countries, including India, Indonesia, Cambodia and many nations in Africa.

The eight manufacturers that hold the license are Biocon Ltd., Cadila Healthcare Ltd., Cipla Ltd., Hetero Labs Ltd., Mylan Laboratories Ltd., Ranbaxy Laboratories Ltd., Sequent Scientific Ltd. and Strides Arcolab Ltd.

India's drug regulator approved Gilead's Sovaldi on Jan. 13, the same week that the nation's patent office rejected claims from Gilead covering an active metabolite of the drug (13 PLIR 118, 1/23/15).

BY KETAKI GOKHALE

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

To contact the editor responsible for this story: Anjali Cordeiro at acordeiro2@bloomberg.net

Canada

Canadian Federal Court Supports Eli Lilly's Effort to Block Generic Cialis

The Federal Court of Canada has blocked Mylan Pharmaceuticals from producing a generic version of Eli Lilly Canada Inc.'s impotence drug Cialis until the patent expires (*Eli Lilly Canada, Inc. v. Mylan Pharmaceuticals*, Fed. Ct., No. T-296-13, 1/7/15).

The court rejected Mylan's claims that Lilly's patent for tadalafil is invalid due to lack of utility and double patenting based on obviousness. It also issued a prohibition order under the Patented Medicines (Notice of Compliance) Regulations prohibiting Health Canada from approving Mylan's generic product until Canadian Patent No. 2, 226,784 (the '784 patent) expires on July 11, 2016.

''I am satisfied on the evidence that Lilly's discovery was truly inventive, and that it has met its legal burden to establish the validity of the '784 Patent on a balance of probabilities,'' Justice Yves de Montigny said in the Jan. 7 ruling, made public Jan. 19. The ruling awarded Eli Lilly its costs.

A Lilly spokesman Jan. 22 said that while the company's policy is not to comment on court rulings in detail, it was pleased with the court's decision to grant a prohibition order. ''We will continue to take every appropriate step to protect our intellectual property,'' the spokesman told Bloomberg BNA.

Mylan Pharmaceuticals didn't respond to a Jan. 21 request from Bloomberg BNA for comment on the ruling and/or whether it planned to appeal to the Federal Court of Appeal.

Lilly filed the '784 patent on July 11, 1996, with a priority date of July 14, 1995, for the use of certain tetracyclic derivatives to treat impotence.

On Dec. 21, 2012, Mylan filed a Notice of Allegation that its generic product wouldn't infringe the patent and that some of the claims on which the patent were based are invalid.

Ruling Rejects Mylan's Allegations. The Federal Court rejected Mylan's allegation that Lilly's patent for tadalafil was invalid because the promise of the patent wasn't soundly predicted. The promise of the '784 patent was treatment of erectile dysfunction with tadalafil or 3-methyl tadalafil, not Mylan's more detailed construction that included oral administration and acceptable side effects, the ruling said.

Only after citing the prevalence of erectile dysfunction and existing therapies does Lilly's patent application refer to administration of the compounds orally, it said. An orally administered drug was seen at the time as the ''Holy Grail'' of erectile dysfunction therapy, but that only made it a ''preferred feature'' of the invention, not the promise of the entire patent, it said.

Mylan incorrectly argued that the patent also promised efficacy in the absence of undue side effects, it said. ''While an inventor may be held to a promise when called upon to prove utility, that promise must have been clear and explicit,'' it said. ''The mere mention of the deleterious effects of existing therapies does not amount to a promise that the compounds will obviate such side effects. Indeed, the '784 Patent is clearly drafted in terms of advantages as opposed to promise.''

No 'Evergreening.' The court also rejected Mylan's arguments that Lilly's patent was invalid on the basis of obviousness-type double patenting. Mylan argued that the patent discloses nothing new as it was previously known, including in an earlier Lilly patent, that compounds like tadalafil could be used to treat erectile dysfunction, it said.

But the use of tadalafil, particularly via oral administration, wouldn't have been obvious to a person skilled in the art at the time the '784 patent application was filed, and it certainly wasn't included in the earlier patent, it said. On that basis, the '784 patent didn't represent an ''evergreening'' of the earlier patent, it said.

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 ruling is available at http://decisions.fct-cf.gc.ca/fc-cf/decisions/en/item/100465/index.do.

United Kingdom

U.K.'s NICE Should Oversee Apps In Mobile Health, Digital Specialist Says

The U.K.'s National Institute for Health and Care Excellence should widen its scope to include the oversight of mobile health apps, the president of the Telemedicine & eHealth section of the Royal Society of Medicine said Jan. 22.

NICE could become responsible for evaluating mHealth apps as the capability for these to replace some drugs, particularly for mental health-related conditions, continues to grow, according to Charles Lowe.

''Mhealth apps can be good to deal with'' conditions like ''anxiety and depression and offer some pain relief but because NICE is not involved in this area, there is no proper mechanism for prescribing them,'' said Lowe, who also is managing director of the Digital Health & Care Alliance.

Evidence Gathering. Lowe referred to how NICE's clinical guidelines are systematically developed recommendations based on the best available evidence.

NICE also is ''well known to pharmaceutical firms'' so ''if and when they take on mobile apps'' the medical industry ''will have much greater confidence that those apps they recommend are efficacious.''

NICE, a body within the Department of Health, is reviewing responses to a triennial review on its role and performance that includes extending its role, as a provider of national guidance and advice to improve health and social care, to mHealth apps.

Lowe spoke at a session on the challenges that mHealth apps pose for the pharma industry during SMi's seventh annual Social Media in the Pharmaceutical Industry conference held Jan. 21-22 in London.

More Harmonization in EU? Commenting more widely on oversight of mobile apps in the European Union, Lowe said that ''currently, every single country in the EU has a different variant'' on the rules governing the use of medical devices which could include mobile apps.

The prospect of a new EU medical devices regulation by 2017 ''will help,'' he said, referring to the process initiated by the European Commission in 2012 to introduce the most sweeping changes to medical device regulation in Europe since the 1990s.

Lowe emphasized that even apps that aren't considered medical devices are subject to rules under the EU's data privacy and consumer protection legislation.

For instance, under the EU legal framework on the protection of personal data, which is being revised, pharmaceutical companies could be liable for any personal data available in apps that a third party decides to use, whether to share or to sell.

''If you pass data in an anonymized form and at a later date someone deanonymizes, you can be fined up to 3 percent of your organization's turnover,'' or sales, under current EU proposals, he said.

Regarding consumer protection legislation, the Misleading and Comparative Advertising Directive 2006/114/EC requires that any product or service making a health or well-being claim must be able to support that claim with good evidence.

Potential to Increase Rx Sales? Reviewing the advantages of mobile apps for pharmaceutical companies, Lowe said they are ''particularly good at assisting medical adherence'' because according to the Academy of Chemical Sciences, only about half of medications that are prescribed to patients are taken. ''Apps, at least in the short term, could improve this very significantly,'' he said.

As an example, Lowe said that he was recently ''talking to a major drug company who told me that their app drove up usage of a particular diabetes drug from 50 to over 80 percent.'' Although ''this rise wouldn't last forever, it clearly is worth having as you get more drug sales. It also means the patient will live a little longer so you can carry on selling to them.''

On the negative side, the apps could prove detrimental to drug companies in that in some cases, by taking more responsibility for their health, a patient can improve their condition and rely less on drugs, Lowe said.

BY ALI QASSIM

To contact the reporter on this story: Ali Qassim in London at correspondents@bna.com

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

  PLIR ISSN 1542-9547

European Union

Pharmaceutical Firms Can Build Trust Through Twitter Conferences, Speaker Says

Online Twitter conferences, or tweet chats, can be an effective way for pharmaceutical firms to build trust with health-care providers and patients, a social media specialist at a major German pharmaceutical firm said Jan. 21 at a London conference.

As pharmaceutical firms in the European Union face strict legal limits on how to promote their brands and products, engaging with their audiences through moderated online discussions is one important way to raise their profiles, said Jaclyn Fonteyne, social media specialist for Boehringer Ingelheim. Fonteyne said a tweet chat is a virtual discussion on Twitter linked by a predefined hashtag to discuss disease awareness topics.

''Even if companies cannot measure the value of these tweet chats in traditional terms of return of investment, they can measure a return on engagement,'' she said.

Increased Engagement. Fonteyne said when a company holds a tweet chat, it can track and measure the number of participants involved, the number of tweets and retweets generated, the amount of followers, the content of discussions and the main contributors to the discussions.

Boehringer was the first company in the pharmaceutical industry to use tweet chats to encourage awareness and engagement within the medical community around a specific disease, she said.

When the German firm held its first real-time tweet chat in 2013 around chronic obstructive pulmonary disease during the European Respiratory Society Congress, it gained 1,200 new followers.

In a separate session at the Social Media in the Pharmaceutical Industry Conference, Silja Chouquet, owner of social media consultancy Whydot Pharma, said managing directors of pharmaceutical companies traditionally have been too wary about the power of social media because they wrongly assume they cannot quantify the influence of a tool like Twitter.

She said, however, that pharmaceutical companies are waking up to the potential. For example, during the annual conference of the American Society of Clinical Oncology, the number of tweets by participants has quadrupled from 10,000 in 2012 to 40,000 in two years.

Brand Attachment. ''In no other industry do you have such a strong attachment to a brand, so we should care more about how to drive a brand in the right direction, and that's what tweet chats can do,'' she said.

Chouquet added that the rise of social media has led pharmaceutical companies to have unprecedented access to data about the views of health-care professionals and patients.

BY ALI QASSIM

To contact the reporter on this story: Ali Qassim in London at correspondents@bna.com

To contact the editor responsible for this story: Michael O. Loatman at mloatman@bna.com

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 January 15 - 22, 2015.

Recent Hatch-Waxman Filings

Matter	NDA Holder / Licensee(s)	ANDA Filer	Patent(s)	Brand Name
Boehringer Ingelheim Pharma GmbH & Co. v. Mylan Pharmaceuticals Inc., No. 1:15-cv-00010, Complaint (N.D. W. Va. Jan. 21, 2015)	Boehringer Ingelheim Pharma GmbH & Co.; Boehringer Ingelheim Pharma GmbH; Boehringer Ingelheim Pharmaceuticals Inc.	Mylan Pharmaceuticals Inc.	U.S. Patent No. 6,087,380 (dabigatran)	PRADAXA (atrial fibrillation)
Teva Pharmaceuticals USA v. AstraZeneca Pharmaceuticals LP, No. 1:15-cv-00050, Complaint (D. Del. Jan. 19, 2015)	Teva Pharmaceuticals USA	AstraZeneca Pharmaceuticals LP; Amylin Pharmaceuticals LLC	U.S. Patent Nos. 7,297,761; 7,741,269 (exenatide)	BYETTA (type 2 diabetes)
Shionogi & Co. v. Aurobindo Pharma Ltd., No. 3:15-cv-00319, Complaint (D.N.J. Jan. 16, 2015)	Shionogi & Co.; Shionogi Inc.	Aurobindo Pharma Ltd.; Aurobindo Pharma USA Inc.	U.S. Patent No. 8,247,402 (doripenem)	DORIBAX (infection)
Supernus Pharamceuticals Inc. v. Par Pharmaceutical Cos., No. 2:15-cv-00326, Complaint (D.N.J. Jan. 16, 2015)	Supernus Pharamceuticals Inc.	Par Pharmaceutical Cos.; Par Pharmaceutical Inc.	U.S. Patent Nos. 8,298,576; 8,298,580; 8,663,683; 8,877,248 (topiramate)	TROKENDI XR (epilepsy)
Supernus Pharamceuticals Inc. v. TWi Pharmaceuticals Inc., No. 1:15-cv-00369, Complaint (D.N.J. Jan.	Supernus Pharamceuticals Inc.	TWi Pharmaceuticals Inc.; TWi International LLC	U.S. Patent Nos. 7,722,898; 7,910,131; 8,617,600; 8,821,930 (oxcarbazepine)	OXTELLAR XR (partial seizures)

  PLIR ISSN 1542-9547

Recent Hatch-Waxman Filings – Continued

Matter	NDA Holder / Licensee(s)	ANDA Filer	Patent(s)	Brand Name
16, 2015)				
Boehringer Ingelheim Pharma GmbH & Co. v. Teva Pharmaceuticals USA Inc., No. 1:15-cv-00048, Complaint (D. Del. Jan. 16, 2015)	Boehringer Ingelheim Pharma GmbH & Co.; Boehringer Ingelheim Pharma GmbH; Boehringer Ingelheim Pharmaceuticals Inc.	Teva Pharmaceuticals USA Inc.; Teva Pharmaceutical Industries Ltd.	U.S. Patent No. 6,087,380 (dabigatran)	PRADAXA (atrial fibrillation)
Sanofi-Aventis US LLC v. Breckenridge Pharmaceutical Inc., No. 9:15-cv-80056, Complaint (S.D. Fla. Jan. 15, 2015)	Sanofi-Aventis US LLC; Aventis Pharma SA; Sanofi	Breckenridge Pharmaceutical Inc.	U.S. Patent Nos. 5,847,170; 7,241,907 (cabazitaxel)	JEVTANA KIT (prostate cancer)
Senju Pharmaceutical Co. v. Paddock Laboratories LLC, No. 1:15-cv-00337, Complaint (D.N.J. Jan. 16, 2015)	Senju Pharmaceutical Co.; Bausch & Lomb Inc.; Bausch & Lomb Pharma Holdings Corp.	Paddock Laboratories LLC; L. Perrigo Co.; Perrigo Co.	U.S. Patent Nos. 8,129,431; 8,669,290; 8,754,131; 8,871,813; 8,927,606 (bromfenac)	PROLENSA (eye inflammation)
Senju Pharmaceutical Co. v. Apotex Inc., No. 1:15-cv-00336, Complaint (D.N.J. Jan. 16, 2015)	Senju Pharmaceutical Co.; Bausch & Lomb Inc.; Bausch & Lomb Pharma Holdings Corp.	Apotex Inc.; Apotex Corp.	U.S. Patent Nos. 8,129,431; 8,669,290; 8,754,131; 8,871,813; 8,927,606 (bromfenac)	PROLENSA (eye inflammation)
Senju Pharmaceutical Co. v. Lupin Ltd., No. 1:15-cv-00335, Complaint (D.N.J. Jan. 16, 2015)	Senju Pharmaceutical Co.; Bausch & Lomb Inc.; Bausch & Lomb Pharma Holdings Corp.	Lupin Ltd.; Lupin Pharmaceuticals Inc.	U.S. Patent Nos. 8,871,813; 8,927,606 (bromfenac)	PROLENSA (eye inflammation)
Sanofi-Aventis US LLC v. Apotex Corp., No. 1:15-cv-00044, Complaint (D. Del. Jan. 15, 2015)	Sanofi-Aventis US LLC; Aventis Pharma SA; Sanofi	Apotex Corp.; Apotex Inc.	U.S. Patent Nos. 5,847,170; 7,241,907 (cabazitaxel)	JEVTANA KIT (prostate cancer)
Sanofi-Aventis US LLC v. Onco Therapies Ltd., No. 3:15-cv-00290, Complaint (D.N.J. Jan. 14, 2015)	Sanofi-Aventis US LLC; Aventis Pharma SA; Sanofi	Onco Therapies Ltd.	U.S. Patent Nos. 5,847,170; 7,241,907 (cabazitaxel)	JEVTANA KIT (prostate cancer)
Sanofi-Aventis US LLC v. Breckenridge Pharmaceutical Inc., No. 3:15-cv-00289, Complaint (D.N.J. Jan. 14, 2015)	Sanofi-Aventis US LLC; Aventis Pharma SA; Sanofi	Breckenridge Pharmaceutical Inc.	U.S. Patent Nos. 5,847,170; 7,241,907 (cabazitaxel)	JEVTANA KIT (prostate cancer)
Sanofi-Aventis US LLC v. Apotex Corp., No. 3:15-cv-00287, Complaint (D.N.J. Jan.	Sanofi-Aventis US LLC; Aventis Pharma SA; Sanofi	Apotex Corp.; Apotex Inc.	U.S. Patent Nos. 5,847,170; 7,241,907 (cabazitaxel)	JEVTANA KIT (prostate cancer)

Recent Hatch-Waxman Filings – Continued

Matter	NDA Holder / Licensee(s)	ANDA Filer	Patent(s)	Brand Name
14, 2015)				
Alcon Laboratories Inc. v. Akorn Inc., No. 2:15-cv-00285, Complaint (D.N.J. Jan. 14, 2015)	Alcon Laboratories Inc.; Alcon Pharmaceuticals Ltd.; Senju Pharmaceuticals Co.; Mitsubishi Chemical Corp.	Akorn Inc.	U.S. Patent No. 6,114,319 (difluprednate)	DUREZOL (eye pain and swelling)
Horizon Pharma Ireland Ltd. v. Paddock Laboratories LLC, No. 1:15-cv-00043, Complaint (D. Del. Jan. 14, 2015)	Horizon Pharma Ireland Ltd.; HZNP Ltd.; Horizon Pharma USA Inc.	Paddock Laboratories LLC; Perrigo Co.	U.S. Patent Nos. 8,217,078; 8,252,838;8,546,450; 8,563,613; 8,618,164; 8,871,809 (diclofenac)	PENNSAID (osteoarthritis of the knee)
Millennium Pharmaceuticals Inc. v. Onco Therapies Ltd., No. 1:15-cv-00040, Complaint (D. Del. Jan. 14, 2015)	Millennium Pharmaceuticals Inc.	Onco Therapies Ltd.; Agila Specialties Inc.	U.S. Patent Nos. 6,713,446; 6,958,319 (bortezomib)	VELCADE (multiple myeloma)
Millennium Pharmaceuticals Inc. v. Hetero Labs Ltd., No. 1:15-cv-00039, Complaint (D. Del. Jan. 14, 2015)	Millennium Pharmaceuticals Inc.	Hetero Labs Ltd.; Hetero USA Inc.	U.S. Patent Nos. 6,713,446; 6,958,319 (bortezomib)	VELCADE (multiple myeloma)
Horizon Pharma Ireland Ltd. v. Paddock Laboratories LLC, No. 1:15-cv-00368, Complaint (D.N.J. Jan. 13, 2015)	Horizon Pharma Ireland Ltd.; HZNP Ltd.; Horizon Pharma USA Inc.	Paddock Laboratories LLC; Perrigo Co.	U.S. Patent Nos. 8,217,078; 8,252,838; 8,546,450; 8,618,164; 8,871,809 (diclofenac)	PENNSAID (osteoarthritis of the knee)

   ISSN 1542-9547

Journal

REGULATORY CALENDAR

Notices

FDA announced that the Center for Drug Evaluation and Research, along with several co-sponsors, will hold a public workshop titled ''Gastroenterology Regulatory Endpoints and the Advancement of Therapeutics (GREAT III)'' March 30-31 in Silver Spring, Md. For more information, contact Kelly Richards, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Room 5237, Silver Spring, Md. 20993-0002, (240) 402-4276, fax (301) 796-9904, GREAT@fda.hhs.gov (80 Fed. Reg. 4,933, Jan. 29, 2015).

FDA announced that the Dermatologic and Ophthalmic Drugs Advisory Committee and the Ophthalmic Devices Panel of the Medical Devices Advisory Committee will hold a public meeting Feb. 24 in Silver Spring, Md., to discuss a new drug application for riboflavin ophthalmic solutions with UV-A irradiation, submitted by Avedro Inc. These combination products are used in corneal collagen cross-linking. For more information, contact Moon Hee V. Choi, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Building 31, Room 2147, Silver Spring, Md. 20993-0002, (301) 796-9001, fax (301) 847-8533, DODAC@fda.hhs.gov, or FDA Advisory Committee Information Line, 800-741-8138 ((301) 443-0572 in the Washington area) (80 Fed. Reg. 4,578, Jan. 28, 2015).

FDA announced it is accepting public comment on a proposal to extend an information collection, ''Biosimilars User Fee Cover Sheet; Form FDA 3792 (OMB Control Number 0910-0718).'' Submit comments by March 30 to http://www.regulations.gov or to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Md. 20852. For more information, contact FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Road, COLE-14526, Silver Spring, Md. 20993-0002, PRAStaff@fda.hhs.gov (80 Fed. Reg. 4,272, Jan. 27, 2015).

FDA announced the availability of a draft guidance for industry and FDA staff titled ''Current Good Manufacturing Practice Requirements for Combination Products.'' Submit comments by March 30 to http://www.regulations.gov or to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Md. 20852. For more information, contact John Barlow Weiner, Office of Combination Products, Food and Drug Administration, 10903 New Hampshire Ave., Building 32, Room 5129, Silver Spring, Md. 20993-0002, (301) 796-8930 (80 Fed. Reg. 4,280, Jan. 27, 2015).

FDA announced the availability of a guidance for industry titled ''S10 Photosafety Evaluation of Pharmaceuticals,'' prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Submit comments at any time to http://www.regulations.gov or to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Md. 20852. For more information, contact Abigail Jacobs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Building 22, Room 6474, Silver Spring, Md. 20993-0002 (80 Fed. Reg. 4,282, Jan. 27, 2015).

FDA announced it is providing the opportunity to submit written comments and to request an informal public meeting concerning recommendations by the World Health Organization to impose international manufacturing and distributing restrictions, under international treaties, on certain drug substances. Submit comments by Feb. 26 to http://www.regulations.gov or to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Md. 20852. Submit requests for a public meeting on or before Feb. 10. For more information, contact James R. Hunter, Center for Drug Evaluation and Research, Controlled Substance Staff, Food and Drug Administration, 10903 New Hampshire Ave., Building 51, Room 5150, Silver Spring, Md. 20993-0002, (301) 796-3156, james.hunter@fda.hhs.gov (80 Fed. Reg. 4,283, Jan. 27, 2015).

FDA announced a public conference titled ''FDA/Xavier University PharmaLink Conference: Leadership in a Global Supply Chain,'' to be held March 25-27 in Cincinnati. For more information, contact Steven Eastham, Food and Drug Administration, Cincinnati South Office, 36 East 7th Street, Cincinnati, Ohio 45202, (513) 246-4134, steven.eastham@fda.hhs.gov (80 Fed. Reg. 4,289, Jan. 27, 2015).

FDA announced that the Dermatologic and Ophthalmic Drugs Advisory Committee will hold a public meeting March 9 in Silver Spring, Md., to discuss a new drug application for moderate to severe convexity or fullness associated with submental fat in adults and pediatric development of systemic products for treating atopic dermatitis with inadequate response to topical prescription therapy. For more information, contact Jennifer Shepherd, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Building 31, Room 2417, Silver Spring, Md. 20993-0002, (301) 796-9001, fax (301) 847-8533, DODAC@fda.hhs.gov, or FDA Advisory Committee Information Line, 800-741-8138 ((301) 443-0572 in the Washington area) (80 Fed. Reg. 3,969, Jan. 26, 2015).

FDA announced that the Pharmacy Compounding Advisory Committee will hold a public meeting Feb. 23-24 in

REGULATORY CALENDAR

Continued from previous page

Silver Spring, Md., to discuss two things: proposed revisions to the list of drug products that may not be compounded under exemptions because the products have been withdrawn or removed from the market because the products or components of them have been found to be unsafe or not effective and proposed criteria for developing the list of bulk drug substances that may be used to compound drug products. For more information, contact Jayne E. Peterson, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Building 31, Room 2417, Silver Spring, Md. 20993-0002, (301) 796-9001, fax (301) 847-8533, PCAC@fda.hhs.gov, or FDA Advisory Committee Information Line, 800-741-8138 ((301) 443-0572 in the Washington area) (80 Fed. Reg. 3,967, Jan. 26, 2015).

FDA announced it is accepting public comment on a proposal to extend an information collection, ''Guidance for Industry on Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application (OMB Control Number 0910-0636).'' Submit comments by March 24 to http://www.regulations.gov or to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, Md. 20852. For more information, contact FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Road, COLE-14526, Silver Spring, Md. 20993-0002, PRAStaff@fda.hhs.gov (80 Fed. Reg. 3,608, Jan. 23, 2015).

CONFERENCES

Suggestions for events to be included in this section may be sent to bbroderick@bna.com.

340B Coalition Winter Conference 2015, Feb. 4-6, 2015, San Francisco (Safety Net Hospitals for Pharmaceutical Access, 1101 15th St. N.W., Suite 910, Washington, D.C. 20005, (202) 552-5850) (http://www.340bconferences.org/conferences/index.htm).

GPhA Annual Meeting 2015, Feb. 9-11, 2015, Miami (Generic Pharmaceutical Association, 777 Sixth St. N.W., Suite 510, Washington, D.C. 20001) (http://www.gphaonline.org/events/upcoming-events/2015-annual-meeting).

Fraud and Abuse in the Sales and Marketing of Drugs, March 12-13, 2015, Boston (American Conference Institute, 45 W. 25th St., 11th Floor, New York, N.Y. 10010, (212) 352-3220) (http://www.americanconference.com/2015/743/fraud--abuse-in-the-sales-and-marketing-of-drugs).

FDA/Xavier PharmaLink 2015, March 24-27, 2015, Cincinnati (Xavier Health, Xavier University, 3800 Victory Parkway, Cincinnati, Ohio 45207-5471) (http://xavierhealth.org/).

Third Annual Biosimilars and Biobetters Conference 2015, April 3-4, 2015, London (Oxford Global Conferences, Part 1st Floor, Godstow Court, Minns Business Park, Botley, Oxford United Kingdom OX2 0JB) (http://www.biosimilars-congress.com/).

Personalized Medicine World Conference, United Kingdom, April 15-17, 2015, Oxford, England (Contact: team@pmwcintl.com, or (650) 961-8877) (http://pmwcintl.com/conferences.php).

Food and Drug Law Institute 2015 Annual Conference, April 20-21, 2015, Washington (Contact: FDLI, 1155 15th St. N.W. #800, Washington, D.C. 20005, (202) 371-1420) (http://www.fdli.org/).

ACI's Ninth Annual Paragraph IV Disputes, April 27-28, 2015, New York (American Conference Institute, 45 W. 25th St., 11th Floor, New York, N.Y. 10010, (212) 352-3220) (http://www.americanconference.com/2015/688/paragraph-iv-disputes).

2015 GPhA CMC Workshop, June 9-10, 2015, Bethesda, Md. (Generic Pharmaceutical Association, 777 Sixth St. N.W., Suite 510, Washington, D.C. 20001) (http://www.gphaonline.org/events/).

BIO 2015, June 15-18, 2015, Philadelphia (Biotechnology Industry Organization, 1201 Maryland Ave. S.W., Suite 900 Washington, D.C. 20024) (http://convention.bio.org/about-bio-convention/).

2015 GPhA Fall Technical Conference, Nov. 2-4, 2015, Bethesda, Md. (Generic Pharmaceutical Association, 777 Sixth St. N.W., Suite 510, Washington, D.C. 20001) (http://www.gphaonline.org/events/).

BIO 2016, June 6-9, 2016, San Francisco (Biotechnology Industry Organization, 1201 Maryland Ave. S.W., Suite 900 Washington, D.C. 20024) (http://convention.bio.org/about-bio-convention/).

  PLIR ISSN 1542-9547