Major Changes for Generic Drugs Were Set Into Motion in 2010

For generic-drug makers, 2010 was a year that began laying the groundwork for changes likely to impact the industry for years to come.

From the long-sought creation of an approval pathway for biosimilars to the FDA’s renewed push for generic user fees and the fight over pay-for-delay deals, stakeholders in and around the generic-drug world began positioning themselves to leave an impression on the future of the industry.

The most immediate change came early in the year when President Barack Obama signed into law the Patient Protection and Affordable Care Act (Generic Line, March 31, 2010).

(See Review, Page 2)

Blockbuster Patent Expirations Loom For Big-Name Drugmakers in 2011

With generic drugs now accounting for more than 70 percent of all prescriptions dispensed in the U.S., the products’ impact on the pharmaceutical industry has never been greater. That trend looks set to continue in 2011 as some of the world’s most-prescribed products lose their patent protection and begin facing generic competition for the first time.

This year, generic competition is expected to dampen sales for about $30 billion worth of drugs facing patent and exclusivity cliffs in the U.S, according to recent reports from IMS Health and Credit Suisse.

Leading the way will be Pfizer’s blockbuster cholesterol treatment Lipitor (atorvastatin calcium), along with Caduet, which combines Lipitor with the blood pressure drug Norvasc (amlodipine besylate). In 2009, Lipitor alone accounted for about 25 percent of
After a hard-fought battle in Congress that lasted more than a year, the final bill contained several provisions affecting the pharmaceutical industry. But for generic-drug makers, the biosimilars pathway is the measure likely to have the most lasting impact.

Even before the legislation was passed, there was a heated debate surrounding the specifics of the pathway, particularly with regard to how long an exclusivity period manufacturers of innovator biologics should be granted to market their products without generic competition.

Despite calls from the Generic Pharmaceutical Association (GPhA) — as well as Obama and Rep. Henry Waxman (D-Calif.) — to cap that exclusivity at seven years, the final legislation included a 12-year period.

**FDA Regulations Forthcoming**

The real debate over the pathway, however, has only just begun.

It is up to the FDA to issue regulations determining what its standards will be for approving the complex drugs, and doing so poses the agency with numerous challenges.

Among the issues that must be sorted out are whether the agency will require clinical trials before approving a biosimilar and, when a drug is approved, how new indications will be granted or how a product will be deemed interchangeable with its brand-name counterpart.

The FDA began its attempts to answer those questions in November when it hosted a public meeting on the pathway, but stark differences between generic and brand-drug makers quickly emerged (Generic Line, Nov. 10, 2010).

While generic-industry heavyweights such as Teva Pharmaceutical Industries called on the agency not to require any additional testing to have a product deemed interchangeable or to approve additional indications, brand companies including Merck and Roche portrayed such proposals as potentially unsafe (Generic Line, Nov. 10, 2010).

Despite both sides’ desire for a quick resolution though, the FDA is under no timetable for setting its regulations and industry experts have predicted it could be years before any formal guidance is issued (Generic Line, Oct. 27, 2010).

**Generic User Fees Revived**

In the meantime, both the agency and generic-drug makers will have their hands full preparing for a separate battle looming over generic user fees.

While past attempts at creating a system of user fees for generic drugs have been met with consternation and ultimately failed, the FDA — which faces a growing backlog of generic drug applications that has now reached more than 2,000 — again revived its efforts last year.

At a public meeting on the issue in September, FDA Commissioner Margaret Hamburg told generic-drug makers that an effective user-fee program would reduce ANDA review times and urged the industry to adopt a unified stance on the topic (Generic Line, Sept. 29, 2010).

“We’re not in a crisis now, but we may soon be,” Hamburg said.

Whether drugmakers will oblige remains to be seen, but GPhA has been generally supportive of adopting the fees. The group has insisted, however, that the FDA develop a program that provides generic-drug makers with specific agency performance goals.

Before a user fee program can even be established though, the FDA must first get approval from Congress.

Legislation authorizing the FDA to impose the fees has not yet been introduced, but negotiations are slowly moving forward and there is a growing sentiment that if a program is going to be created it will happen this year, Kurt Karst, an attorney with Hyman, Phelps & McNamara, said.

(See Review, Page 4)
Teva Upbeat Despite FDA Denial Of New Copaxone Indication

The FDA has denied Teva Pharmaceutical Industries’ attempt to gain a new indication for its multiple sclerosis treatment Copaxone, but the decision may turn out to be a blessing in disguise for the company by delaying generic competition to the blockbuster drug.

In a complete response letter sent to Teva last month, the agency noted that it could not approve the company’s application for a lower-dose version of Copaxone (glatiramer acetate) because the drug’s mechanism of action is not fully understood and even a formulation change could impact clinical outcomes.

“Unless you can provide a convincing argument that the new higher concentration/lower volume formulation does not have an impact on efficacy, an adequate and well controlled efficacy study will be needed to support efficacy of this new formulation,” the FDA told Teva in its letter.

**Surprise Reaction**

But rather than appearing downcast, the company trumpeted the news, saying that the agency’s decision supports its case that any future generic versions of Copaxone should require full clinical trials before being approved.

The FDA’s response “supports Teva’s belief that even slight changes to a glatiramoid like Copaxone can significantly and unpredictably influence the efficacy, toxicity and immunogenicity profile of the compound,” the company said last month.

Indeed, analysts covering Teva agreed with the company, with J.P. Morgan analyst Chris Schott noting in a Dec. 23 report that the FDA’s complete response letter highlighted the “high hurdle” potential generic manufacturers of Copaxone will face in gaining approval.

“While we are unlikely to have full clarity on this issue for some time, today’s news, in our view, increases the probability of clinical data requirements for generic Copaxone manufacturers,” Schott says.

If the FDA does eventually require clinical trials for any generic Copaxone, it would be a major boost to Teva, which has been lobbying for such a move for some time.

The company has filed multiple citizen petitions with the agency, most recently in December, and has hit several of its competitors with patent-infringement lawsuits after they filed applications to market a generic version of the drug.

With $2.8 billion in worldwide sales in 2009 — 18 percent of Teva’s net sales for the year — it is not difficult to see why the company is putting up such a vigorous fight to require the trials for Copaxone.

**Lovenox Precedent**

Looming in the background, however, is an FDA decision from last year to approve Sandoz and Momenta Pharmaceuticals’ generic version of Sanofi-Aventis’ Lovenox (enoxaparin sodium for injection), another complex molecule, without requiring clinical trials (Generic Line, Aug. 4, 2010).

Like Teva, Sanofi had sought to have the FDA require clinical trials for generic Lovenox, filing citizen petitions with the agency and launching lawsuits against generic-drug makers.

The company’s efforts ultimately proved fruitless though.

Following its approval in July, generic Lovenox went on to erode more than half of Sanofi’s market share in its first nine weeks on the market and post sales of nearly $300 million (Generic Line, Nov. 10, 2010).

While Teva will certainly have one eye on that decision as generic Copaxone applications — including from Sandoz and Momenta — move forward, the company is hedging its bets with its own application for a generic version of Lovenox.

— David Belian
With generic and brand-drug makers continually sparring in court over patent infringement and other cases, it is not often the two sides find an issue that brings them together.

2010 offered that rare feat, though, as the two sides joined together to oppose a strong push from the FTC to put an end to so-called pay-for-delay deals, which the agency says delays consumers’ access to generic drugs.

The deals, in which a brand manufacturer pays a generic competitor to delay marketing a generic version of a drug, are defended by the pharmaceutical companies as a means of avoiding a costly and often drawn-out legal process.

But the agency made its intention to stop the agreements known early in the year, stating in April that eliminating the deals was among its top priorities in 2010 (Generic Line, May 12, 2010).

Enforcing that goal proved to be rather more difficult for the FTC, however, as the agency failed to sway several courts to its arguments against the deals and became entangled in a dispute with Watson Pharmaceuticals over a deal in an attempt to induce testimony from the company’s CEO, Paul Bisaro (Generic Line, Sept. 1, 2010).

The FTC’s efforts to enact a legislative ban on the deals also failed to materialize, as a provision from Sen. Herb Kohl (D-Wis.) that would have outlawed the agreements was added, and then dropped, from several different bills.

Still, the agency has shown no intention of giving up its fight, appealing to the Supreme Court in December to take on its case challenging a pay-for-delay deal between Bayer and Barr Laboratories over the antibiotic Cipro (ciprofloxacin).

And even if that is not successful, drugmakers will still want to keep an eye on the agency in 2011, as an FTC commissioner said in November that the agency is considering issuing its own rule as a “Plan C” in putting a stop to the deals (Generic Line, Nov. 24, 2010). — David Belian

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FDA to Hold Stakeholder Meetings On Developing Biosimilar User Fees

The FDA is planning to hold consultation meetings with drugmakers and other industry stakeholders to seek their views on the development of a user fee program for biosimilars.

The meetings, which are expected to occur early this year, were outlined by the agency in a notice published in the Federal Register Dec. 8. Stakeholders interested in attending are asked to respond by Jan. 10.

While the approval pathway for biosimilars — passed as part of healthcare overhaul legislation last year — allowed the FDA to assess user fees on biosimilars under the Prescription Drug User Fee Act (PDUFA), the agency is required to develop separate fees for the products beginning in fiscal 2013, the FDA says.

**Planned Topics**

The agency is planning to ask stakeholders at the meetings what the goals for the user fees should be and invite input on the review process for biosimilar applications, according to the notice.

The development of the fees comes, however, before the FDA has issued any guidelines on what its standards for approving biosimilars will be.

The agency held a two-day public meeting on the topic in November, at which brand and generic companies differed strongly on the approval standards and other requirements they felt the agency should adopt (Generic Line, Nov. 10, 2010).

Despite receiving that input, experts have predicted that any guidance from the FDA on biosimilars could still be years away (Generic Line, Oct. 27, 2010).

Meanwhile, skepticism has been growing among drugmakers about the effectiveness of user fees in general.

A survey released in November by Price-waterhouseCoopers found that nearly half of the 50 life science companies asked were unclear on the purpose of user fees and only 24 percent of companies felt that the FDA is applying the fees as intended (Generic Line, Dec. 8, 2010).

Still, the FDA has pushed ahead with its plans to rely on the fees. Negotiations to reauthorize PDUFA have been ongoing for months, and the agency is lobbying generic-drug makers to accept user fees for their products as well.

— David Belian

Shionogi Hits Mylan With Suit Over Generic Orapred ANDA

Shionogi Pharma has filed a patent-infringement lawsuit against Mylan Pharmaceuticals in an attempt to prevent the generic-drug maker from gaining approval for its version of the anti-inflammatory drug Orapred ODT.

In the suit, filed in December in the U.S. District Court for the District of Delaware, Shionogi claims that Mylan’s ANDA for generic Orapred ODT (prednisolone sodium phosphate) 10-, 15- and 30-mg orally disintegrating tablets would violate the company’s ’341 patent on the drug.

Shionogi is asking the Delaware court to issue an injunction preventing Mylan from marketing or manufacturing its generic prednisolone until the ’341 patent expires in November 2019.

In a Paragraph IV certification filed with the FDA last year, however, Mylan claims that the ’341 patent is invalid and would not be infringed by the company’s generic version of the drug.

The company also believes it is the first generic-drug maker to file an ANDA for Orapred ODT and would thus be entitled to 180 days of marketing exclusivity if its application is approved, Mylan said Dec. 17.

Orapred ODT had U.S. sales of approximately $28 million for the 12 months ending Sept. 30, 2010, Mylan says. — David Belian
Pfizer's revenue and maintained its position as the biggest-selling drug in the world with about $11.4 billion in sales. Norvasc generics first appeared in 2007.

While Pfizer will be able to hold on to its Lipitor exclusivity for much of the year, Indian drugmaker Ranbaxy will enter the market in November and will have six months of marketing exclusivity on its generic version of the drug, based on an agreement between the two companies.

Pfizer is also set to lose exclusivity on another of its blockbuster drug franchises when its glaucoma treatments Xalatan (latanoprost) and Xalacom (latanoprost/timolol maleate) go off patent in March, and the hemophilia treatment BeneFIX (Coagulation Factor IX recombinant) is also due to face generic competition this year.

The patent-expiration pain will not be limited to Pfizer, however, as Eli Lilly also faces a looming deadline for losing exclusivity on its own best-selling product, the antipsychotic Zyprexa (olanzapine).

Like Pfizer, Lilly will be able to hold on to its blockbuster for much of the year as Zyprexa, which had nearly $5 billion in sales in 2009, is not set to lose patent protection until October.

The company will have to couple that loss, though, with generic competition to Symbyax (olanzapine/fluoxetine HCl), a combination of Zyprexa and the antidepressant Prozac, which is also going off patent. These developments follow the November launch of a generic of its oncologic Gemzar (gemcitabine HCl) and ongoing legal challenges on its attention-deficit drug Strattera (atomoxetine HCl).

For Johnson & Johnson, 2010 was dominated by turmoil surrounding the company’s manufacturing practices. This year, J&J will also have to deal with the loss of exclusivity on its blockbuster antibiotic Levaquin (levofloxacin).

While J&J’s patent protection on the drug actually expired on Dec. 20, the company was granted pediatric exclusivity by the FDA that will ward off generic competition until June.
— David Belian

**Court Allows Generic Companies To Bypass Patents on Crestor**

A federal court has allowed several drug-makers to continue pursuing approval for their generic versions of AstraZeneca’s blockbuster cholesterol drug Crestor, saying the companies’ applications would not violate patents on the drug.

In a ruling issued Dec. 15, the U.S. District Court for the District of Delaware found that ANDAs filed by companies including Apotex and Teva Pharmaceutical Industries seek approval for methods of use on Crestor (rosuvastatin calcium) that are different than those claimed by AstraZeneca’s ’618 and ’152 patents on the drug.

While AstraZeneca responded by arguing that, if the FDA approved the ANDAs, it would require the generic-drug makers to change their labels to match those of the brand drug, thus violating the ’618 and ’152 patents, the court disagreed.

“Because the Hatch-Waxman Act allows ANDAs to carve out FDA-approved indications, and because there is no reason to believe that the FDA will not continue to approve qualified ANDAs, plaintiffs’ claims are based on contingent future events that are unlikely to occur,” the court says.

If the ruling stands it would be a big loss for AstraZeneca because it would allow generic-drug makers to bypass the ’618 and ’152 patents on Crestor and knock at least two years off the drug’s exclusivity. The two patents expire in 2018 and 2022.

The case is AstraZeneca Pharmaceuticals LP et al. v. Apotex Corp, et al. — David Belian
Supreme Court Agrees to Rule On Generic Preemption

The Supreme Court has agreed to hear the matter of whether generic-drug makers are preempted by federal law from unilaterally modifying the label of their products.

In a ruling issued Dec. 10, the court granted certiorari to three cases involving the issue, consolidating them and allowing one hour for oral arguments. The court is expected to hear the case later this year.

The ruling comes despite a request from acting Solicitor General Neal Katyal for the court not to take up the issue (Generic Line, Nov. 10, 2010).

Katyal said in an amicus brief filed in November that two federal appeals courts that heard the cases were correct in their rulings that generic-drug makers can be found liable for not providing sufficient warnings of risks on labeling, even if such warnings are not found on the brand product’s labeling.

Brand-Drug Precedent

The Supreme Court itself took on the issue of preemption for brand-drug makers last year, ruling in Wyeth v. Levine that companies could be found liable for failing to modify their products’ labeling, even without FDA approval.

The court’s decision to take up the generic-drug makers’ cases, however, may be a sign that the justices are thinking differently than they did in Wyeth, Kurt Karst, an attorney with Hyman, Phelps & McNamara, told Generic Line.

“It’s certainly a possibility here that they want to clarify their Wyeth v. Levine ruling with respect to generics,” Karst said.

The cases the court will hear revolve around a generic version of Wyeth’s gastroesophageal reflux disease drug Reglan (metoclopramide HCl).

The plaintiffs in the cases, Gladys Mensing and Julie Demahy, took generic Reglan and subsequently developed the neurological disorder tardive dyskinesia, which causes uncontrollable body movements, particularly around the face.

Mensing and Demahy then sued the generic manufacturers of Reglan, and two federal appeals courts — the Eighth Circuit and the Fifth Circuit — ruled that the companies could be found liable in the cases (Generic Line, Feb. 3, 2010).

Aside from generic-drug makers, manufacturers of OTC products will also closely be watching the case, as they await word from the Supreme Court on whether it will take up a case determining preemption for their products.

— David Belian

Teva Calls on Supreme Court To Deny Cozaar, Hyzaar Suit

Teva Pharmaceutical Industries is calling on the Supreme Court to deny a case challenging how the company was awarded marketing exclusivity on Merck’s hypertension drugs Cozaar and Hyzaar.

The case, which generic-drug maker Apotex asked the court to hear in October, centers on a dispute over what actions can lead a generic manufacturer to lose their initial 180-day marketing exclusivity for a product.

Apotex had argued that Teva should not get the exclusivity on Cozaar (losartan potassium) and Hyzaar (hydrochlorothiazide/losartan potassium) because Merck had delisted its patent on the drugs from the FDA’s Orange Book, which under the Medicare Prescription Drug, Improvement and Modernization Act (MMA) is a valid reason for canceling a generic-drug maker’s marketing exclusivity.

The U.S. Court of Appeals for the District of Columbia Circuit ruled in Teva’s favor, however, saying that any unilateral action by a brand-drug maker, such as delisting a patent or letting it expire, cannot be used as a means for canceling a generic-drug maker’s exclusivity (Generic Line, March 17, 2010).

(See Cozaar, Page 8)
Sun Files Supreme Court Petition In Prandin Patent-Use Code Dispute

Sun Pharmaceutical has filed an appeal with the U.S. Supreme Court in a case that could determine how brand-drug makers can use patent-use codes to protect their products from generic competition in the future.

The case was originally brought by Sun subsidiary Caraco Pharmaceutical, which was seeking to market a generic version of Novo Nordisk's diabetes drug Prandin (repaglinide).

In its ANDA, Caraco claimed that its version of Prandin would be marketed only for uses that were not patented by Novo Nordisk, and the agency agreed and accepted the drug’s proposed label.

Novo Nordisk responded by changing its patent use codes on Prandin to include the uses that Caraco was seeking approval for, which prompted the FDA to reverse its decision and reject Caraco’s proposed label.

Lower Court Disagreements

Caraco took its case to federal court, where the U.S. District Court for the Eastern District of Michigan ruled in the company’s favor.

On appeal, though, the U.S. Court of Appeals for the Federal Circuit reversed that decision, saying that nothing in the Hatch-Waxman Act prevented Novo Nordisk from changing its patent-use codes (Generic Line, April 28, 2010).

In its petition to the Supreme Court filed on Dec. 23, Sun argues that, if upheld, the appeals court’s decision would set a precedent allowing all brand-drug makers to submit overbroad patent descriptions to the FDA to prevent generic competition to their products.

“Brands may now craft highly generalized use codes … which effectively allows them to extend their monopolies to unpatented uses,” Sun says. “In other words, brands can insulate Section viii — a critical [Hatch-Waxman] provision that facilitates the approval and marketing of lower-cost generic drugs for uses no longer protected by a patent — a dead letter.”

Sun’s petition has received support from several other generic-drug makers, as well as the Generic Pharmaceutical Association. Novo Nordisk’s response is due to the Supreme Court by Jan. 27. — David Belian

Cozaar, from Page 7

Despite saying that it disagreed with the appellate court’s ruling, the FDA nonetheless approved Teva’s exclusivity, saying the court’s interpretation of the MMA gave it no choice (Generic Line, March 31, 2010).

While Teva’s exclusivity on the drugs has since expired, Apotex maintains that its suit is still valid because the means by which exclusivity is awarded in all future cases is at stake (Generic Line, Oct. 13, 2010).

But in its response, filed with the high court on Dec. 10, Teva says that the fact that its exclusivity has already expired makes Apotex’s appeal “moot on arrival.”

“Needless to say, this court is not in the business of exercising its discretionary jurisdiction to render advisory opinions on purely academic matters, and it should not do so here,” Teva says.

Even if Apotex’s case was still relevant, though, the court should still decline to hear it because the appeals court ruled correctly and there were no dissenting opinions from other courts, Teva adds.

“As three different panels of the D.C. Circuit now have recognized, it upends both law and logic to think that Congress created an incentive scheme designed to encourage generic companies to challenge dubious brand-name patents, but simultaneously empowered the brand companies who assert those dubious patents to eviscerate that incentive scheme,” Teva says.

— David Belian
Supreme Court Asked to Rule On Cipro Pay-for-Delay Case

The legality of pay-for-delay deals could be decided by the U.S. Supreme Court now that plaintiffs challenging one such deal between Bayer and Barr Laboratories over the antibiotic Cipro have petitioned the court to hear their case.

In the petition for a writ of certiorari, filed Dec. 6 by direct purchasers of Cipro (ciprofloxacin), plaintiffs contend that the Supreme Court should take up the case because there has been a split among lower courts in deciding whether the deals are legal.

In addition, an earlier ruling from the U.S. Court of Appeals for the Second Circuit permitting the Cipro deal conflicted with Supreme Court precedent, plaintiffs argue, adding that they believe this case is the right vehicle to decide the issue once and for all.

Long-Running Case

The case at hand stems from a patent dispute between Bayer and Barr that began in 1991 when Barr filed an ANDA to market a generic version of Cipro and challenged the validity of Bayer’s ’444 patent on the drug.

Bayer sued Barr in the U.S. District Court for the Southern District of New York. But about two weeks before a trial was scheduled to begin in 1997, the companies reached a pay-for-delay settlement.

Since that time, the deal has been upheld by a federal district court and, despite objections from the FTC and the Justice Department, the appeals court (Generic Line, Sept. 15, 2010).

Whether the Supreme Court will agree to hear the case, however, remains to be seen. The court has twice before declined petitions to hear pay-for-delay cases, most recently a case in 2007 that involved Barr Laboratories agreeing not to market a generic version of AstraZeneca’s Nolvadex (tamoxifen citrate) (Generic Line, June 27, 2007).

The court also declined in 2006 to hear a case brought by the FTC against Schering-Plough involving its potassium deficiency drug K-Dur 20 (potassium chloride) (Generic Line, June 28, 2006).

The commission is among the most ardent opponents of the deals and has said that it will continue to look for other means of outlawing them if its is not successful in court.

While efforts to enact a legislative ban on the agreements have also stalled, Thomas Rosch, an FTC commissioner, said in November that the agency is considering issuing its own rule as a “Plan C” in bringing an end to the deals (Generic Line, Nov. 24, 2010).

The petition was filed in Louisiana Wholesale Drug Co., Inc., et al. v. Bayer AG, et al., which can be found at www.fdanews.com/ext/files/Cipro Petition.pdf. — David Belian

FTC Urges Pay-for-Delay Deals To Be Judged by Patent Strength

As the FTC struggles to gain ground in its ongoing legal battles against pay-for-delay deals, the agency is trying out a new strategy — urging a federal court to acknowledge that the strength of a brand-drug maker’s patents on a drug should be considered before determining whether an agreement violates antitrust laws.

The argument was put forth by the FTC in a brief filed Dec. 15 with the U.S. Court of Appeals for the Eleventh Circuit. The court is considering an agency challenge to an alleged pay-for-delay deal between Watson Pharmaceuticals and Abbott Laboratories over the male hypogonadism treatment AndroGel (testosterone).

The court also declined in 2006 to hear a case brought by the FTC against Schering-Plough involving its potassium deficiency drug K-Dur 20 (potassium chloride) (Generic Line, June 28, 2006).

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The petition was filed in Louisiana Wholesale Drug Co., Inc., et al. v. Bayer AG, et al., which can be found at www.fdanews.com/ext/files/Cipro Petition.pdf. — David Belian

(See Pay-for-Delay, Page 10)
Teva Files Another Petition To Delay Generic Copaxone

In its latest effort to throw down barriers to any company that attempts to bring to market a generic form of its multiple sclerosis (MS) drug, Copaxone, Teva Pharmaceutical Industries has filed a third citizen's petition with the FDA, this time asking the agency to convene a multidisciplinary advisory panel to consider the approval of any follow-on glatiramer acetate products.

Teva cited three reasons for its Dec. 13 request: “an inability” to establish sameness of Copaxone (glatiramer acetate injection), the level of complexity associated with the mechanisms of action for glatiramoids and the inapplicability of bioequivalence confirmation through pharmacokinetic and pharmacodynamic testing methods.

Therefore, Teva asked the FDA to include preclinical testing and full-scale clinical trials as requirements for applications for generic versions of Copaxone.

Earlier Petitions

This most recent citizen petition follows earlier petitions to the FDA, both of which asked the agency to refuse approval for generic ANDAs (Generic Line, May 26, 2010).

Teva also is involved with several patent-infringement lawsuits with potential competitors.

A trial date has not been set for a lawsuit against Sandoz and Momenta Pharmaceuticals regarding Copaxone, although a federal court ruled last year that the companies do not have to notify Teva if they bring a generic Copaxone to market (Generic Line, Oct. 27, 2010).

Sandoz says it is first to file an ANDA.

“The FDA is actively reviewing our application for generic Copaxone,” Sandoz spokeswoman Marija Mandic, told Generic Line. She declined to comment on the lawsuit.

Teva also has filed two lawsuits against Mylan, accusing the company of infringing patents on Copaxone (Generic Line, Sept. 29, 2010).

Mylan and Momenta did not respond to requests for comment by press time.

So far, the FDA has not made a decision on any Copaxone ANDAs or answered Teva’s most recent citizen petition. — Molly Cohen

Pay-for-Delay, from Page 9

Their argument was buoyed by the U.S. District Court for the Northern District of Georgia, which ruled in February that patent litigation is too complex and the results too uncertain to assert such a claim (Generic Line, March 3, 2010).

But in its reply brief, the FTC says that the strength of a brand drug’s patents is a crucial factor in determining whether a pay-for-delay deal prevented a generic drug from entering the market as early as possible.

“The likelihood of the patent holder prevailing in its infringement action helps define the patent’s potential exclusionary scope, and the size of payments relative to the profits the infringers could expect is relevant to assessing that likelihood,” the FTC says.

And while Watson and Abbott argued that the Eleventh Circuit’s own rulings in previous cases have set a precedent against considering a brand drug’s patent strength, the FTC disagrees and says that, if that is the case, the court should reconsider those rulings.

 “[Watson and Abbott] draw several lessons from this court’s cases, but get them all wrong,” the agency says. “Regardless of what other courts have held, this court has not held that reverse payments, or the patentee’s odds of success in infringement litigation, are irrelevant.”

Sanofi Alleges Rifts Within FDA Before Generic Lovenox Approval

As Sanofi-Aventis continues its fight to have Sandoz and Momenta’s generic version of Lovenox pulled from the market, the company is alleging that rifts occurred within the FDA about the criteria used to approve the drug.

In a request for summary judgment filed Dec. 13 in the U.S. District Court for the District of Columbia, Sanofi expands on its argument that in granting approval for generic Lovenox (enoxaparin sodium) last year, the FDA ignored its own precedent regarding approval of generic versions of drugs that have not been fully characterized and has failed to ensure that Sandoz’s drug has the same active ingredient as Sanofi’s product.

Those arguments were initially deemed insufficient by the court in August to grant Sanofi a temporary injunction halting sales of the drug (Generic Line, Sept. 1, 2010).

Approval Criteria Questioned

But in its latest summary judgment request, Sanofi alleges scientists within the FDA’s Office of New Drug Quality Assessment (ONDQA) were hesitant to approve a generic Lovenox and took particular concern with the agency’s set of five criteria that it later said was used to approve the drug (Generic Line, Aug. 4, 2010).

“ONDQA further explained that [the Office of Generic Drugs’ (OGD)] five criteria are inadequate to demonstrate sameness and criticized OGD for relying on ‘inference’ to do so,” Sanofi says. “ONDQA asserted that OGD’s proposed methodology was contrary to both the law and FDA policies.”

Despite the ONDQA’s concerns, the dispute was eventually resolved by Keith Webber, deputy director of the FDA’s Office of Pharmaceutical Science, in an intra-agency memorandum sent in July, Sanofi says.

According to the company, Webber determined that OGD’s five criteria were acceptable, stating that “depending on the kind of drug at issue, there may be different ways to show active ingredient sameness.”

The agency went on to approve Sandoz and Momenta’s ANDA just two days after Webber’s memo and the drug has since brought in huge sales for the companies, earning about $292 million in sales and capturing more than half of the brand drug’s market share in its first nine weeks on the market (Generic Line, Nov. 10, 2010).

For its part, Sanofi put forth several other arguments against generic Lovenox’s approval in its most recent court filing, including that even if the FDA’s five-step test were acceptable, Sandoz and Momenta’s drug failed to meet all of the criteria.

The case is Sanofi-Aventis US LLC v. Food and Drug Administration, et al. and Sandoz Inc. — David Belian

Amphastar Amends FDA Lawsuit To Force Generic Lovenox Approval

Amphastar Pharmaceuticals has amended a lawsuit against the FDA and is now asking a federal court to force the agency to approve its ANDA for generic Lovenox, which the company says has been unfairly delayed.

In an amended complaint filed Dec. 22 in the U.S. District Court for the District of Columbia, Amphastar, which claims it is the first company to file an ANDA for generic Lovenox (enoxaparin sodium), argues that the FDA has continually denied its application without proper justification.

“Amphastar has repeatedly met the standards set by the FDA, only to see those standards shift or to have new standards arbitrarily and capriciously created,” Amphastar says in its complaint. “Every time Amphastar clears the agency’s latest obstacle to approval, a new one is created.”

The most recent delay came Nov. 30 when the FDA informed Amphastar that its raw heparin supplier in China would need to be inspected again, Jason Shandell, vice president and general

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counsel for Amphastar, told Generic Line. The supplier has been cited for good manufacturing practice violations in the past.

Although the letter also showed a path to approval, the company has not yet decided whether it will proceed with the reinspection, Shandell added.

Amphastar filed suit against the FDA in October accusing the agency of unfairly detaining two shipments of semi-purified heparin last year, saying the holdup was part of arbitrary regulatory treatment that has delayed approval of its ANDA (Generic Line, Nov. 10, 2010).

However, in November, the FDA released the detained heparin, just days after Amphastar filed for an injunction to force the agency to do so (Generic Line, Nov. 24, 2010).

Amphastar’s desire to have its application quickly approved has been buoyed by the huge sales Sandoz and Momenta have seen from their generic version of Lovenox, approved in July.

The generic brought in about $292 million in sales and captured more than half of the brand drug’s market share in its first nine weeks on the market (Generic Line, Nov. 10, 2010).

In its complaint, Amphastar also accuses the agency of showing favoritism to Sandoz and Momenta. Shandell told Generic Line he believes the FDA is “manipulating” the company’s application and that CDER Director Janet Woodcock is to blame.

“While Amphastar’s enoxaparin ANDA has languished, the FDA’s favored competitor, which filed its enoxaparin ANDA more than two years after Amphastar, has been allowed to be the exclusive producer of a generic enoxaparin sodium injection product in the United States, reaping a financial windfall in the process,” the complaint says.

The FDA declined to comment on the lawsuit.

Amphastar’s amended complaint is available at www.fdanews.com/ext/files/AmendedComplaint.pdf. — David Belian, Jonathan Block

Takeda, Teva Reach Settlement On Generic Actos, Actoplus Met

Takeda Pharmaceuticals and Teva Pharmaceutical Industries have settled their patent-infringement lawsuit over the diabetes treatments Actos and Actoplus Met, paving the way for Teva to bring generic versions of the drugs to the market in 2012.

Under the terms of the deal announced by the companies Dec. 21, Teva will be able to introduce authorized generic versions of Actos (pioglitazone HCl) in the U.S. in August 2012, followed by Actoplus Met (pioglitazone HCl/metformin HCl) in December 2012.

Those are the same dates that generic-drug maker Mylan will be allowed to introduce generic versions of the drugs under a settlement agreement reached with Takeda in March. Mylan, though, says it believes it will have 180 days of marketing exclusivity on its products (Generic Line, March 31, 2010). — David Belian