Portfolio Media. Inc. | 111 West 19th Street, 5th Floor | New York, NY 10011 | www.law360.com
Phone: +1 646 783 7100 | Fax: +1 646 783 7161 | customerservice@law360.com

Does Indication-Specific Pricing Fit Generics With Carveouts?

By **Michael Cottler and Natasha Daughtrey**
December 15, 2017, 12:03 PM EST

Michael Cottler

Natasha Daughtrey

Indication-specific pricing (ISP) is often proposed as a solution to rising health care costs, particularly for branded drugs that have multiple indications. But it is unclear whether such a model could work with generic and biosimilar products that have labels from which one or more approved uses have been carved out.

Introduction

Public officials and the media regularly lament the high cost of prescription drugs. Indeed, prescription drugs account for about 17 percent of all health care spending in the U.S.,[2] and that figure is expected to increase.[3] Criticism about the cost of drugs is often coupled with the allegation that such drugs are no better than existing, less expensive treatments. This may be the case for a drug, for example, with multiple indications, and the relative clinical benefit of the drug varies between the indications.[4] Historically, drugs are priced on a per unit basis, meaning the price of the drug is the same, regardless of the indication. To many, this makes little sense for drugs with multiple indications. As the Institute for Clinical and Economic Review has reported, "price and clinical value do not necessarily align well across multiple indications. With multi-indication drugs on the rise, it is important for payers and manufacturers to consider the options through which pricing can better reflect differential benefit by indication."[5]

That is where ISP (or indication-based pricing) comes in. ISP is a form of value-based pricing that sets different prices for the same drug, depending on the indication for which it is used.[6] Many have touted it as one solution to rising prescription drug cost because it allows drug reimbursements to reflect the actual value delivered by the drug, leading to more informed choices by patients and doctors. [7] Interested parties have published the pros and cons of ISP, and have provided solutions as to how it may work.[8] ISP programs can be implemented in different ways: (1) the same drug product is branded under a different name (and price) depending on the indication; (2) no brand differentiation, but discounts apply to a drug depending on the indication for which it is used, requiring tracking the indication for each prescription; and (3) using a single "blended" rate for a drug rate based on estimates of how much a drug will be used for each indication.[9]

Recently, pharmacy benefit managers[10] (PBMs) have started to use ISP programs.[11] Express Scripts,

the largest PBM, has rolled out an ISP program for drugs to treat certain cancers. An example of such a drug is Tarceva (erlotinib), which when used to treat non-small cell lung cancer provides an additional five months of life compared to chemotherapy, whereas when it is used to treat pancreatic cancer, it provides only an additional 12 days of life compared to chemotherapy.[12] For this reason, Express Scripts has suggested it will pay less when the drug is used to treat pancreatic cancer compared to lung cancer. It has taken a similar approach to anti-inflammatory drugs too.

While ISP is intended to address some economic concerns for branded products, it is not clear whether ISP is compatible with existing regulatory and legal frameworks relating to generic products and biosimilars, particularly those with drug labeling that has carveouts. A brief discussion of regulatory and patent infringement issues regarding such products is provided below.

ANDA Label Carveouts

The Hatch-Waxman Act provides a framework for the approval process for "small molecule," generic drugs and a means for resolving patent infringement disputes arising out of the filing of an applicant's Abbreviated New Drug Application.[13] In a Hatch-Waxman litigation, the infringement inquiry focuses on the drug as described in the applicant's ANDA; when a method of use patent is asserted, the question is how would the product be used according to its proposed drug label.[14] While a proposed label for a generic product must generally have the same information as the brand product's label,[15] 21 U.S.C. § 355(j)(2)(A)(viii) permits an ANDA applicant to "carve out" (or remove) from its label indications that are covered by method of use patents, as long as there is at least one indication remaining in the label and the product is safe and efficacious for the remaining use(s). Carving out a patented use would ideally avoid a claim of induced infringement of that patent because by removing the use from the label, the company is not instructing or encouraging others to practice it.

Generics drugs with such "skinny" labels, however, have been prescribed and dispensed for carved-out uses. Doctors are permitted to prescribe drugs, both branded and generic, "off label," that is for indications that do not specifically appear on the drug's label. Once a generic drug is approved, insurance carriers and PBMs may only cover the generic form, and state generic substitution laws may require pharmacists to dispense the generic version,[16] regardless of the use. But that does not mean the generic product sponsor is inducing infringement. In a Hatch-Waxman litigation, evidence that physicians would prescribe a proposed generic drug in an infringing manner, where the patented indication is carved out of the label, is insufficient to establish induced infringement.[17] This defense is not absolute, however. Courts have found liability under such circumstances, based on other information in the label,[18] and the generic drug manufacturer's correspondence to the U.S. Food and Drug Administration.[19]

BPCIA Label Carveouts

The Biologics Price Competition and Innovation Act ("BPCIA")[20] was created to establish a regulatory pathway for follow-on biologics (i.e., "big molecules"), known as biosimilars, and a framework for resolving patent disputes stemming from the filing of an abbreviated biologics license application ("aBLA"). If a reference biologic product has multiple indications, the aBLA applicant could include all those indications in its proposed biosimilar label by conducting clinical trials for each indication, or by extrapolating clinical data regarding one indication to the others so long as there is sufficient scientific justification of biosimilarity for the other indications.[21] Like ANDA applicants, however, aBLA applicants can choose to not seek FDA approval for certain indications and have label carveouts.[22]

There is little, if any, real-world data available regarding off-label use of biosimilars; just a few are commercially marketed, and none of those have label carveouts. Many states have passed laws paving the way for substitution of brand products for biosimilars that are deemed "interchangeable"[23] but no marketed biosimilar is currently designated as such.[24] Therefore, while it remains to be seen whether biosimilars, including interchangeables, will be prescribed or dispensed, it is certainly possible for carved-out uses, given the high costs of biologics.

Furthermore, there has only been one BPCIA case where the issue of infringement has made its way to the Federal Circuit, Amgen v. Apotex.[25] While that case relates to process claims, the lower court and Federal Circuit opinions suggest that the test for infringement in a BPCIA case, including for method claims, may be substantially similar to the test in a Hatch-Waxman litigation, discussed above.

Indication-Specific Pricing For Generic And Biosimilar Products With Carveouts

That brings us back to ISP. It is unclear how generic products and biosimilars with label carveouts will be priced, or reimbursed, under ISP. An ISP program may work best if the uses for which a drug is prescribed are reasonably forecasted at the time the manufacturer negotiates pricing with the insurer or PMB. But how would a generic or biosimilar manufacturer negotiate a price with an insurer or PBM with respect to a product that has a "skinny" label, from which patented uses were carved out? Would pricing be based on all expected uses (based on how the branded product is used), or just on those uses that appear in the "skinny" label? And let's assume for the sake of argument it is the former. Would there be induced infringement implications? In other words, could the manufacturer's mandatory, price negotiations reflecting off-label use be used as evidence of induced infringement against the manufacturer?

Moreover, ISP of generic and biosimilar products with carveouts might undermine the policy behind such pricing, which is to match the value of the drug with its costs. For example, imagine that a doctor prescribes a drug, for which a generic product is available, but according to an FDA-approved indication that is carved out from the generic product. And let's assume when the patient fills the drug it is automatically substituted at the pharmacy with the generic product. If the generic drug company is reimbursed based on only the uses not carved out from its label, then the drug company may not be reimbursed according to the true value of drug's use.

Conclusion

Practitioners should pay close attention to see whether, and how, ISP is adopted for generic and biosimilar products, particularly those with "skinny" labels. In view of the questions raised above, it is unclear whether ISP is compatible with the current legal frameworks in play.

Michael B. Cottler is a partner in the New York office of Goodwin. Natasha Daughtrey is an associate in the firm's New York office.

[1] Dep't of Health and Human Services, ASPE Issue Brief: Observations on Trends in Prescription Drug Spending (March 8, 2016) at 8, https://aspe.hhs.gov/system/files/pdf/187586/Drugspending.pdf.

[2] IQVIA Inst. for Human Data Sci., Medicines Use and Spending in the U.S. (May 2017) at 6, https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicines-use-and-spending-in-the-us.pdf.

[3] Inst. for Clinical and Econ. Review, Indication-Specific Pricing of Pharmaceuticals in the United States Health Care System 2 (March 2016) at 2, https://icer-review.org/wp-content/uploads/2015/03/Final-Report-2015-ICER-Policy-Summit-on-Indication-specific-Pricing-March-2016_revised-icons-002.pdf (hereinafter "ICER").

[4] Id.

[5] Id. at 6-7.

[6] See, e.g., Roxanne Nelson, ASCO Addresses High Cost of Cancer Drugs, Medscape (July 19, 2017), https://www.medscape.com/viewarticle/883115.

[7] See, e.g., ICER, supra note 4, at 2; Steven Pearson, et al., Indication-Specific Pricing of Pharmaceuticals in the US Healthcare System, 6 J. Comparative. Effectiveness Research 397, 400-02 (2017).

[8] Thomas Beaton, Medicaid Drug Pricing Rule May Inhibit Value-Based Contracts, HealthPayer Intelligence (Oct. 4, 2017), https://healthpayerintelligence.com/news/medicaid-drug-pricing-rule-may-inhibit-value-based-contracts; ICER, supra note 4, at 3.

[9] See American Association of Colleges of Pharmacy, Pharmacy Benefit Management (2007), https://www.pharmacist.com/sites/default/files/files/Profile_24_PBM_SDS_FINAL_090707.pdf (describing the role of a pharmacy benefit manager).

[10] See Troy Brennan, M.D., Aligning Drug Prices with Value, CVS Health (July 11, 2017), https://payorsolutions.cvshealth.com/insights/aligning-drug-prices-with-value.

[11] Steven Miller, M.D., We Have to Change How We Pay for Cancer Drugs, Express Scripts (June 15, 2015), http://lab.express-scripts.com/lab/insights/drug-options/we-have-to-change-how-we-pay-for-cancer-drugs.

[12] 21 U.S.C. § 355(j).

[13] Glaxo Inc. v. Novopharm Ltd., 110 F.3d 1562, 1568 (Fed. Cir. 1997); Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1359 (Fed. Cir. 2003).

[14] 21 U.S.C. § 355(j)(2)(A)(v).

[15] See, e.g., Jesse C. Vivian, Generic-Substitution Laws, 33 U.S. Pharmacist 30 (2008).

[16] See AstraZeneca Pharm. LP v. Apotex Corp., 669 F.3d 1370, 1379 (Fed. Cir. 2012); Warner-Lambert, 316 F.3d at 1354–56; see also Aventis Pharma Deutschland GmbH v. Cobalt Pharms. Inc., 355 F. Supp. 2d 586, 599 (D. Mass. 2005).

[17] See AstraZeneca LP v. Apotex Inc., 633 F.3d 1042, 1060 (Fed. Cir. 2010).

[18] See Aventis Pharm. Inc. v. Barr Labs. Inc., 411 F. Supp. 2d 490, 517-18 (D.N.J.), aff'd, 208 F. App'x 842 (Fed. Cir. 2006), and aff'd, 208 F. App'x 843 (Fed. Cir. 2006).

[19] 42 U.S.C. § 262.

[20] See US. Dep't of Health and Human Services Food and Drug Admin., Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Guidance for Industry (Draft guidance) 21, https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291128.pdf.

[21] See US. Dep't of Health and Human Services Food and Drug Admin., Labeling for Biosimilar Products: Guidance for Industry (Draft guidance), at 5, fn. 11. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM493439.pdf.

[22] Id. at 2 (describing the requirements for interchangeability).

[23] Richard Cauchi, State Laws and Legislation Related to Biologic Medications and Substitution of Biosimilars, NCSL.org (Sept. 1, 2017), http://www.ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-and-substitution-of-biosimilars.aspx.

[24] Amgen Inc. v. Apotex Inc., No. 15-61631-JIC, D.I. 267 (S.D. Fla. Sept. 6, 2016) (affirmed at Amgen Inc. v. Apotex Inc., No. 2017-1010, 2017 WL 5256264, at *5 (Fed. Cir. Nov. 13, 2017)).