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GSK v. Teva: The Skinny On Induced Infringement And Label Carve-Outs

by Tina Williams McKeon , April Abele Isaacson

An update posted on February 10 provides the most recent update on this matter.

Statutory Basis For Label Carve-Outs

Section viii of the Hatch-Waxman Act permits an Abbreviated New Drug Application (ANDA) applicant to obtain FDA approval to market a generic version of a drug for a non-patented use where the reference listed drug (RLD) has multiple indications, not all of which are covered by a method-of-use patent.[1] To meet the requirements of this provision, the generic manufacturer must file an ANDA with a "section viii statement" for indications not covered by claims of Orange Book-listed method of use patents.[2] If an ANDA applicant submits a section viii statement, it must propose labeling for its generic product that "carves out" the patented methods of use. [3] The FDA will approve the proposed labeling only if (a) the proposed carve-out label does not overlap with the "use code" listed in the Orange Book for the product [4] and (b) the FDA determines sale of the drug with the modified labeling will not "render the proposed drug product less safe or effective than the listed drug for all remaining, nonprotected conditions of use."[5] These section viii carve-outs, or "skinny labels," however, do little to dissuade substitution of an AB-rated[6] generic drug for all approved indications of a branded drug, including the carved-out patented indication, resulting in ensuing patent litigation based on induced infringement.

Induced Infringement

The issue of induced infringement in this context was recently addressed by the Federal Circuit in *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*[7] In 2007, Teva launched its AB-rated generic drug with a skinny label that stated, "Carvedilol is indicated to reduce cardiovascular mortality in clinically stable patients who have survived the acute phase of myocardial infarction and have a left ventricular ejection fraction of ≤ 40% (with or without symptomatic heart failure)."[8] Teva marketed the product as a generic of GSK's branded drug, COREG®.[9] In 2008, a reissue of a follow-on patent directed to treatment of congestive heart failure using carvedilol in combination with other agents was listed in the Orange Book.[10] In 2011, the FDA subsequently required Teva to amend the label to be identical to the GSK approved label, including the patented indication for treatment of heart failure.[11] In 2014, GSK sued Teva for infringing claims in the reissue patent.[12] Teva argued in the jury trial that it could not be found to have induced infringement at least until the time of the amended label

because the patented use was carved out on the skinny label. Teva further argued that GSK had to prove Teva's communications caused the direct infringement.[13] Although the jury determined that Teva willfully induced infringement during the periods before and after amendment of the label and awarded damages of $235.5 million, the court granted Teva's motion for judgment as a matter of law (JMOL) and held that GSK failed to prove Teva caused direct infringement during either period because the infringement was caused by non-Teva factors (e.g., prior knowledge of cardiologists regarding the uses for carvedilol). GSK appealed the JMOL.[14]

On appeal, GSK argued that Teva's promotion of its generic product as being the same as the branded product, along with its marketing with knowledge of potential infringing uses constituted substantial evidence of active inducement.[15] Judges Newman and Moore agreed with GSK, reversing the JMOL and remanding for entry of the jury verdict. Chief Judge Prost, the third member of the panel, wrote a strong dissent and accused the majority of misapplying the law and misconstruing the facts. She framed the question as whether Teva infringed by marketing its generic carvedilol for an unpatented use through a skinny label and reasoned Teva did not infringe in view of Congress's intent to allow such use. Chief Judge Prost further reasoned that nothing changed in the marketplace when the label was amended, thus Teva's actions could not be said to be inducing infringement even after the label was amended. She also asserted that GSK failed to show any evidence of inducement by Teva under either the skinny or amended label because doctors did not rely on the labels, and AB-rated generics were substituted automatically at the pharmacy without the doctors' knowledge. [16]

Future of Skinny Labels

Teva has since filed a petition for rehearing *en banc* to answer two questions: (1) can a generic manufacturer induce infringement based only on a skinny label and product materials that identify the generic product as an equivalent of a branded product without any mention of the patented use and (2) if found to have encouraged infringement, can the generic manufacturer be found to have induced in the absence of a direct infringer seeing the encouragement?

Eight amicus briefs were filed in support of rehearing. Former Rep. Henry Waxman (D-Calif.), who cosponsored the Hatch-Waxman Act, argued the majority's decision "is flatly inconsistent with the language of the Act and congressional intent."[17] Waxman stated that, if the decision is left in place, "it will have a devastating impact on the Hatch-Waxman Act's generic drug program, which has saved patients, the federal government, and other payers trillions of dollars."[18] The Federal Circuit invited GSK to respond to Teva's *en banc* petition. GSK's response is due January 29.

We expect a decision regarding the petition for rehearing sometime after January 29, and, given the concern generic manufacturers have regarding the threat to routine section viii carve-outs, we anticipate Teva will file a petition for certiorari for Supreme Court review.

Issues regarding section viii carve-outs remain unresolved in the context of small molecules, and use of

carve-outs has yet to be litigated in the context of biosimilars. The FDA previously signaled an intent to permit carve-outs in biosimilars, and, in February 2020, the FDA issued draft guidance which makes it explicitly clear that carve-outs are indeed permissible for biosimilars.[19] The outcome of the *GSK v. Teva* case could prove informative as to carve-out use with biosimilars and the proofs required for inducing infringement.

Please contact the authors with any questions and stay tuned for updates regarding this important topic.

Footnotes

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[1] *See* 21 U.S.C. § 355(j)(2)(A)(viii).

[2] *Id.*

[3] *See Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S* , 566 U.S. 399, 406 (2012).

[4] For an approved New Drug Application (NDA), the NDA holder that owns a patent covering an FDA-approved method of using the drug must submit to the FDA a brief "description of the patented method of use," known as a "use code." *See* 21 C.F.R. § 314.53(c)(2)(ii)(P)(3), (f)(1)(i)(B).

[5] *See* 21 C.F.R. § 314.127(a)(7); *see also Caraco*, 566 U.S. at 406.

[6] "AB rating" is an FDA coding system "allow[ing] users to determine quickly whether the Agency has evaluated a particular approved product . . . as therapeutically equivalent to other pharmaceutically equivalent products (first letter) and to provide additional information on the basis of FDA's evaluations (second letter)." Food & Drug Admin., U.S. Dep't of Health & Hum. Servs. , Approved Drug Products with Therapeutic Equivalence Evaluations, at xii-xiii (40th ed. 2020) (FDA Orange Book).

[7] 976 F.3d 1347 (Fed. Cir. 2020).

[8] *Id.* at 1350.

[9] *Id.*

[10] *Id.* at 1362-63.

[11] *Id.* at 1350.

[12] *Id.*

[13] *Id.*

[14] *Id.* at 1351-52.

[15] *Id.* at 1352.

[16] *Id.* at 1358.

[17] *See* Brief of Amicus Curiae Former Congressman Henry A. Waxman in Support of Petition for Rehearing En Banc [Corrected] at 1-2, *GlaxoSmithKline LLC*, Nos. 18-1976, 18-2023 (Fed. Cir. Dec. 30, 2020).

[18] *Id.* at 2.

[19] Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed (2020) (draft guidance); *see also* Ctr. for Drug Evaluation & Rsch., U.S. Food & Drug Admin., Biosimilarity and Interchangeability: Additional Draft Q&As on Biosimilar Development and the BPCI Act (2020).