Nos. 18-1976, 18-2023

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

GLAXOSMITHKLINE LLC and SMITHKLINE BEECHAM (CORK) LIMITED,

*Plaintiffs-Appellants*,

v.

TEVA PHARMACEUTICALS USA, INC.,

*Defendant-Cross-Appellant.*

Appeal from the U.S. District Court for the District of Delaware,
No. 1:14-cv-00878-LPS-CJB (Stark, C.J.)

# BRIEF FOR THE ASSOCIATION FOR ACCESSIBLE MEDICINES AS *AMICUS CURIAE* IN SUPPORT OF REHEARING EN BANC

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December 16, 2020

# CERTIFICATE OF INTEREST

Counsel for *amicus curiae* Association for Accessible Medicines certifies:

1. The full name of every party or amicus represented by me is:

Association for Accessible Medicines.

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

See above.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the amicus curiae represented by me are:

Not applicable.

4. The names of all law firms and the partners or associates that appeared for the amicus curiae now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

Not applicable.

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal is:

*GlaxoSmithKline LLC et al. v. Glenmark Pharmaceuticals Inc., USA*, No. 1:14-cv-877 (D. Del.).

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| | |
|---|---|
| AAM | Association of American Medicines |
| ANDA | Abbreviated New Drug Application (generic drug application) |
| CHF | Congestive heart failure |
| FDA | Food and Drug Administration |
| FDCA | Food, Drug and Cosmetic Act |
| GSK | Plaintiffs-Appellants GlaxoSmithKline LLC and SmithKline Beecham (Cork) Limited |
| Hatch-Waxman | Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (formally, Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585) |
| Section viii | 21 U.S.C. § 355(j)(2)(A)(viii) |
| Teva | Defendant-Cross-Appellant Teva Pharmaceuticals USA, Inc. |

## INTEREST OF *AMICUS CURIAE*[1]

The Association for Accessible Medicines (AAM) is a nonprofit, voluntary association representing manufacturers and distributors of generic and biosimilar medicines and bulk active pharmaceutical chemicals, as well as suppliers of other goods and services to the generic pharmaceutical industry. AAM's members provide patients with access to safe and effective generic and biosimilar medicines at affordable prices. AAM's core mission is to improve the lives of patients by providing timely access to safe, effective, and affordable prescription medicines. Generic drugs constitute 90% of all prescriptions dispensed in the United States, yet account for only 22% of total drug spending. AAM regularly participates in litigation as *amicus curiae*.

*Amicus* and its members have a significant interest in the issues raised by Teva's petition for rehearing en banc: namely, whether generic pharmaceutical manufacturers can be held liable for inducing infringement when (1) their FDA-approved labeling excludes patented uses of the drug

[1] No counsel for any party authored this brief in any part, and no party, counsel, or person other than *Amicus*, its members, and its counsel contributed money to fund the preparation and submission of this brief, and all parties consent to the filing of this brief. *See* Fed. R. App. P. 29(a)(4)(E).

consistent with the Federal Food, Drug and Cosmetic Act (FDCA) and (2) they make truthful statements that their generics have been found by the FDA to be therapeutically equivalent to a brand-name drug. By threatening massive damages whenever pharmacists fill prescriptions with generics for patented off-label uses—even when generics purposely carve those uses out of FDA-approved labeling and do not encourage off-label use—the panel's decision nullifies the skinny-label regime Congress adopted in the FDCA.

## INTRODUCTION

The panel's erroneous ruling in this case is of enormous concern to AAM and its members, and it is already threatening to deprive patients of low-cost generic medicines. The decision takes elements that are, by definition, present in every carve-out case and holds that they can suffice to make inducement claims jury-worthy. As commenators have already recognized, the panel decision exposes generic manufacturers to punishing liability "even if they have followed the law."[2] Review is urgently warranted.

Congress made the policy judgment that generic manufacturers should be able to bring their lower-cost alternatives to market even if the

[2] Dani Kass, *Generics Worry Fed. Circ. Blew Up 'Routine' Labeling Practice*, Law360 (Oct. 7, 2020), https://tinyurl.com/yxsjbhpk.

brand-name drug manufacturer still holds patents on select uses. Congress's solution, adopted as part of the 1984 Hatch-Waxman Amendments, was to create a "skinny-label" regime in which the generic manufacturer could carve out patented uses from its label and enter the market with its product labeled for non-patented uses. Since 1984, patients (and the taxpayers who fund public health programs like Medicare) have saved billions of dollars by obtaining generic versions of expensive drugs for unpatented uses. Skinny labels have proven particularly important for generic competitors of blockbuster drugs where patent owners frequently seek to extend their monopolies by obtaining seriatim method-of-use patents.

As commentators have already recognized, the panel decision undermines Congress's skinny-label regime—and with it a major pathway for patients to obtain low-cost generics for uses not subject to any valid patent. According to the panel majority, a generic manufacturer can potentially be liable for inducing infringement for a use expressly carved out of its label merely because it accurately describes its product as therapeutically equivalent to the branded drug. The panel reached this conclusion notwithstanding the fact that equivalence determinations are based on *the labeled uses*—and that patented uses may comprise only a small

fraction of generics' sales. That definition of inducement makes a dead letter of Congress's skinny-label regime because its very purpose is to bring equivalent generics to market for non-patented uses.

By turning what was supposed to be a safe harbor into dangerous waters, the panel decision will greatly hinder the development of low-cost generic medicines. And the ultimate losers will be the patients and taxpayers of this country who will be deprived of cost-effective medicines. Generic manufacturers will not take the risk of bringing generics to market if they may be subjected to enormous damages just for accurately identifying their product as a generic equivalent with a statutorily authorized labeling carve-out.

Take this case. Teva was subjected to a $234 million judgment across the skinny- and full-label periods, simply for using a template skinny label the FDA *itself* provided, and then repeating the therapeutic equivalence rating the FDA *itself* had determined. Because Teva made only $74 million in sales during those periods, "it was ultimately more costly for Teva to sell an unpatented drug for unpatented uses than it would have been to stay out of the market altogether." Dissent 33.

Indeed, lawsuits are already being filed using—and expanding—the erroneous theory of inducement liability that the panel applied. One has even been threatened against a *pre-launch* generic. Today, more and more drugs—especially cancer drugs—are approved (and receive patents) for many indications, any of which could result in off-label usage. Thus, the risk of inducement liability under the panel's new rule will only grow.

To secure the patent regime that Congress chose, and to ensure that the American public has access to generic and biosimilar medicines as Congress intended, this Court must act now to correct the panel's ruling.

## ARGUMENT

### I. The Skinny-Label Provision Lets Manufacturers Carve Out Patented Uses To Speed The Availability Of Low-Cost Generic Drugs To Patients And Thereby Save The Public Billions of Dollars.

In the Hatch-Waxman Amendments, Congress made the policy decision to let generics "'seek approval for less than all of th[e] indications'" for which a brand-name was approved. *Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625, 630 (Fed. Cir. 2015). This way, brands could not use new method-of-treatment patents to block competitors from selling generics for old, unpatented methods of use. *See Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 414-5 (2012). Congress thus

allowed generic applicants to inform the FDA that they seek approval only for unpatented uses. 21 U.S.C. § 355(j)(2)(A)(viii). This path gives generics an alternative to challenging patents via paragraph IV certifications, which typically trigger litigation and—in some instances—a thirty-month stay of approval. *Id.* § 355(j)(5)(B)(iii).

Congress understood that "enabl[ing] the sale of drugs for non-patented uses … would result in some off-label infringing uses." *Takeda*, 785 F.3d at 631, 633. Not least because, when physicians prescribe drugs for patented uses, pharmacies often fill those prescriptions with generics. However, the law's sponsors accepted that tradeoff to bring generics to market "as soon as the [first] patent expires." 130 Cong. Rec. 23,764 (1984) (statement of Sen. Hatch); *see* H.R. Rep. No. 98-857(I), at 21-22 (1984), *as reprinted in* 1984 U.S.C.C.A.N. 2647, 2654-55 (discussing skinny-label regime).

The skinny label provisions have saved patients and taxpayers billions of dollars. Take the example of Crestor, a branded drug used to treat high cholesterol. Before the entry of generics, patients and payors spent $6.2

billion annually on Crestor.[3] AstraZeneca's patent on the compound expired in 2016, but AstraZeneca had two method-of-use patents that did not expire until 2018 and 2022.[4] Because the generics were able to carve out those patented uses and obtain a skinny label from the FDA, they were able to enter the market in 2016 rather than waiting until 2022.[5] Patients benefitted immediately from the introduction of generics—the average wholesale cost for the generics was 70% lower than for the branded drug.

## II. The Panel Decision Renders The Skinny-Label Provision A Nullity And Cannot Be Reconciled With This Court's Inducement Precedents.

The panel decision directly conflicts with Hatch-Waxman. It turns Congress's decision to allow skinny labels against itself. As Chief Judge Prost explained in her dissent, Teva sought FDA approval to sell a generic equivalent to GSK's Coreg®, and carved out an indication for congestive heart failure (CHF) that was subject to a method patent. Dissent 7-9.

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[3] Eric Palmer, *Nexium, AstraZeneca*, FiercePharma (Oct. 28, 2013), https://www.fiercepharma.com/special-report/nexium-astrazeneca.

[4] FDA, *Petition Denial Response – Final* 19 n.59, Dkt. No. FDA 2016-P-1485 (July 20, 2016).

[5] *Id.* at 1.

Nonetheless, the panel held that a jury properly found that Teva induced infringement, and thus, was liable for hundreds of millions of dollars in lost profits and royalties. The panel noted that Teva described its drug as bioequivalent to Coreg®, and that Teva "knew" that some CHF prescriptions would be filled with its product notwithstanding the carved-out label. Maj. 16. In the panel's view, Teva was liable because "[t]he jury received evidence that Teva's promotional materials referred to Teva's carvedilol tablets as AB rated equivalents of" Coreg, and "doctors … read" manufacturers' publications. Maj. 12, 17.

That reasoning contradicts Hatch-Waxman and undermines both the skinny-label regime and this Court's precedents on inducement. Congress did not design the skinny-label regime as a trap where the very label Congress authorized serves as the basis for inducement liability. The very point of permitting carve-outs is to let a generic manufacturer sell a bioequivalent drug for non-patented uses. Indeed, the notion that therapeutic equivalence for labeled uses amounts to inducement of carved-out patented uses is particularly misguided since the Orange Book *itself* states that AB-equivalence extends only to labeled uses. FDA, *Orange Book Preface* § 1.2 (40th ed. current as of Feb. 13, 2020), https://www.fda.gov/

drugs/development-approval-process-drugs/orange-book-preface ("[Therapeutic equivalents] can be expected to have the same clinical effect and safety profile when administered to patients *under the conditions specified in the labeling*." (emphasis added)). If Teva's actions suffice to make out an inducement claim, then no carve-out is safe from litigation.

Nor is it any answer to say, as the panel did, that Teva was aware that doctors might prescribe its generic for CHF. It is certainly true that pharmacies frequently substitute generics for branded drugs, but this Court has already concluded that such "market realities" cannot undergird inducement claims. *AstraZeneca Pharm. LP v. Apotex Corp.*, 669 F.3d 1370, 1380 (Fed. Cir. 2012). And for good reason: inducement requires "affirmative steps" by the defendant, not passive awareness. *Glob.-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 760 (2011); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003) (inducement requires defendant to "promote or encourage doctors to infringe").

Indeed, this Court made exactly this point in *Takeda*, in words that could have (and should have) been written for this opinion. "Given the statutory scheme" Hatch-Waxman created, this Court held there that non-encouraging "label language cannot be combined with speculation about how

physicians may act to find inducement." 785 F.3d at 632. Otherwise, courts could "too easily transform that which we have held is 'legally irrelevant' … into induced infringement." *Id.* (citation omitted).

## III. The Panel Decision Will Deprive Patients of Low-Cost Generic Medicines.

The panel's attack upon the skinny-label regime will inflict harm on the millions of American patients who benefit from cost-effective generic drugs. The decision provides a road-map for bringing inducement claims that will chill generic development—even for manufacturers that "did everything right," as Teva did here. Dissent 8. With a single use patent, brand-name manufacturers can now threaten inducement suits to scare generics out of the market, even for non-patented uses. If allowed to stand, the panel decision "would confer substantial additional rights on pioneer drug patent owners that Congress quite clearly did not intend to confer." *Warner-Lambert*, 316 F.3d at 1359. For patients, this means one thing: higher prices.

Imagine a generic manufacturer considering whether to bring a generic to market. The manufacturer could file an ANDA seeking to bring the generic to market when the brand-name drug's compound patent expires—just like Teva. It could carve-out a subsequent method-of-use patent and use the label provided by the FDA—just like Teva. Appx1234-

1235. It could then carefully sell its generic without encouraging the carved-out use—just like Teva. Yet playing by the rules that Congress set out could expose that manufacturer to an enormous jury verdict—just like Teva. Generic manufacturers will simply be unwilling to take that risk if the protection that Congress provided is diluted. And as low-cost generics drop out of markets or fail to enter them, higher prices will follow.

Industry observers immediately recognized the boon the panel decision gives brand-name manufacturers and the harm it poses for patients. One said the panel decision "essentially undermines Congress' directive that generics are permitted to carve-out indications from their generic labels without facing liability" and "effectively upset[s] the expected scope of liability for most generic launches with skinny labels."[6] The decision therefore poses "a big threat tha[t] any individual generic must consider before entering the market."[7] Other observers have reached similar conclusions. *See, e.g.*, Kyu Yun Kim et al., *A Major Decision Evaluating the*

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[6] Zachary Silbersher, *Can Amarin benefit from the GSK v. Teva decision regarding induced infringement for off-label sales?*, Markman Advisors (Oct. 7, 2020), https://www.markmanadvisors.com/blog/2020/10/7/can-amarin-benefit-from-the-gsk-v-teva-decision-regarding-induced-infringement-for-off-label-sales.

[7] *Id.*

*Effect of a Skinny Label in a Post-Launch, Non-Hatch Waxman Litigation, Jury Trial World*, Finnegan (Oct. 13, 2020), https://tinyurl.com/y2x987xu (labeling the case "a major decision" that "will likely have practical implications"). Practitioners in the field agree: generics now have "every reason to be afraid that they're going to be facing lawsuits even if they have followed the law." Kass, *supra*.

Indeed, the panel decision has already transformed brand companies' legal strategies. One prominent example is Amarin, manufacturer of Vascepa® (icosapent). In September 2020, this Court held that Amarin's patents for treating high trigycerides were invalid, paving the way for Hikma's launch of an FDA-approved generic icosapent. *Amarin Pharma, Inc. v. Hikma Pharm. USA Inc.*, 819 F. App'x 932 (Fed. Cir. 2020). Soon after the panel's decision here, Amarin's President and CEO acknowledged on an earnings call that Amarin personnel "have been tracking the GSK versus Teva case for some time," and teased Amarin's new "legal options" in its fight against generic competitors. Motley Fool Transcribing, *Amarin (AMRN) Q3 2020 Earnings Call Transcript* (Nov. 5, 2020), https://tinyurl.com/y2dd8wrp. On November 30, Amarin filed another suit against generic manufacturer Hikma for allegedly inducing infringement of its

cardiovascular patents, relying on the panel's holding in this case, even though Hikma had explicitly carved out that indication. Compl. ¶¶ 121-143, *Amarin Pharma, Inc. v. Hikma Pharmaceuticals USA Inc.*, No. 1:20-cv-01630 (D. Del. filed Nov. 30, 2020), https://tinyurl.com/y4jzgf88.

Amarin's suit looks eerily familiar. Like Teva, Hikma stands accused of inducement solely because it allegedly knew its generic *could* be prescribed for the patented cardiovascular indication—notwithstanding that it received approval of a skinny label—and because it noted receiving a generic AB-rating from the FDA. *Id.* ¶¶ 12, 95-113. If successful, generics of Vascepa® could be pulled off the market, costing patients hundreds of millions of dollars annually.

Nor will the woes end with generics already on the market. One AAM member recently received infringement contentions regarding a *pending* ANDA. The ANDA's proposed label carves out all mention of the claimed use. Yet the brand-name plaintiff asserts the *potential* for inducement, based on the generic's *anticipated* AB-equivalent rating and physicians' *historical* prescription practices. Not only does this threatened action indicate an improper expansion of the panel decision's logic to pre-launch generics, it also illustrates how thoroughly the panel decision eviscerates the

skinny-label provision. Brand-name manufacturers can always allege that a generic will obtain an AB rating, and that doctors will prescribe the generic for all the brand-name's uses. If those allegations are sufficient, carving out patented indications will become meaningless, and millions of patients and taxpayers will be deprived of more affordable medicines.

## CONCLUSION

*Amicus* respectfully requests that the Court grant Teva's petition for rehearing en banc.

Respectfully submitted,

Dated: December 16, 2020

*/s/ Matthew S. Hellman*

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## CERTIFICATE OF SERVICE

I hereby certify that on December 16, 2020, I caused the foregoing brief to be electronically filed with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit by using the CM/ECF system, which caused a copy of the foregoing to be delivered by electronic means to counsel of record.

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## CERTIFICATE OF COMPLIANCE

I hereby certify that:

1. This Brief complies with the type-volume limitation of Fed. R. App. P. 29(b)(4) because this Brief contains 2,590 words, excluding the parts of the Brief exempted by Fed. R. App. P. 32(f) and Federal Circuit Rule 32(b).

2. This Brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this Brief has been prepared in a proportionately spaced typeface using Microsoft Office Word 2016 in Century Expanded LT Std, Font Size 14.

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