United States Court of Appeals for the Federal Circuit

ELI LILLY AND COMPANY AND TRUSTEES OF PRINCETON UNIVERSITY,
Plaintiffs-Appellees,

v.

TEVA PARENTERAL MEDICINES, INC. AND BARR LABORATORIES, INC.,
Defendants-Appellants,

and

APP PHARMACEUTICALS, LLC,
Defendant-Appellant.

2011-1561, -1562

Appeals from the United States District Court for the District of Delaware in consolidated Case Nos. 08-CV-0335, 08-CV-0384, 08-CV-0860, and 09-CV-0272, Chief Judge Gregory M. Sleet.

ELI LILLY AND COMPANY AND TRUSTEES OF PRINCETON UNIVERSITY,
Plaintiffs-Appellees,

v.

APP PHARMACEUTICALS, LLC,
Defendant-Appellant.

2012-1037

Appeal from the United States District Court for the District of Delaware in Case No. 11-CV-0628, Chief Judge Gregory M. Sleet.

Decided: August 24, 2012

ADAM L. PERLMAN, Williams & Connolly, LLP, of Washington, DC, argued for plaintiff-appellee. With him on the brief were BRUCE R. GENDERSON, KANNON K. SHANMUGAM, DOV P. GROSSMAN, and DAVID M. KRINSKY. Of counsel was ELLEN E. OBERWETTER.

JOHN C. ENGLANDER, Goodwin Procter, LLP, of Boston, Massachusetts, argued for defendants-appellants. With him on the brief were DARYL L. WIESEN and EMILY L. RAPALINO. Of counsel on the brief were ERIC H. YECIES and MICHAEL B. COTTLER.

Before LOURIE, DYK, and WALLACH, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Appellants Teva Parenteral Medicines, Inc., Barr Laboratories, Inc., and APP Pharmaceuticals, LLC appeal from the judgment of the United States District Court for the District of Delaware holding that U.S. Patent 5,344,932 (the "'932 patent") is not invalid for obviousness-type double patenting. *See Eli Lilly & Co. v. Teva Parenteral Meds. Inc.*, No. 08-335-GMS, 2011 U.S. Dist.

LEXIS 83124, 2011 WL 3236037 (D. Del. July 28, 2011). We affirm.

BACKGROUND

This patent infringement dispute concerns applications filed by several generic pharmaceutical manufacturers seeking regulatory approval to market generic formulations of the chemotherapy agent pemetrexed. To begin, we outline the necessary background information and procedural history, as set forth below.

A. Antifolate Drugs

Folates, which include the B vitamin folic acid and its derivatives,[1] play a critical role in nucleic acid synthesis within human cells and, as such, are required for cell growth and division. To that end, numerous cellular enzymes recognize and process folates—some folate-specific enzymes such as dihydrofolate reductase ("DHFR") and glycinamide ribonucleotide formyltransferase ("GARFT") catalyze biochemical reactions important for making both DNA and RNA, while others such as thymidylate synthetase ("TS") selectively affect DNA production.[2]

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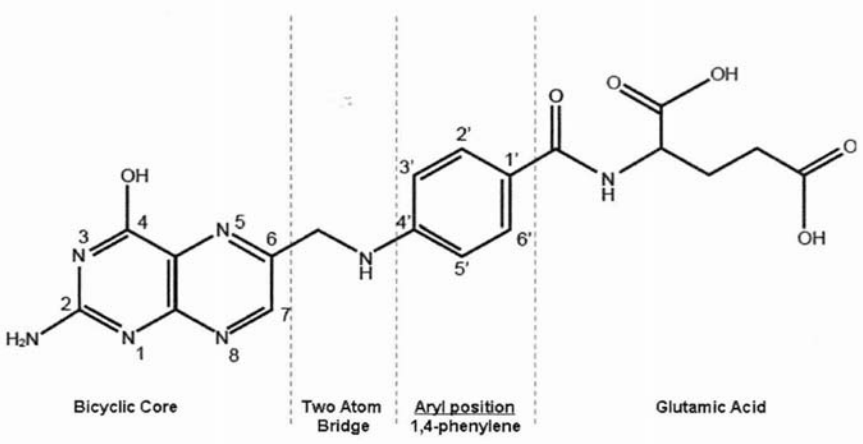
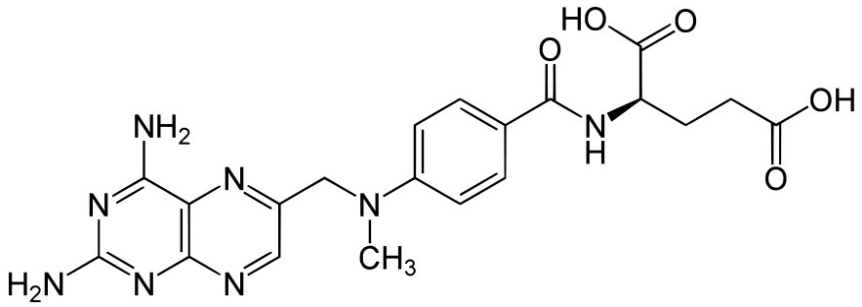
[1] Although folic acid itself predominates in most dietary supplements and fortified foods, the compound naturally occurs in various other chemical forms including folic acid salts and esters. For convenience, we refer to folic acid and such related compounds collectively as "folates."

[2] Purines and pyrimidines are key building blocks in the production of both RNA and DNA. DHFR and GARFT participate in global purine synthesis, so those enzymes affect both DNA and RNA production. In contrast, TS serves only in the production of deoxythymidine monophosphate, a pyrimidine nucleotide that is incorporated into DNA but not RNA.

Given the key role of folates in DNA synthesis, and thus in cellular replication, folate metabolism presents an attractive target for cancer treatments because cancerous cells characteristically exhibit rapid, unchecked division and proliferation. Accordingly, researchers and physicians have developed numerous compounds, known as "antifolates," intended to inhibit one or more of the folate-specific enzymes necessary for DNA synthesis. Structurally analogous to natural folates, antifolates induce initial recognition by one or more of the folate-specific enzymes yet contain important structural differences that prevent the target enzyme from carrying out its normal function. For example, the chemical structure of folic acid is represented below—highlighting key structural features including the bicyclic core, bridge region, aryl position, and glutamic acid domain—along with the closely related structure of methotrexate, a well-known antifolate that was first introduced around 1950.



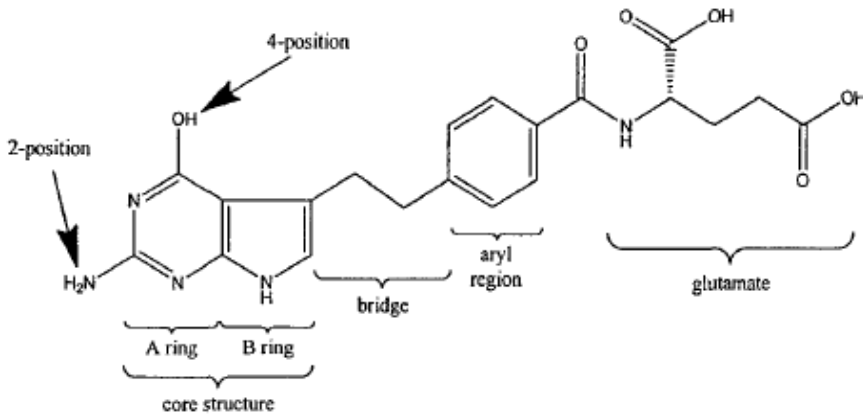
Folic Acid



Methotrexate

Methotrexate is used as a chemotherapy agent for treating certain cancers, including leukemias, lymphomas, and osteosarcoma, among others. In addition to its anticancer effects, however, methotrexate, like many antifolates, exhibits significant toxicity due to deleterious effects on non-cancerous, healthy cells. Such toxicity is thought to arise at least in part because methotrexate primarily inhibits DHFR and therefore substantially impairs DNA *and* RNA synthesis. While DNA synthesis is of principal importance for actively dividing cells (*e.g.*, cancer cells), ongoing RNA synthesis is necessary for essentially all living cells in the body. Methotrexate and other antifolate drugs that inhibit both the DNA and RNA synthesis pathways are thus prone to undesirable off-target effects.

In the 1980s, researchers sought to develop antifolates capable of inhibiting TS, which would selectively impede DNA synthesis and presumably mitigate the toxicity issues associated with methotrexate and other then-existing antifolates. One such effort led by Prof. Edward Taylor, a chemist at Princeton University, yielded pemetrexed, the antifolate at the heart of this appeal:



Pemetrexed

As with methotrexate, pemetrexed exhibits some structural similarity to folic acid. One key difference that distinguishes pemetrexed from folic acid and methotrexate is that pemetrexed contains a pyrrolo[2,3-d]pyrimidine bicyclic core, characterized by a five-member ring fused with a six-member ring, rather than the dual six-member rings found in the pteridine cores of folic acid and methotrexate. After synthesizing pemetrexed, the Princeton group collaborated with researchers at Eli Lilly to test the new compound for antifolate activity, and the results soon revealed that pemetrexed acts as a potent inhibitor of TS. Princeton and Eli Lilly (together, "Lilly") thereafter began exploring for related compounds with similar activity as TS inhibitors and pursuing preclinical and clinical studies to evaluate promising candidates for therapeutic use.

Among the many pemetrexed-related compounds that were developed and tested, pemetrexed itself proved to be the best therapeutic candidate and ultimately won FDA approval in 2004 for use in treating mesothelioma and then in 2008 for treatment of non-small cell lung cancer.

Lilly manufactures and distributes pemetrexed under the brand name Alimta®.

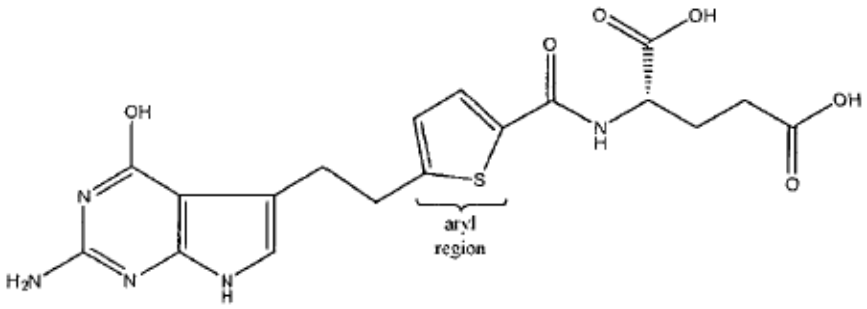
B. Lilly's Patents

In conjunction with their antifolate research, the inventors filed U.S. patent application 07/448,742 (the "'742 application") on December 11, 1989. The '742 application disclosed and claimed pemetrexed as well as a broader group of related antifolates containing pemetrexed's characteristic core structure. The '742 application, though itself eventually abandoned, founded a family of related applications that ultimately yielded the three patents at issue in this appeal.

The '932 patent issued on September 6, 1994, from an application filed on March 22, 1991, claiming priority from the '742 application through a series of continuations. Claim 3 of the '932 patent claims pemetrexed. Claims 1, 2, and 7 are generic, Markush-style claims that encompass pemetrexed as well as other structurally related antifolates.

U.S. Patent 5,028,608 (the "'608 patent") issued on July 2, 1991, from an application filed on May 24, 1990, as a continuation-in-part of the '742 application. The '608 patent claims, *inter alia*, an antifolate (the "'608 Compound") that differs from pemetrexed only in its aryl region—the '608 Compound contains a five-member thiophene ring in place of pemetrexed's six-member benzene ring.[3]

[3] The parties use the expressions "thienyl group" and "phenyl group"; accordingly, we will also.

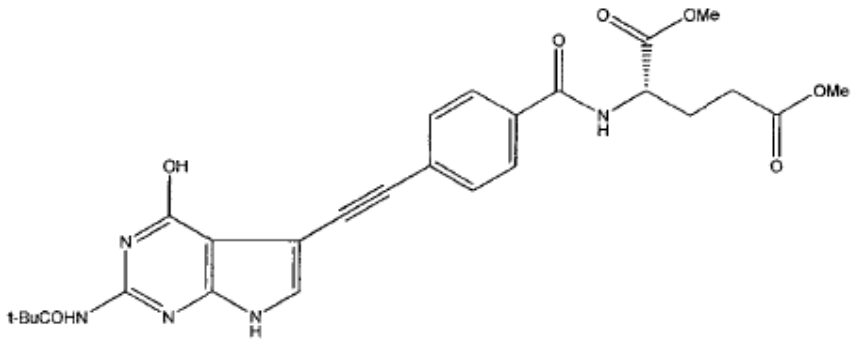


The '608 Compound

U.S. Patent 5,248,775 (the "'775 patent") issued on September 28, 1993, from an application filed January 31, 1992, as a continuation-in-part of the application that led to the '932 patent. The '775 patent discloses a family of chemical intermediates that can be used to make a variety of antifolates, including pemetrexed, that contain a pyrrolo[2,3-d]pyrimidine bicyclic core. Among others, the '775 patent claims a compound (the "'775 Intermediate") that is used as an intermediate in one method for making pemetrexed. The '775 Intermediate differs from pemetrexed in having a carbon-carbon triple bond in its bridge region and three protecting groups at substituent positions in its core and glutamate domains.[4] In addition,

[4] Protecting groups are selectively reversible chemical modifications often used to prevent unwanted side reactions during multistep organic syntheses. In general, protecting groups are introduced at one or more particularly reactive positions in a complex molecule to stabilize or "protect" those parts of the molecule during later chemical manipulation of other target sites. Once a desired modification has been achieved elsewhere in the molecule, the protecting groups can be removed to reconstitute a reactive substituent at each protected position. The '775 Intermediate contains a pivaloyl protecting group (denoted "*t*-BuCO") in its core region and two methyl ester protecting groups (denoted "OMe") in its glutamate domain.

Examples 6 and 10 of the '775 patent disclose reduction and hydrolysis reactions, respectively, that could together be used to derive pemetrexed from the '775 Intermediate. '775 patent col. 9, l. 59 – col. 10, l. 5; col. 12, ll. 51–66.



The '775 Intermediate

The '932, '608, and '775 patents were assigned to the Trustees of Princeton University and exclusively licensed to Eli Lilly. The '608 and '775 patents have expired, but the '932 patent remains in effect until July 24, 2016, due to a patent term extension of over four years to compensate for delays in the regulatory approval of Alimta®. *See* 35 U.S.C. § 156. Lilly holds a further six months of market exclusivity over pemetrexed pursuant to 21 U.S.C. § 355a.

C. District Court Proceedings

Teva Parenteral Medicines, Inc., Barr Laboratories, Inc., and APP Pharmaceuticals, LLC (collectively, "Teva") filed abbreviated new drug applications ("ANDAs") seeking approval to manufacture and sell generic versions of Alimta® before the expiration of the '932 patent. Those ANDAs each included a Paragraph IV certification asserting that the '932 patent was invalid, unenforceable, or would not be infringed by the proposed generic products.

See 21 U.S.C. § 355(j)(2)(A)(vii)(IV). In response, Lilly brought suit in the United States District Court for the District of Delaware, alleging infringement of claims 1, 2, 3, and 7 of the '932 patent pursuant to 35 U.S.C. § 271(e)(2)(A).

During the proceedings, Teva conceded infringement but maintained that the asserted claims of the '932 patent were invalid for obviousness-type double patenting over two earlier-issued claims: (1) claim 3 of the '608 patent, which claims the '608 Compound, and (2) claim 7 of the '775 patent, which claims the '775 Intermediate.

Regarding the '608 Compound, Teva presented evidence that various antifolates known at the time of the invention contained a phenyl group in the aryl position, and Teva contended that it would have been obvious to incorporate a phenyl group into the '608 Compound consistent with such "conventional wisdom" in the field. As to the '775 Intermediate, Teva argued that the asserted claims of the '932 patent constitute a use for the '775 Intermediate—*i.e.*, synthesizing pemetrexed—that had already been disclosed in the specification of the earlier-issued '775 patent, rendering such claims invalid for obviousness-type double patenting. In addition, Teva argued that even ignoring the specification of the '775 patent, an ordinarily skilled chemist presented with the '775 Intermediate immediately would have recognized pemetrexed as an obvious potential end product.

Following a bench trial, the district court rejected Teva's arguments and held that claims 1, 2, 3, and 7 of the '932 patent were not invalid for obviousness-type double patenting over either the '608 Compound or the '775 Intermediate. *Eli Lilly*, 2011 WL 3236037, at *2–4. Specifically, the district court rejected Teva's "focus[] only on the aryl region of the ['608 Compound] in isolation,"

finding persuasive other evidence indicating that one of skill in the art would have pursued changes outside of the aryl region to improve TS inhibition and would have avoided introducing a phenyl group into the '608 Compound based on previous reports of toxicity with analogous antifolate structures. *Id.* at *4. The district court also declined to hold the asserted claims invalid over the '775 Intermediate. The court held (1) that the '932 patent "does not claim the use of the ['775 Intermediate]," so the teachings from the '775 patent's specification were inapplicable to its obviousness-type double patenting analysis, and (2) that pemetrexed would not have been obvious from the structure of the '775 Intermediate because, among many possible choices, a person of ordinary skill would not have made the structural changes necessary to derive pemetrexed. *Id.* at *2–3.

Accordingly, the district court entered a final judgment in Lilly's favor and enjoined approval of Teva's proposed generic pemetrexed products until after the expiration of Lilly's exclusive rights on January 24, 2017. *Eli Lilly & Co. v. Teva Parenteral Meds. Inc.*, Nos. 08-335-GMS, 08-384-GMS, 08-860-GMS, and 09-272-GMS (D. Del. Aug. 22, 2011) (Am. Final J. Order), ECF No. 115. Teva timely appealed, and we have jurisdiction under 28 U.S.C. § 1295(a)(1).[5]

[5] After trial, individual appellant APP Pharmaceuticals supplemented its ANDA to add a further Paragraph IV certification relating to a particular pemetrexed dosage form. Appellees initiated a new infringement suit to address APP's supplemental ANDA filing, and the parties agreed to be bound in that action by any judgment in the antecedent litigation. Accordingly, following its August 22, 2011, judgment in favor of Lilly, the district court entered a stipulated judgment against APP as to its supplemental ANDA filing. *Eli Lilly & Co. v. APP Pharm., LLC*, No. 11-628-GMS (D. Del. Oct. 17, 2011)

DISCUSSION

The sole disputed issue in this appeal is whether the asserted claims of the '932 patent are invalid for obviousness-type double patenting. The doctrine of obviousness-type double patenting is intended to "prevent the extension of the term of a patent . . . by prohibiting the issuance of the claims in a second patent not patentably distinct from the claims of the first patent." *In re Longi*, 759 F.2d 887, 892 (Fed. Cir. 1985). "A later patent claim is not patentably distinct from an earlier claim if the later claim is obvious over, or anticipated by, the earlier claim." *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001). As with statutory obviousness under 35 U.S.C. § 103, obviousness-type double patenting is an issue of law premised on underlying factual inquiries. *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1290 (Fed. Cir. 2012). Accordingly, we consider the district court's ultimate conclusion on obviousness-type double patenting without deference, but we review any predicate findings of fact for clear error. *Id.*

A. The '608 Compound

We first address the '608 Compound. Claim 3 of the '608 patent recites the '608 Compound, an antifolate that is structurally related to pemetrexed but never advanced to clinical use. As described, the '608 patent issued in July 1991, more than three years before the '932 patent issued with its claims covering pemetrexed. The question, then, is whether the asserted claims of the '932 patent are

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(Stipulation and J. Order), ECF No. 10. We granted APP's unopposed motion to consolidate that action with the related matters on appeal. *Eli Lilly & Co. v. Teva Parenteral Meds. Inc.*, Nos. 2011-1561, -1562, 2012-1037 (Fed. Cir. Nov. 29, 2011) (Order Consolidating Appeals).

patentably distinct from Lilly's earlier-issued claim to the '608 Compound.

On appeal, Teva contends that the district court erred by failing to invalidate the claims for obviousness-type double patenting. Teva's primary argument concerns the appropriate legal standard for evaluating obviousness-type double patenting. Relying on our decision in *Amgen Inc. v. Hoffmann-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), Teva contends that the correct analysis involves only the *differences* between the claims at issue, so that any features held in common between the claims—in this case, all but the aryl regions of the '608 Compound and pemetrexed—would be excluded from consideration. In *Amgen*, we explained that once the differences between claims are established, the obviousness-type double patenting analysis entails determining "whether the differences in subject matter between the claims render the claims patentably distinct." 580 F.3d at 1361. But those differences cannot be considered in isolation—the claims must be considered as a whole. *Amgen* expressly noted that "[t]his part of the obviousness-type double patenting analysis is analogous to an obviousness analysis under 35 U.S.C. § 103." *Id.* And just as § 103(a) requires asking whether the claimed subject matter "as a whole" would have been obvious to one of skill in the art, so too must the subject matter of the '932 claims be considered "as a whole" to determine whether the '608 Compound would have made those claims obvious for purposes of obviousness-type double patenting. *Gen. Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1278 (Fed. Cir. 1992) ("Claims must be read as a whole in analyzing a claim of double patenting."). Thus, the district court did not err by examining whether one of ordinary skill in the art would have been motivated to modify the '608 Com-

pound to create pemetrexed, considering the compounds as a whole.

On the merits, Teva also disputes the district court's findings and conclusions in view of the evidence presented. Specifically, Teva contends (1) that placing a phenyl group in the aryl position represented inescapable "conventional wisdom" in the field based on antifolate structures known at the time, (2) that the district court erred in finding that one of skill in the art would have considered a phenyl group undesirable within the structural context of the '608 Compound, and (3) that the district court erred by discounting its theory that principles of bioisosterism[6] would have suggested replacing the '608 Compound's thienyl with phenyl.

Lilly defends the district court's findings, arguing that the evidence amply supported the court's view that a person of ordinary skill would not have had reason to manipulate the '608 Compound to produce pemetrexed. Lilly contended, and the district court found, that a chemist at the time seeking to develop TS inhibitors would have looked specifically to data from that emerging sub-discipline rather than attempting to emulate the "conventional" antifolates highlighted by Teva. In fact, according to Lilly, the contemporary experience and understanding in the TS field not only would have failed to suggest substituting a phenyl group into the '608 Compound, but earlier reports of associated inefficacy and toxicity would have actively dissuaded one from doing so. Finally, Lilly maintains that bioisosterism provides no

[6] Bioisosterism refers to a process that involves replacing one atom or functional group in a molecule with another of similar chemical, physical, or electronic properties in hopes that the substitution will result in similar or enhanced activity.

basis for predicting whether a substituted compound will prove more or less effective than the original.

Based on the evidence presented at trial, we discern no error in the district court's findings or its conclusion that the asserted claims are patentably distinct from the '608 Compound. In the chemical context, we have held that an analysis of obviousness-type double patenting "requires identifying some reason that would have led a chemist to modify the earlier compound to make the later compound with a reasonable expectation of success." *Otsuka*, 678 F.3d at 1297. Here, the district court considered the parties' arguments and evidence, particularly their conflicting expert testimony as to how an ordinarily skilled chemist presented with the '608 Compound would have been motivated to proceed at the time. In its decision, the court credited Lilly's evidence to find that "the ways in which a person of ordinary skill in the art would modify [the '608 Compound] would not result in pemetrexed." *Eli Lilly*, 2011 WL 3236037, at *4. We owe that finding considerable deference on appeal, and we see no clear error based on the record before us. Moreover, a complicated compound such as the '608 Compound provides many opportunities for modification, but the district court did not find that substituting a phenyl group into the aryl position was the one, among all the possibilities, that would have been successfully pursued. Thus, absent any motivation to derive pemetrexed from the '608 Compound or reason to expect success in doing so, the district court correctly concluded that the asserted claims were not invalid for obviousness-type double patenting over the '608 Compound.

B. The '775 Intermediate

As with the '608 Compound, Lilly's claim covering the '775 Intermediate was issued before the '932 patent. As

an independent basis for holding the '932 claims invalid for obviousness-type double patenting, Teva similarly contends that pemetrexed is not patentably distinct from the '775 Intermediate.

Teva's arguments regarding the '775 Intermediate can be summarized as follows. According to Teva, the '775 Intermediate is used to make pemetrexed, and Lilly disclosed that use in the '775 patent. By later claiming pemetrexed itself, Teva maintains, the '932 patent appropriates a previously disclosed use for a previously patented compound, which renders the asserted '932 claims invalid for obviousness-type double patenting under a line of our precedent including *In re Byck*, 48 F.2d 665 (CCPA 1931), and *Sun Pharmaceutical Industries, Ltd. v. Eli Lilly & Co.*, 611 F.3d 1381 (Fed. Cir. 2010). We conclude that Teva's reliance on *Byck*, *Sun*, and related cases is unsound and that the district court did not err when it upheld the asserted claims of the '932 patent over the '775 Intermediate.

As a general rule, obviousness-type double patenting determinations turn on a comparison between a patentee's earlier and later claims, with the earlier patent's written description considered only to the extent necessary to construe its claims. *E.g.*, *In re Avery*, 518 F.2d 1228, 1232 (CCPA 1975). This is so because the non-claim portion of the earlier patent ordinarily does not qualify as prior art against the patentee and because obviousness-type double patenting is concerned with the improper extension of exclusive rights—rights conferred and defined by the *claims*. The focus of the obviousness-type double patenting doctrine thus rests on preventing a patentee from claiming an obvious variant of what it has previously *claimed*, not what it has previously *disclosed*. *See generally Gen. Foods*, 972 F.2d at 1280–82.

The cases on which Teva relies represent a limited exception to this customary framework. In *Byck*, our predecessor court considered obviousness-type double patenting rejections against claims to an insulated coil made up of a conductive winding material coated with an "infusible, flexible, phenol-fatty oil composition." 48 F.2d at 665. The patent applicant, Byck, had earlier obtained a patent claiming the same phenol-oil composition, and the prior art disclosed similar coils coated with other insulating compositions. *Id.* at 665–66. Moreover, Byck's earlier patent had discussed using his phenol-oil composition to produce adherent insulating films on metal substrates. *Id.* at 666. The court concluded that, in view of the prior art and Byck's earlier patent, the pending claims were drawn not to a second, distinct invention "but only . . . an obvious use of the composition there patented." *Id.* The court explained:

> It would shock one's sense of justice if an inventor could receive a patent upon a composition of matter, setting out at length in the specification the useful purposes of such composition, manufacture and sell it to the public, and then prevent the public from making any beneficial use of such product by securing patents upon each of the uses to which it may be adapted.

Id. Thus, even though Byck's earlier patent was not prior art, the court held that its disclosure of an intended use for the previously claimed phenol-oil composition could be used in the obviousness-type double patenting analysis to reject a later claim directed to that use of the same compound. *Id.* at 667.

A trio of our more recent decisions applied the same exception to allow limited consideration of teachings in an earlier-issued patent's specification. In *Geneva Pharma-*

ceuticals, Inc. v. GlaxoSmithKline PLC, 349 F.3d 1373 (Fed. Cir. 2003), the plaintiff had patented methods of using clavulanic acid to mitigate antibiotic resistance when treating bacterial infections. The plaintiff then acquired a preexisting patent that claimed clavulanic acid compositions and disclosed their utility for treating patients harboring antibiotic-resistant bacteria. *Id.* at 1377, 1385. In that case, we relied on *Byck* to hold the plaintiff's method claims invalid for double patenting: "Our predecessor court recognized that a claim to a method of using a composition is not patentably distinct from an earlier claim to the identical composition in a patent disclosing the identical use." *Id.* at 1385–86 (citing *Byck*, 48 F.2d at 666). Similarly, in *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc.*, 518 F.3d 1353, 1363 (Fed. Cir. 2008), we held claims to methods of administering a particular anti-inflammatory drug invalid for obviousness-type double patenting where the patentee's earlier patent claimed the drug itself and disclosed the same methods of administering the drug. And in *Sun*, the patent holder had developed an antiviral compound, gemcitabine, that also proved useful for treating cancer. An initial patent issued with composition claims covering gemcitabine as well as method claims drawn to using the drug to treat herpesvirus infections; also mentioned in the specification, but not claimed, was gemcitabine's potential anticancer activity. *Sun*, 611 F.3d at 1383. As in *Geneva* and *Pfizer*, we held the patentee's subsequent claims to methods of using gemcitabine to treat cancer invalid for double patenting, looking to the disclosure of anticancer utility in the first patent's specification. *Id.* at 1386–89.

Byck, *Geneva*, *Pfizer*, and *Sun* thus "address the situation in which an earlier patent claims a compound, disclosing the utility of that compound in the specification, and a later patent claims a method of using that

compound for a particular use described in the specification of the earlier patent." *Sun*, 611 F.3d at 1389. Furthermore, in each of those cases, the claims held to be patentably indistinct had in common the same compound or composition—that is, each subsequently patented "use" constituted a, or the, disclosed use for the previously claimed substance.

That is not the case before us. Rather than a composition and a previously disclosed use, the claims at issue recite two separate and distinct chemical compounds: the '775 Intermediate and pemetrexed, differing from each other in four respects. That alone suffices to undermine Teva's argument regarding the '775 Intermediate, for the asserted claims of the '932 patent do not recite a *use* of the *same compound*, but a *different compound* altogether. The cited cases therefore do not govern.

Furthermore, even if one composition could somehow be considered a "use" of another, the record makes clear that, unlike in the cited cases, Lilly's successive claims are wholly independent of one another. For example, pemetrexed and the '775 Intermediate exhibit substantial structural differences, and neither embodies or subsumes the other. Moreover, pemetrexed can be made via any of several synthetic techniques, many of which do not involve the '775 Intermediate. The '775 Intermediate and pemetrexed are thus separate and independent chemical compounds; Lilly's original claim to the '775 Intermediate offered no protection for pemetrexed, and its claims to pemetrexed do not incorporate or require use of the '775 Intermediate. The particular concerns motivating our prior decisions are thus absent here. In sum, although the specification of the '775 patent discloses one method for deriving pemetrexed using the '775 Intermediate, we agree with the district court's conclusion that that disclo-

sure does not render Lilly's claims to pemetrexed invalid for obviousness-type double patenting.

As the district court recognized, the correct double patenting analysis in this case turns on an evaluation of what Lilly has claimed, not what it has disclosed. Putting aside the teachings in the '775 patent's specification, Teva's double patenting contentions evaporate. The evidence of record characterizes the '775 Intermediate as a versatile compound from which a skilled chemist could derive innumerable final products beyond just pemetrexed, and the district court found that there would have been "no reason" to pursue pemetrexed among the various other avenues that would have been considered possible at the time. We see no error in the district court's findings or its conclusion on this point, and, although not controlling, we further note that its analysis comports with PTO guidelines on the patentability of related products. *See* Manual of Patent Examining Procedure § 806.05(j) (8th ed., rev. 8, 2010) ("[A]n intermediate product and a final product can be shown to be distinct inventions if the intermediate and final products are mutually exclusive inventions (not overlapping in scope) that are not obvious variants, and the intermediate product as claimed is useful to make other than the final product as claimed."). In sum, the district court correctly concluded that the asserted claims are not invalid for obviousness-type double patenting over the '775 Intermediate.

C. Objective Indicia of Nonobviousness

Finally, Lilly presented evidence at trial that pemetrexed exhibited unexpected clinical properties and achieved considerable commercial success. But the district court disregarded that evidence, holding that "secondary considerations are not relevant to the analysis of

invalidity for obviousness-type double patenting." *Eli Lilly*, 2011 WL 3236037, at *1 n.1. For that proposition, the district court relied on a footnote in *Geneva*, in which we remarked only that inquiry into secondary considerations is not required in every obviousness-type double patenting analysis, not that such evidence is off-limits or irrelevant. *See Geneva*, 349 F.3d at 1378 n.1. The district court's categorical repudiation of Lilly's evidence was therefore erroneous. When offered, such evidence should be considered; a fact-finder "must withhold judgment on an obviousness challenge until it has considered all relevant evidence, including that relating to the objective considerations." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1079 (Fed. Cir. 2012). Given that the district court nonetheless rejected Teva's double patenting arguments, however, such error was, in this instance, harmless.

CONCLUSION

In view of the foregoing, we hold that the asserted claims of the '932 patent are not invalid for obviousness-type double patenting over claim 3 of the '608 patent or claim 7 of the '775 patent. We have considered each of Teva's remaining arguments and find them unpersuasive. Accordingly, the judgment of the district court is

AFFIRMED