395 F.3d 1364 (2005)

MERCK & CO., INC., Plaintiff-Appellee,

v.

TEVA PHARMACEUTICALS USA, INC., Defendant-Appellant.

No. 04-1005.

United States Court of Appeals, Federal Circuit.

Decided: January 28, 2005.

1365 *1365 John F. Lynch, Howrey Simon Arnold & White, LLP, of Houston, Texas, argued for plaintiff-appellee. With him on the brief were Nicolas G. Barzoukas and Richard L. Stanley. Of counsel on the brief were Paul D. Matukaitis, Edward W. Murray and Gerard M. Devlin, Merck & Co., Inc., of Rahway, New Jersey.

James Galbraith, Kenyon & Kenyon, of New York, New York, argued for defendant-appellant. With him on the brief were Maria Luisa Palmese and William G. James, II.

Before RADER, GAJARSA, and PROST, Circuit Judges.

GAJARSA, Circuit Judge.

Teva Pharmaceuticals USA, Inc. ("Teva") appeals the final judgment of the United States District Court of Delaware, which, after a bench trial, found Merck & Co.'s ("Merck") U.S. Patent No. 5,994,329 (issued Nov. 1366 30, 1999) ("the '329 patent") *1366 not invalid as anticipated or obvious. The district court further found the '329 patent to be enforceable, and the ' 329 patent claims 23 and 37 constructively infringed by Teva's Abbreviated New Drug Application ("ANDA") under 35 U.S.C. § 271(e)(2)(A) of the Hatch-Waxman Act. *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 288 F.Supp.2d 601 (D.Del.2003) ("*Merck*"); *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, No. 01-CV-0048, Order (D.Del. Sept. 24, 2003) (Final Judgment Order Pursuant to Fed.R.Civ.P. 54(b)) ("*Final Judgment Order*").[1]

We disagree with the district court's construction of the claim term "about" in claims 23 and 37 of the '329 patent. Because we further hold claims 23 and 37 obvious in light of the prior art, we vacate the judgment of the district court and hold the claims invalid and not infringed.

I. BACKGROUND

A. *'329 Patent*

Merck owns the '329 patent. The '329 patent, entitled "Method for Inhibiting Bone Resorption," teaches a method of treating and preventing osteoporosis through less-than-daily administration of bisphosphonate compounds. '329 patent, col. 1, ll. 15-25. The patent was filed on August 14, 1998, and Merck stipulated at trial that it would not allege an invention date prior to July 22, 1997 for the claims at issue. *Merck*, 288 F.Supp.2d at 606.

Bisphosphonates are a family of chemical compounds that are known to selectively inhibit the bone destruction process that contributes to osteoporosis and other bone diseases. '329 patent, col. 1, ll. 45-50. Bisphosphonates include, among other compounds, alendronate, risedronate, tiludronate, pamidronate, ibandronate, zolendronate, and etidronate. *Id.* at col. 1, ll. 54-65; col. 2, ll. 28-31. At issue in this case are once-weekly dosages of alendronate monosodium trihydrate.

Bisphosphonates are not readily absorbed by the gastrointestinal ("GI") tract. The medications thus require rigorous dosing instructions: a patient must take the medicine on an empty stomach and remain upright and fasting for thirty minutes after ingestion. '329 patent, col. 2, ll. 3-24. In addition, the compounds are known to have adverse GI side effects that physicians believed to be related, in part, to (a) irritation to the patient's esophagus, or (b) the size of the dose. *Id.* at col. 2, ll. 23-46.

Before the '329 patent issued, standard osteoporosis treatments consisted of small daily doses of bisphosphonates to avoid GI complications. *Id.* at col. 1, ll. 54-61; col. 2, ll. 34-35, 44-46. According to the patent, however, the adverse GI side-effects resulting from repetitive irritation to the GI tract were the primary concern in the field. *Id.* at col. 2, ll. 65-67; col. 3, l. 57 — col. 4, l. 13. The inventors trumpeted the reduced-frequency dosing schedule disclosed in the '329 patent as decreasing the irritating effect of the compounds, as well as increasing patient compliance with the rigorous dosing instructions. *Id.* at col. 3, ll. 57-64; col. 4, ll. 14-23.

This case involves dependent claims 23 and 37 of the '329 patent. At trial, the parties agreed to cast the text of these claims in independent form, incorporating all the dependent limitations:

> 23. A method *for treating* osteoporosis in human comprising orally administering *about 70 mg* of alendronate monosodium trihydrate, on an alendronic acid basis, as a unit dosage according to a continuous schedule having a dosing interval of once-weekly.
>
> 1367 *1367 37. A method *for preventing* osteoporosis in human comprising orally administering *about 35 mg* of alendronate monosodium trihydrate, on an alendronic acid basis, as a unit dosage according to a continuous schedule having a dosing interval of once-weekly.

'329 patent, col. 21, ll. 24-27 (claim 23) (emphasis added); col. 22, ll. 24-26 (claim 37) (emphasis added). We note that the only differences between claim 23 and claim 37 are (1) the dosage amount of alendronate monosodium trihydrate (70 mg or 35 mg) and (2) whether the method is directed to treating or preventing osteoporosis.

Merck has Food and Drug Administration ("FDA") approval to market both a once-weekly and a relatively diminished daily dose of alendronate monosodium trihydrate, which it does under the trade name Fosamax. *Merck*, 288 F.Supp.2d at 605.

B. *Litigation*

In late 2000, Teva amended an existing ANDA and sought FDA approval to market generic versions of Merck's once-weekly Fosamax supplement in 35 mg and 70 mg quantities.[2] *Merck*, 288 F.Supp.2d at 605-06; Teva Br. at 4. Merck subsequently filed suit against Teva under 35 U.S.C. § 271(e)(2)(A), alleging Teva's ANDA filing was an act of infringement.[3]

According to the trial court, Merck acted as its own lexicographer and through the specification redefined the ordinary meaning of "about" in claims 23 and 37 — which both parties agree has the ordinary meaning "approximately" — to something quite different. *Merck*, 288 F.Supp.2d at 612-16. Thus, the district court concluded the terms "about 35 mg" in claim 37 and "about 70 mg" in claim 23 mean *exactly* 35 (or 70) mg of alendronic acid.[4]

Relying on this construction of "about," the district court dismissed Teva's allegations that the claims at issue were (1) anticipated by a July 1996 *Lunar News* article or (2) rendered obvious by an April 1996 *Lunar News* article combined with the July 1996 article.[5] The trial court found both articles qualified as prior art
1368 publications under 35 U.S.C. § 102(a). *Merck*, 288 F.Supp.2d at 618-19. The *1368 April 1996 article in *Lunar News* recommends weekly dosages of alendronate to improve patient compliance:

> [O]ne of the difficulties with alendronate is its low oral bioavailability. When taken with water in a fasting state, only about 0.8% of the oral dose is bioavailable. Even coffee or juice reduces this by 60%, and a meal reduces it by >85%. Alendronate must be taken, after an overnight fast, 30-60 minutes before breakfast. Subjects should remain seated or standing; a very small group of patients have reported some upper gastrointestinal distress if this is not done. This regime may be difficult for the elderly [to] maintain chronically. *An intermittent treatment program (for example, once per week, or one week every three months), with higher oral dosing, needs to be tested.*

Update: Bisphosphonate, Lunar News, Apr. 1996, at 31 (emphasis added).

The July 1996 *Lunar News* article further emphasizes the need for a once-weekly dose of Fosamax because "[s]ome United States physicians are reluctant to treat [patients with Fosamax] because of: a) side effects; b) difficulty of dosing; and c) high costs ($700/year)." The author suggests:

> The difficulties with oral bisphosphonates may favor their episodic (*once/week*) or cyclical (one week each month) administration. Even oral alendronate potentially could be given in a *40 or 80 mg dose once/week* to avoid dosing problems and reduce costs.[6]

Update: Bisphosphonate, Lunar News, July 1996, at 23 (emphasis added).

Regarding anticipation, the trial court held the July 1996 article does not "expressly or inherently disclose the dosage amounts for alendronate in claims 23 and 37" because there was no evidence that 40 mg and 80 mg of alendronate contains "the same number of alendronate core molecules" as found in 35 mg and 70 mg, respectively, of alendronic acid. *Merck*, 288 F.Supp.2d at 618-20.

As for obviousness, the district court concluded the suggestion of weekly treatment was not "clinically useful or obvious in July 1997 because of the known dose-related gastrointestinal side effects" associated with the daily formulation of Fosamax. *Merck*, 288 F.Supp.2d at 628. Although it is undisputed that a once-weekly dosage was known to be efficacious, the court determined that the *Lunar News* articles could not overcome doctors' concerns associated with higher dosages because the *Lunar News* articles were not published in peer-reviewed journals or authored by one skilled in the art. *Merck*, 288 F.Supp.2d at 628-29.

Finding the '329 patent not invalid as anticipated or obvious, the district court delayed the effective date of the FDA approval of Teva's ANDA until the '329 patent expires and enjoined commercial sale of Teva's generic

1369 *1369 # II. DISCUSSION

A. *Standard of Review*

On appeal from a bench trial, this court reviews the district court's conclusions of law *de novo* and findings of fact for clear error. *Golden Blount, Inc. v. Robert H. Peterson Co.*, 365 F.3d 1054, 1058 (Fed.Cir.2004); *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1123 (Fed.Cir.2000). A finding is clearly erroneous when, despite some supporting evidence, "the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed." *United States v. United States Gypsum Co.*, 333 U.S. 364, 395, 68 S.Ct. 525, 92 L.Ed. 746 (1948).

The court reviews claim construction, a question of law, *de novo. Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1456 (Fed.Cir.1998) (en banc). Obviousness is a question of law based on underlying factual determinations. *Richardson-Vicks, Inc. v. Upjohn Co.*, 122 F.3d 1476, 1479 (Fed.Cir.1997). The court reviews an obviousness ruling *de novo,* but reviews the underlying factual findings for clear error. *Graham v. John Deere Co.*, 383 U.S. 1, 17, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966); *Golden Blount,* 365 F.3d at 1058. The underlying factual determinations include (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the claimed invention and the prior art, and (4) objective indicia of nonobviousness. *Graham,* 383 U.S. at 17-18, 86 S.Ct. 684.

B. *Claim Construction*

In finding that Merck acted as its own lexicographer, the district court relied on the following passage from the specification:

> Because of the mixed nomenclature currently in use by those or [sic] ordinary skill in the art, reference to a specific weight or percentage of bisphosphonate compound in the present invention is on an active weight basis unless otherwise indicated herein. *For example the phrase "about 70 mg of bone resorption inhibiting bisphosphonate selected from the group consisting of alendronate, pharmaceutically acceptable salts thereof and mixtures thereof, on an alendronic acid weight basis" means that the amount of bisphosphonate compound selected is calculated based on 70 mg of alendronic acid.*

'329 patent, col. 10, l. 65 — col. 11, l. 8 (emphasis added). According to the district court's opinion, the patentee uses the phrase "about 35 [or 70] mg" to account for variations in the molecular weight of the different derivatives of alendronic acid and to deliver *exactly* 35 (or 70) mg of alendronic acid. *Merck,* 288 F.Supp.2d at 613. For example, the court noted that alendronate monosodium trihydrate, which is used in Fosamax, requires an atom of sodium for each molecule. *Id.* at 613-14. If a heavier metal were chosen, such as potassium, the weight of the derivative compound would have to increase to deliver exactly the same number of molecules of the active alendronate compound found in 35 [or 70] mg of alendronic acid. *Id.* at 614. The district court thus construed the term "about 35 [or 70] mg" to mean the amount of the derivative compound that gives *exactly* 35 [or 70] mg of the active compound.

We reverse the district court's construction of "about" and hold that such term should be given its ordinary

1370 meaning of "approximately."[7] To properly construe *1370 a claim term, a court first considers the intrinsic

(Fed.Cir.1996). Generally claim terms should be construed consistently with their ordinary and customary meanings, as determined by those of ordinary skill in the art. *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 (Fed.Cir.2003). While in some cases there is a presumption that favors the ordinary meaning of a term, *Tex. Digital Sys. v. Telegenix Inc.*, 308 F.3d 1193, 1202 (Fed.Cir.2002), the court must first examine the specification to determine whether the patentee acted as his own lexicographer of a term that already has an ordinary meaning to a person of skill in the art. *See, e.g., Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed.Cir.1998); *Brookhill-Wilk*, 334 F.3d at 1299.

When a patentee acts as his own lexicographer in redefining the meaning of particular claim terms away from their ordinary meaning, he must clearly express that intent in the written description. *See, e.g., Bell Atl. Network Servs. v. Covad Communications Group, Inc.*, 262 F.3d 1258, 1268 (Fed.Cir.2001). We have repeatedly emphasized that the statement in the specification must have sufficient clarity to put one reasonably skilled in the art on notice that the inventor intended to redefine the claim term. *Id.; see also Elekta Instrument S.A. v. O.U.R. Sci. Int'l, Inc.*, 214 F.3d 1302, 1307 (Fed.Cir.2000) ("Absent an express intent to impart a novel meaning, claim terms take on their ordinary meaning."); *Renishaw*, 158 F.3d at 1249 ("The patentee's lexicography must, of course, appear `with reasonable clarity, deliberateness, and precision' before it can affect the claim.") (quoting *In re Paulsen*, 30 F.3d 1475, 1480 (Fed.Cir.1994)); *Union Carbide Chems. & Plastics Tech. Corp. v. Shell Oil Co.*, 308 F.3d 1167, 1177-78 (Fed.Cir.2002) (stating that the "presumption in favor of the claim term's ordinary meaning is overcome, however, if a different meaning is clearly and deliberately set forth in the intrinsic evidence"). In the present case, the passage cited by the district court from the specification for Merck's definition of "about" is ambiguous. It fails to redefine "about" to mean "exactly" in clear enough terms to justify such a counterintuitive definition of "about."

1371 The phrase's ambiguity arises from the fact that it can easily be read as Teva *1371 does — as a way of explaining what is meant by the use of the phrase "alendronate acid active basis" rather than as a way of radically redefining what is meant by "about." The district court construed the phrase "about 70 [or 35] mg" to mean that one should administer approximately 70 (or 35) mg of the *derivative compound,* such that the end result is that the patient is administered exactly 70 (or 35) mg of alendronic acid. In other words, the district court determined that the quantity specified in the claims (35 or 70 mg) modifies the amount of the *derivative compound* rather than the *active compound.* Under such a construction, the term "about" informs one of ordinary skill in the art to select whatever quantity of the derivative compound necessary to give exactly 35 (or 70) mg of alendronic acid; for alendronate monosodium trihydrate, the word "about" thus meant that 45.68 mg (or 91.35 mg) of that compound should be delivered — the amount necessary to give exactly 35 (or 70) mg of alendronic acid.

Unlike the limiting definition of "about" adopted by the district court, Teva's interpretation of the paragraph in question would mean that "70 [or 35] mg" refers to the amount of the *active compound* to be administered rather than the amount of the derivative compound. The term "about" in the claims would then serve to modify the quantity of the *active compound* in a way consistent with its normal definition of "approximately." Under this construction, the modifying phrase "about 70 [or 35] mg" would refer to approximately 70 (or 35) mg of *alendronic acid*.[8]

The claim construction urged by Merck and adopted by the district court reads the sentence of the passage underlined above out of context. In the sentence before the highlighted sentence, the patentee informs those of ordinary skill in the art that, when the patent refers to a certain amount of a bisphosphonate compound, it is actually instructing them to administer a certain amount of the active component of the compound rather than

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