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Client Alert

APRIL 3, 2020

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D.C. Circuit Concludes that Serial Periods of Exclusivity May Be Available Under the Orphan Drug Act

On March 13, 2020, the U.S. Court of Appeals for the D.C. Circuit affirmed the D.C. District Court's 2018 summary judgment ruling in favor of Eagle Pharmaceuticals and against the FDA, finding that (1) the Orphan Drug Act[1] ("ODA") allows for multiple, sequential seven-year periods of Orphan Drug Exclusivity ("ODE") for the same drug and same indication, and (2) the FDA was not authorized to implement regulations requiring an applicant seeking Orphan Drug designation for a previously approved drug and indication to demonstrate "clinical superiority" to benefit from an additional ODE period.[2] Click here for the opinion.

The effect of this decision may be limited to certain products (like Eagle's Bendeka®) approved as Orphan Drugs before Congress's 2017 codification of "clinical superiority" requirements for sequential ODE periods[3] – but the decision hints at the potential for broader impact.

BACKGROUND

The Orphan Drug Act

In 1983, the Congress passed the ODA, which provided economic incentives encouraging the development of "orphan drugs" – *i.e.*, drugs "designed to treat a rare disease or condition," which "became 'orphaned' because the comparatively small demand for treatment left little motive for research and development."[4] Under the ODA, the FDA's granting of an "Orphan Drug" designation to an investigational drug leads to certain benefits that ease the cost of clinical development.[5] And upon FDA approval of a designated Orphan Drug for a certain rare disease or condition, the ODA grants a seven-year ODE period, during which time the FDA may not approve another application "for such drug for such disease or condition."[6]

Prior to 2017 amendments, the ODA was silent on whether multiple, serial periods of ODE could be granted for the same drug (*i.e.*, with the same

active moiety) for the same rare disease or condition. The FDA addressed this issue through regulation, and concluded that ODE is unavailable for a drug that "is otherwise the same drug as a previously approved drug for the same use or indication" – unless the sponsor demonstrates that "the drug is ***clinically superior*** to the previously approved drug."[7]

Following amendment in 2017, the ODA now requires that a sponsor seeking ODE for a new drug, where the "same drug" was previously approved for the same rare disease or condition, must show that the new drug is "clinically superior" to the previously approved drug.[8] This amendment is not retroactive for FDA determinations on ODE made before the amendment's effective date.[9]

Eagle's Bendeka® and the Disputes Below

The dispute between Eagle and the FDA arose from the FDA's denial of a seven-year ODE period following the 2015 approval of Eagle's product Bendeka® (bendamustine HCl) injection. Applying its regulations, the FDA found that Bendeka® was not entitled to ODE because Eagle failed to show "clinical superiority" of Bendeka® over Treanda® – a bendamustine HCl injection product previously approved in 2007 and 2008 with the same indications (but a different formulation) as Bendeka®. Treanda® was also previously designated an Orphan Drug, and the ODE period for Treanda® expired in 2015.

In 2018, Eagle filed a lawsuit in D.D.C. under the Administrative Procedure Act, challenging the FDA's denial of exclusivity for Bendeka®.[10] The district court ruled in Eagle's favor that Bendeka® is entitled to its own seven-year period of ODE. The district court granted summary judgment to Eagle under step one of the U.S. Supreme Court's decision in *Chevron*, which "ask[s] whether the agency-administered statute is ambiguous on the 'precise question at issue.'"[11] Evaluating the text of the ODA, the district court found that it "unambiguously require[d] the FDA to afford Bendeka® the benefit of orphan-drug exclusivity."[12] The FDA and certain intervening parties appealed.

THE D.C. CIRCUIT'S DECISION

Writing for the appeals court in a 2-1 decision, Circuit Judge Karen L. Henderson affirmed the grant of summary judgment to Eagle, upholding the ruling that Bendeka® is entitled to its own ODE period. The majority found that "the text of § 360cc(a) unambiguously entitles a manufacturer to marketing exclusivity upon designation and approval."[13] "[I]f the FDA approves a previously-designated orphan drug, it cannot approve another such drug for the same condition for seven years," the majority wrote.[14] Applying *Chevron* step one, the statutory "language leaves no room for the FDA," Judge Henderson explained, "to add an after-the-fact requirement that a designated and approved drug prove clinical superiority before receiving that exclusive approval benefit."[15] In sum, "the district court correctly determined at *Chevron* step one that the FDA's post-approval clinical superiority requirement was forbidden and that Eagle was automatically entitled to a seven-year period of exclusive approval when it approved Bendeka® for marketing."[16]

Notably, the majority expressly stated that its decision does ***not*** impact the FDA's ability to require that sponsors seeking Orphan Drug designation show a "plausible hypothesis of superiority" if the same drug had been previously approved for the proposed orphan condition – explaining that the FDA has "unchallenged statutory authority" to impose requirements at the Orphan Drug designation stage.[17]

Circuit Judge Stephen F. Williams dissented, arguing that the majority's reasoning "upsets the basic economic bargain that Congress so carefully struck."[18] In allowing multiple sponsors of the same drug to obtain exclusivity, Judge Williams asserted, the majority ignores the text, structure, and purpose of the ODA, all of which demonstrate that "Congress clearly did not intend the same drug to enjoy multiple seven-year periods of exclusivity."[19]

POTENTIAL IMPACT OF THE D.C. CIRCUIT'S RULING IN *EAGLE V. AZAR*

The D.C. Circuit's decision will have a significant impact on a certain subset of products – "at least 11," according to the FDA – that, like Bendeka®, were approved for marketing but denied ODE because the FDA found that they were not "clinically superior" to a previously-approved product that was the same drug for the same disease.[20] We expect to see the sponsors of such products approach the FDA to have their ODE periods instated, as well as possibly requesting that the approval of any previously approved generic products be revoked. For products first approved after the 2017 amendments to the ODA, however, the statutory "clinically superior" requirement still controls.[21]

One potential open issue was raised by the FDA in a last-minute letter to the D.C. Circuit: at least one sponsor has apparently argued that a supplemental NDA for a manufacturing change to a previously approved product might be entitled to a new ODE period.[22] The FDA has said it will oppose that request, so this will be a dispute to monitor if it proceeds to litigation.

Another potential open issue is the argument brought by the intervenors that any judicial order requiring the FDA to grant ODE for a product such as Bendeka®, or the "at least 11" similarly situated products, would be a "new determination subject to the 2017 amendments."[23] The majority rejected this argument on procedural grounds (as not properly raised below), and so it remains to be seen whether it is raised and addressed on the merits in any subsequent challenges.[24]

[1] 21 U.S.C. § 360aa *et seq.*, as drafted before 2017 amendments)
[2] *Eagle Pharms. Inc. v. Azar*, No. 18-5207 (D.C. Cir., Mar. 13, 2020).
[3] *See* 21 U.S.C. § 360cc(c).
[4] *Spectrum Pharms., Inc. v. Burwell*, 824 F.3d 1062, 1064 (D.C. Cir. 2016).
[5] *See* 26 U.S.C. § 45C; 21 U.S.C. §§ 360aa(a), 360ee.
[6] 21 U.S.C. § 360cc(a) (pre-2017 amendment).
[7] 21 C.F.R. § 316.34(c) (emphasis added).
[8] 21 U.S.C. § 360cc(c)(1).
[9] *See* FDA Reauthorization Act of 2017, Pub. L. N. 115-52, § 607(b), 131 Stat. 1005 ("Nothing in the amendments made by subsection (a) shall affect any determination under sections 526 and 527 of the Federal Food, Drug, and Cosmetic Act made prior to the date of enactment of the FDA Reauthorization Act of 2017.").
[10] *See* 5 U.S.C. § 706.
[11] *Guedes v. Bureau of Alcohol, Tobacco, Firearms & Explosives*, 920 F.3d 1, 28 (D.C. Cir. 2019) (quoting *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 842–43 (1984)).
[12] *Eagle Pharms., Inc. v. Azar*, No. No. 16-790 (TJK), 2018 U.S. Dist. LEXIS 101735, *16 (D.D.C. June 8, 2018) (Kelly, J).
[13] Slip Op. at 2.
[14] *Id.* at 32.
[15] *Id.*
[16] *Id.* at 33.
[17] *Id.* at 21–22.
[18] *Id.* at 1 (Williams, J, dissenting).
[19] *Id.* at 1, 7.
[20] *See Eagle Pharms. Inc. v. Azar*, No. 18-5207, Transcript 11:1–6 (D.C. Cir., Oct. 17, 2019).
[21] *See* 21 U.S.C. § 360cc(c).
[22] *See* FDA FRAP Rule 28(j) Letter (March 2, 2020).
[23] *See* Slip Op. at 34 (majority).
[24] *See id.* ("Because they raise this argument for the first time on appeal, it is waived.").