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Paper No. 12
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ETON PHARMACEUTICALS, INC,
Petitioner,

v.

EXELA PHARMA SCIENCES, LLC,
Patent Owner.

PGR2020-00064
Patent US 10,478,453 B1

Before ULRIKE W. JENKS, SUSAN L.C. MITCHELL, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge.*

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 324

Eton Pharmaceuticals Inc. ("Petitioner") filed a Petition requesting a post-grant review of claims 1–22 ("the challenged claim") of Patent US 10,478,453 B1(Ex. 1001, "the '453 patent"). Paper 1 ("Pet."). Exela Pharma Sciences, LLC ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp."). With our authorization (Paper 7), Petitioner filed a reply to Patent Owner's Preliminary Response (Paper 9 ("Pet. Reply")), and Patent Owner filed a Sur-reply (Paper 11 ("Sur-reply")). We granted additional briefing to allow Petitioner to clarify the record with respect to assertions made in Patent Owner's preliminary response, and to allow Patent Owner the opportunity to address alleged conflicting arguments made in a related proceeding.

We have authority to determine whether to institute a post-grant review. 35 U.S.C. § 324. After considering all the papers submitted, for the reasons discussed below, we deny the Petition and do not institute a post-grant review.

I. BACKGROUND

A. Real Parties in Interest

Petitioner identifies itself as the real party in interest. Pet. 2. Patent Owner identifies itself as the real party in interest. Paper 3, 2.

B. Related Proceedings

Petitioner identifies as related matter *Exela Pharma Sciences, LLC v. Eton Pharms., Inc.*, Case No. 1:20-cv-00365-MN (D. Del., filed March 16, 2020) ("District Court Action"); *Exela Pharma Sciences LLC v. Avadel Legacy Pharms., LLC*, No. 1:20-cv-00024-MN (D. Del., filed January 7, 2020); *Exela Pharma Sciences LLC v. Sandoz Inc.*, Case No. 1:20-cv-00645-MN (D. Del., filed May 14, 2020); and *Exela Pharma Sciences LLC v.*

Sandoz Inc., Case No. 1:20-cv-01393 (D. Colo., filed May 15, 2020). Pet. 3; Paper 3, 1.

Petitioner also identifies U.S. Patent No. 10,583,155, U.S. Patent Appl. No. 16/746,028, U.S. Patent Appl. No.16/773,563 (now U.S. Patent No. 10,653,719), U.S. Patent Appl. No.16/773,641, U.S. Patent Appl. No.16/850,726, U.S. Patent Appl. No.16/850,962, and U.S. Patent Appl. No.16/850,973 as claiming benefit of priority to U.S. Application No. 16/248,460 which issued as the '453 patent. Pet. 3–4; Paper 3, 2.

C. The '453 Patent (Ex. 1001)

The '453 patent is titled "STABLE, HIGHLY PURE L-CYSTEINE COMPOSITIONS FOR INJECTION AND METHODS OF USE." Ex. 1001, (54). The '453 patent issued from Application No. 16/248,460 ("the '460 application"), filed January 15, 2019. *Id.* at (21), (22).

The '453 patent describes stable L-cysteine compositions for injection, comprising: L-cysteine or a pharmaceutically acceptable salt thereof and/or hydrate thereof in an amount from about 10 mg/mL to about 100 mg/mL, and aluminum in an amount from about 1.0 parts per billion (ppb) to about 250 ppb. *Id.* at (57).

"L-cysteine is a sulfur-containing amino acid that can be synthesized de novo from methionine and serine in adult humans." *Id.* at 1:14–16. Because L-cysteine can be synthesized by the body, it is considered a non-essential amino acid. *Id.* at 1:20. "L-cysteine can be conditionally essential in preterm infants due to biochemical immaturity of the enzyme cystathionase that is involved in L-cysteine synthesis. Thus, there are a number of circumstances in which L-cysteine supplementation can be desirable." *Id.* at 1:26–31.

According to the specification, "[i]t has now been found that L-cysteine compositions for injection can be prepared using the methods described herein whereby the compositions unexpectedly comprise exceedingly low levels of Aluminum and other undesirable impurities, such as cystine, pyruvic acid, certain heavy metals and certain ions." *Id.* at 4:25–30. Moreover, the specification discloses that:

> [T]he problems of safety, purity and stability are results not simply or directly from the level of Aluminum, but are also intertwined with dissolved oxygen levels in the composition and oxygen in the headspace as well as certain heavy metals and certain ions that may leach or be extracted out of the container closure.

Id. at 4:37–43.

The specification discloses that "known L-cysteine compositions contain up to 5000 ppb Aluminum." *Id.* at 7:8–9. In contrast, the specification describes "compositions that provide a therapeutically effective amount of L-cysteine, while containing less than 250 ppb Aluminum." *Id.* at 7:10–13. The specification discloses that reduced aluminum compositions "permit[ ] exposure to less than or equal to 4–5 micrograms per kilogram per day (µg/kg/d) to avoid or minimize Aluminum toxicity while still providing therapeutically effective L-cysteine in a stable composition." *Id.* at 7:21–25.

The specification expressly defines the term "stable" as a composition that will contain the specified levels of all components, e.g., Aluminum, cystine, and pyruvic acid, "for [a] sufficient period of time to enable the composition to be commercially manufactured, stored, shipped, and administered in a clinical setting." *Id.* at 16:41–52. For example, the specification discloses compositions wherein "cystine is present in the

composition in an amount not more than 2.0 wt % relative to L-cysteine after storage at ambient temperature for a period of 6 months." *Id.* at 25:6–9. The specification also discloses compositions wherein "pyruvic acid is present in the composition in an amount not more than 2.0 wt % relative to L-cysteine after storage at ambient temperature for a period of 6 months." *Id.* at 26:5–8.

D. Illustrative Claim

Claim 1 of the '453 patent is illustrative and reproduced below (with added bracketing for reference):

> A stable L-cysteine composition for parenteral administration, comprising:
>
> [(A)] L-cysteine or a pharmaceutically acceptable salt thereof and/or hydrate thereof in an amount from about 10 mg/mL to about 100 mg/mL;
>
> [(B)] Aluminum (Al) in an amount from about 1.0 parts per billion (ppb) to about 250 ppb;
>
> [(C)] L-cystine in an amount from about 0.001 wt% to about 2.0 wt % relative to L-cysteine;
>
> [(D)] pyruvic acid in an amount from about 0.001 wt% to about 2.0 wt % relative to L-cysteine;
>
> [(E)] a pharmaceutically acceptable carrier, comprising water;
>
> [(F)] headspace oxygen that is from about 0.5% v/v to 4.0% v/v from the time of manufacture to about 1 month from manufacture when stored at room temperature;
>
> [(G)] dissolved oxygen present in the carrier in an amount from about 0.1 parts per million (ppm) to about 5 ppm from the time of manufacture to about 1 month from manufacture when stored at room temperature,
>
> [(H)] wherein the composition is enclosed in a single-use container having a volume of from about 10 mL to about 100 mL.

Ex. 1001, 59:2–25.

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