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Paper 11
Entered: December 15, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ETON PHARMACEUTICALS, INC.,
Petitioner,

v.

EXELA PHARMA SCIENCES, LLC,
Patent Owner.

PGR2020-00068
Patent 10,583,155 B1

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

PAULRAJ, *Administrative Patent Judge*.

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

I. INTRODUCTION

Eton Pharmaceuticals, Inc. (collectively, "Petitioner") filed a Petition requesting post-grant review of claims 1–30 (the "challenged claims") of U.S. Patent No. 10,583,155 (Ex. 1001, "the '155 patent"). Paper 1 ("Pet."). Exela Pharma Sciences, LLC ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp."). We have jurisdiction under 35 U.S.C. § 324.

To institute a post-grant review, we must determine whether the information presented in the petition "would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." 35 U.S.C. § 324(a). After considering the Petition and the Preliminary Response, we determine, for the reasons set forth below, that Petitioner has failed to demonstrate that it is "more likely than not" that any of the challenged claims are unpatentable based on the grounds presented. Therefore, we do not institute a post-grant review of those claims.

A. Real Parties in Interest

Petitioner identifies itself as the real party in interest. Pet. 3–4. Patent Owner identifies itself as the real party in interest. Paper 4, 2.

B. Related Matters

The '155 patent is the subject of the following litigation matters: *Exela Pharma Sciences, LLC v. Eton Pharms., Inc.*, Case No. 1:20-cv-00365-MN (D. Del., filed March 16, 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. 3–4; Paper 4, 2.

Petitioner filed a petition for post-grant review against a related patent, U.S. Patent No. 10,478,453 B1 ("the '453 patent"), for which we previously denied institution. Pet. 4; PGR2020-00064, Paper 12.

Petitioner lists the following related patents and published applications: Appl. No. 16/248,460 ("the '460 application," which issued as the '453 patent); Appl. No. 16/746,028; U.S. Appl. No. 16/773,563 (issued as U.S. Patent No. 10,653,719 B1); U.S. Appl. No. 16/850,726; U.S. Appl. No. 16/850,962; and U.S. Application No. 16/850,973. Pet. 4–5.

C. The '155 Patent

The '155 patent, titled "Stable, Highly Pure L-Cysteine Compositions for Injection and Methods of Use," discloses stable L-cysteine compositions for injection. Ex. 1001, (54), (57). The '155 patent issued from Application No. 16/665,702, which is a continuation of the '460 application filed on January 15, 2019. *Id.*, (63).

L-cysteine is a "conditionally essential" sulfur-containing amino acid involved in growth and protein synthesis. *Id.* at 1:21–29. L-cysteine supplements may be administered to preterm infants who lack the natural ability to synthesize L-cysteine due to biochemical immaturity of the enzyme cystathionase. *Id.* at 1:29–37. Although L-cysteine compositions were known in the prior art, the '155 patent states that these prior art compositions for infusion failed to address issues related to aluminum and cystine impurities, and thus were considered less safe for preterm infants, pediatric patients, and critically ill adults. *Id.* at 4:25–31.

According to the '155 patent, "[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 4:31–36. Moreover, the patent discloses that:

> the 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 4:43–49.

The '155 patent discloses that "known L-cysteine compositions contain up to 5000 ppb Aluminum." *Id.* at 7:16–17. In contrast, the patent describes "compositions that provide a therapeutically effective amount of L-cysteine, while containing less than 250 ppb Aluminum." *Id.* at 7:18–22. The patent further discloses that reduced aluminum compositions "permits 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 7:29–35.

The '155 patent 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 25:4–9. 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 25:51–59.

Example 1 of the '155 patent describes a method of compounding an L-cysteine composition as follows:

> 40±1.0 kg of Water for Injection, USP (WFI) was added . . . A target 65 water temperature of NMT 60° C. was maintained throughout WFI addition using a heat exchanger. With continuous mixing at a speed of 126 rpm, Argon overlaying of the WFI began in the mixing bag and continued until the dissolved oxygen was NMT 1 ppm; then the mixing bag was allowed to cool to a temperature of NMT 30° C.
>
> . . . L-Cysteine Hydrochloride, Monohydrate, USP (L-Cysteine) was added . . . The mixing continued for NLT 15 minutes or until complete dissolution was observed. . . . Argon overlaying continues until the dissolved 15 oxygen was NMT 1 ppm.
>
> . . . [T]he solution's pH was adjusted to a target of 1.8 with concentrated Hydrochloric Acid, NF and/or 5.0 N Sodium Hydroxide, NF.
>
> . . . [T]he solution was q.s.'d with the WFI to a final weight of 50.6 kg and allowed to mix for approximately 10 minutes. The final solution weight, solution temperature, solution pH, and dissolved oxygen was then measured and recorded. Following these steps, the mixing bag was fully inflated with Argon and capped, and the solution was transferred from the mixing bag to the solution holding bag.

Id. at 41:60–42:32.

Example 2 describes a test for aluminum levels in L-Cysteine injections compounded as per Example 1. *Id.* at 42:34–60. The bulk solution was filled into uncoated Schott Type 1 USP glass vials. *Id.* Although "[t]he product was quite stable for all the time points tested up to 12 months[,] . . . the product resulted in an unacceptably high aluminum content." *Id.* at 43–49. The aluminum levels are shown in Table 6, reproduced below. *Id.*

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