October 10, 2022

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Subject: **Citizen Petition Requesting Therapeutic Equivalence Rating Assignment for NDA 209552**

Request Eugia Pharma Specialities Limited's Argatroban in Sodium Chloride Injection, 50 mg/50 mL approved under 505(b)(2) NDA 209552 be assigned a therapeutic equivalence rating of 'AP' to the pharmaceutically equivalent Reference Listed Drug, Argatroban in Sodium Chloride Injection, 50 mg/50 mL NDA 212035, held by Accord Healthcare Inc.

Dear Sir/Madam,

The undersigned submits this petition on behalf of Eugia Pharma Specialities Ltd. (Eugia) pursuant to 21 CFR §10.30 requesting the Commissioner of the Food and Drug Administration to designate Eugia's Argatroban in Sodium Chloride Injection, 50 mg/50 mL approved under 505(b)(2) NDA 209552 as therapeutically equivalent with an 'AP' rating to the Reference Listed Drug (RLD) Argatroban in Sodium Chloride Injection, 50 mg/50 mL NDA 212035, held by Accord Healthcare Inc.

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration designate Eugia's Argatroban in Sodium Chloride Injection, 50 mg/50 mL approved under 505(b)(2) NDA 209552 as therapeutically equivalent with an 'AP' rating to the RLD Argatroban in Sodium Chloride Injection, 50 mg/50 mL NDA 212035, held by Accord Healthcare Inc.

B. Statement of Grounds

FDA has approved four NDAs for pharmaceutically equivalent versions of Argatroban in Sodium Chloride Injection, 50 mg/50 mL:

- Eagle Pharma's Argatroban in Sodium Chloride Injection, 50 mg/50 mL (NDA 022434)
- Hikma's Argatroban Injection, 50 mg/50 mL (NDA 203049)
- Eugia's Argatroban in Sodium Chloride Injection, 50 mg/50 mL (NDA 209552)
- Accord Healthcare's Argatroban in Sodium Chloride Injection, 50 mg/50 mL (NDA 212035)

NDA 020883 currently held by Novartis Pharmaceuticals Corp. is the original RLD referenced in the 505(b)(2) applications submitted by Sandoz (NDA 022485), Eagle Pharma (NDA 22434) and Hikma (NDA 203049). Thus, these three previously-approved 505(b)(2) NDAs and 505(b)(2) variations on these approvals (including Eugia's NDA) all refer to the original innovator product approved under NDA 020883. This is indicated in their approval documents which are posted on the Agency's website as linked below.

Eagle 505(b)(2) NDA 022434
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022434_argatroban_toc.cfm

Sandoz 505(b)(2) NDA 022485
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/022485_argatroban_toc.cfm

Hikma 505(b)(2) NDA 203049 *(Original approval for 250 mg/2.5 mL)*
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203049_argatroban_toc.cfm

(S-004 (for 50 mg/50 mL presentation)
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/203049Orig1s004.pdf

Accord Healthcare's Argatroban in Sodium Chloride Injection, 50 mg/50 mL 505(b)(2) NDA 212035 referenced Eagle's 505(b)(2) NDA 022434 as the Reference Listed Drug. This is indicated in the approval documents which are posted on the Agency's website as linked below.

Accord Healthcare 505(b)(2) NDA 212035
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/212035Orig1s000TOC.cfm

The Eagle 505(b)(2) NDA 022434 was granted a waiver of *in-vivo* bioequivalence testing based on formulation comparison to the RLD 020883, and certain *in-vitro* comparison data.

The Sandoz 505(b)(2) NDA 022485 was also granted a waiver of *in-vivo* bioequivalence testing pursuant to 21 CFR §320.22(d)(3) based on formulation comparison to the RLD 020883, and certain *in-vitro* comparison data.

Eugia's 505(b)(2) NDA 209552 (citing Sandoz's NDA 022485 as RLD) was granted a waiver of *in-vivo* bioequivalence testing pursuant to 21 CFR §320.22(d)(1) based on formulation comparison to the Sandoz product.

Accord Healthcare's 505(b)(2) NDA 212035 was a granted biowaiver granted based on qualitative and quantitative sameness to the cited RLD.

Eugia's formulation approved under 505(b)(2) NDA 209552 is qualitatively and quantitatively *identical* to the formulation of Accord Healthcare's Argatroban in Sodium Chloride Injection, 50 mg/50 mL approved under NDA 212035.

A side-by-side pharmaceutical equivalence comparison of NDA 209552 (Eugia) and the RLD NDA 212035 (Accord Healthcare) is provided in Table 1:

Table 1: Side-by-Side Pharmaceutical Equivalence Comparison of NDA 209552 and NDA 212035

Attribute	Eugia's NDA 209552	Accord Healthcare's RLD NDA 212035	Comparison
Strength	50 mg/50 mL	50 mg/50 mL	Same
Route of Administration	Intravenous	Intravenous	Same
Dosage form	Injectable	Injectable	Same
Active Ingredient	Argatroban	Argatroban	Same

Attribute	Eugia's NDA 209552	Accord Healthcare's RLD NDA 212035	Comparison
Indications	Argatroban Injection is a direct thrombin inhibitor indicated: • For prophylaxis or treatment of thrombosis in adult patients with heparin-induced thrombocytopenia (HIT) • As an anticoagulant in adult patients with or at risk of HIT undergoing percutaneous coronary intervention (PCI)	Argatroban Injection is a direct thrombin inhibitor indicated: • For prophylaxis or treatment of thrombosis in adult patients with heparin-induced thrombocytopenia (HIT) • As an anticoagulant in adult patients with or at risk of HIT undergoing percutaneous coronary intervention (PCI)	Same
Excipients	Sodium Chloride 9 mg/mL Sorbitol 3 mg/mL Water for Injection q.s.	Sodium Chloride 9 mg/mL Sorbitol 3 mg/mL Water for Injection q.s.	Same

Approved Drug Products with Therapeutic Equivalence Evaluations, ("The Orange Book"), defines *pharmaceutically equivalent* drug products as follows:

1. Contain identical amounts of the same active drug ingredient in the same dosage form and route of administration
2. Meet compendial or other applicable standards of strength, quality, purity and identity

The Orange Book defines *therapeutically equivalent* drug products as follows:

1. Are approved as safe and effective.
2. Contain identical amounts of the same active drug ingredient in the same dosage form and route of administration
3. Meet compendial or other applicable standards of strength, quality, purity and identity
4. Are bioequivalent
5. Are adequately labeled
6. Were manufactured under cGMP

Eugia Pharma Specialities Limited's approved 505(b)(2) NDA 209552 Argatroban in Sodium Chloride Injection, 50 mg/50 mL meets all of the above-listed requirements.

Table 1 demonstrates that the Accord Healthcare's RLD and Eugia Pharma's NDA drug products are qualitatively and quantitatively *identical* in formulation.

Based on all the above-mentioned reasons, Eugia Pharma Specialities Limited hereby requests the Agency to grant our NDA 209552, Argatroban in Sodium Chloride Injection a therapeutic equivalence rating of 'AP' to the RLD Argatroban in Sodium Chloride Injection, 50 mg/50 mL NDA 212035, held by Accord Healthcare, Inc.

C. Environmental Impact

Issuance, amendment, or revocation of procedures for submission of applications for product development, testing and investigational use, and approval are categorically excluded from the requirements of an environmental assessment or impact statement under 21 CFR § 25.30(h).

D. Economic Impact

Information regarding economic impact will be submitted upon request by the Commissioner.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all the information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Please contact the undersigned at Eugia US LLC, 279 Princeton-Hightstown Road, East Windsor, NJ 08520, if you have any questions regarding this submission.[1]

Sincerely,
Eugia US LLC
(U.S. Agent for Eugia Pharma Specialities Limited)

Vincent P. Andolina

Digitally signed by Vincent P. Andolina
DN: cn=Vincent P. Andolina, o=Eugia US LLC, ou=Regulatory Affairs, email=vandolina@eugiaus.com, c=US
Date: 2022.10.10 18:42:58 -04'00'

Vincent P. Andolina
Vice President, Regulatory Affairs

[1] Alternate contact person: Ms. Apexa Chudasama, Sr. Director Regulatory Affairs (achudasama@eugiaus.com)