generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug or biologic product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: a testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Director of USPTO may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA has approved for marketing the human drug product, Onpattro (patisiran), indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. Subsequent to this approval, the USPTO received patent term restoration applications for Onpattro (U.S. Patent Nos. 8,168,775; 8,741,866; 9,234,196) from Alnylam Pharmaceuticals, Inc., and the USPTO requested FDA's assistance in determining the patents' eligibility for patent term restoration. In a letter dated July 14, 2020, FDA advised the USPTO that this human drug product had undergone a regulatory review period and that the approval of Onpattro represented the first permitted commercial marketing or use of the product. Thereafter, the USPTO requested that FDA determine the product's regulatory review period.

II. Determination of Regulatory Review Period

FDA has determined that the applicable regulatory review period for Onpattro is 1,901 days. Of this time, 1,658 days occurred during the testing phase of the regulatory review period, while 243 days occurred during the approval phase. These periods of time were derived from the following dates:

1. The date an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(i)) became effective: May 29, 2013. Alnylam Pharmaceuticals, Inc. claims that June 7, 2013, is the date the investigational new drug application (IND) became effective. However, FDA's records indicate that the effective date of the IND was May 29, 2013, which was the first date after receipt of the IND that the investigational studies could proceed.

2. The date the application was initially submitted with respect to the human drug product under section 505 of the FD&C Act: December 11, 2017. FDA has verified the applicant's claim that the new drug application (NDA) for Onpattro (NDA 210922) was initially submitted on December 11, 2017.

3. The date the application was approved: August 10, 2018. FDA has verified the applicant's claim that NDA 210922 was approved on August 10, 2018.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the USPTO applies several statutory limitations in its calculations of the actual period for patent extension. In its applications for patent extension, this applicant seeks 593 days, 887 days or 1,025 days of patent term extension.

III. Petitions

Anyone with knowledge that any of the dates as published are incorrect may submit either electronic or written comments and, under 21 CFR 60.24, ask for a redetermination (see **DATES**). Furthermore, as specified in § 60.30 (21 CFR 60.30), any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period. To meet its burden, the petition must comply with all the requirements of § 60.30, including but not limited to: must be timely (see **DATES**), must be filed in accordance with § 10.20, must contain sufficient facts to merit an FDA investigation, and must certify that a true and complete copy of the petition has been served upon the patent applicant. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41–42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Submit petitions electronically to *https://www.regulations.gov* at Docket No. FDA–2013–S–0610. Submit written petitions (two copies are required) to the Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Dated: May 10, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2023–10317 Filed 5–12–23; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–N–2029]

Final Decision on Withdrawal of MAKENA (Hydroxyprogesterone Caproate) and Eight Abbreviated New Drug Applications Following Public Hearing; Availability of Final Decision

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of the final decision withdrawing approval of MAKENA (hydroxyprogesterone caproate injection, 250 milligrams (mg) per milliliter (mL), once weekly), under the new drug application (NDA) 021945, held by Covis Pharma Group/Covis Pharma GmbH (Covis), and the eight abbreviated new drug applications (ANDAs) from multiple ANDA holders that reference NDA 021945. The Commissioner of Food and Drugs (the Commissioner) and the Chief Scientist jointly issued the decision following an October 2022 public hearing.

DATES: Approval of MAKENA and the ANDAs that reference MAKENA is withdrawn as of April 6, 2023.

FOR FURTHER INFORMATION CONTACT: Patrick Raulerson, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6260, Silver Spring, MD 20993–0002, 301–796–3522, *Patrick.Raulerson@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

On February 3, 2011, FDA's Center for Drug Evaluation and Research (CDER) approved NDA 021945 for MAKENA (hydroxyprogesterone caproate) Injection to reduce the risk of preterm birth (PTB) in women with a singleton pregnancy who have a history of singleton spontaneous PTB (sPTB). FDA approved MAKENA under the accelerated approval pathway, pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 356(c)) and 21 CFR 314.510, based on evidence of the drug's effect on

an intermediate clinical endpoint that was considered reasonably likely to predict the drug's clinical benefit.

As a condition of MAKENA's approval, the sponsor was required to complete a postmarketing trial to verify and describe the clinical benefit of MAKENA in reducing neonatal morbidity and mortality from complications of PTB among babies born to women with a singleton pregnancy who had a previous singleton sPTB. This postmarketing confirmatory trial, Trial 003, failed to show that MAKENA reduced the risk of neonatal morbidity and mortality from complications of PTB and failed to show a treatment effect of MAKENA on the intermediate clinical endpoint that was the basis of MAKENA's approval.

On October 5, 2020, CDER issued a proposal to withdraw approval of MAKENA and a notice of opportunity for hearing (NOOH) on two independent grounds using expedited procedures under section 506(c)(3) of the FD&C Act and 21 CFR 314.530(a): (1) the confirmatory trial failed to verify the clinical benefit of the drug and (2) the evidence demonstrates that the drug is not shown to be effective under its conditions of use. CDER's NOOH and proposal to withdraw approval of MAKENA also provided notice to all holders of approved ANDAs referencing the NDA for MAKENA (NDA 021945) that, if the Agency were to withdraw approval of MAKENA, CDER would withdraw approval of those ANDAs under 21 CFR 314.151(b)(3).

MAKENA's sponsor submitted a hearing request dated October 14, 2020, followed by a submission of data and information in support of the hearing request. The Agency granted the sponsor's hearing request on August 18, 2021, and on August 17, 2022, published a notice of hearing (87 FR 50626). The hearing was held on October 17, 18, and 19, 2022. The Obstetrics, Reproductive and Urologic Drugs Advisory Committee was present at the hearing to review the issues involved and to provide advice and recommendations to the Commissioner. The presiding officer issued a report, dated January 19, 2023, that summarized the legal and factual background, content of the hearing, and her analysis and recommendations. On April 6, 2023, after considering CDER's and Covis' March 6, 2023, post-hearing submissions, the Commissioner and Chief Scientist jointly issued a final decision withdrawing approval of MAKENA and the ANDAs that referenced MAKENA.

FDA has withdrawn approvals of the following NDA and eight ANDAs:

Application No.	Drug	Holder/sponsor
NDA 021945	Makena (hydroxyprogesterone caproate) Injection, 250 mg per mL	Covis Pharma Group/Covis Pharma GmbH.
ANDA 208381	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Sun Pharmaceutical Industries, Ltd.
ANDA 210618	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Slayback Pharma LLC.
ANDA 210723	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	American Regent, Inc.
ANDA 210724	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Do.
ANDA 210877	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Slayback Pharma LLC.
ANDA 211070	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Eugia Pharma Specialities Ltd.
ANDA 211071	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Do.
ANDA 211777	Hydroxyprogesterone Caproate Injection USP, 250 mg/mL	Aspen Pharma USA Inc.

Withdrawal of approval of the applications listed in the table includes all strengths, dosage forms, amendments, and supplements to these applications, effective April 6, 2023. As discussed in the decision of the Commissioner and Chief Scientist, FDA has withdrawn approval of the MAKENA NDA for reasons of safety or effectiveness, as well as approval of the ANDAs that reference MAKENA.

Section 505(j)(7) of the FD&C Act (21 U.S.C. 355(j)(7)) requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the ''Approved Drug Products With Therapeutic Equivalence Evaluations,'' which is known generally as the ''Orange Book,'' available at *https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm.* Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness 21 CFR 314.162. Accordingly, the Agency has removed the applications listed in the table from the list of drug products published in the Orange Book. FDA will not accept or approve ANDAs that reference MAKENA.

II. Electronic Access

Persons with access to the internet may obtain the final decision at *https://downloads.regulations.gov/FDA-2020-N-2029-0385/attachment_1.pdf.* The final decision, a transcript of the hearing, and other documents pertaining to the withdrawal of the NDA for MAKENA (NDA 021945) are available at *https://www.regulations.gov* under the docket number found in brackets in the heading of this document.

Dated: May 8, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2023–10264 Filed 5–12–23; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA–2020–E–1905 and FDA–2020–E–1896]

Determination of Regulatory Review Period for Purposes of Patent Extension; Tack Endovascular System (6F)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or the Agency) has determined the regulatory review period for Tack Endovascular System (6F) and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of applications to the Director of the U.S. Patent and Trademark Office (USPTO), Department of Commerce, for the extension of patents which claim that medical device.

DATES: Anyone with knowledge that any of the dates as published (see