



# U.S. FDA APPROVES NEXTSTELLIS<sup>®</sup>, NEW ORAL CONTRACEPTIVE

*First approved product containing estetrol (E4), the first new estrogen introduced in the U.S. in over 50 years*

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**April 16, 2021, Greenville, North Carolina:** Mayne Pharma announced today that the U.S. Food and Drug Administration (FDA) has approved NEXTSTELLIS (3 mg drospirenone [DRSP] and 14.2 mg estetrol [E4] tablets) for the prevention of pregnancy. NEXTSTELLIS is the first and only contraceptive pill containing E4, a naturally occurring estrogen, now produced from a plant source, with a unique mechanism of action that offers potential advantages over other estrogens.

“When speaking with patients about their contraceptive options, one of the most common concerns is side effects,” said Mitchell Creinin, Professor and Director of Family Planning at the University of California, Davis. “NEXTSTELLIS is an innovative contraceptive that has been shown to be not only safe and effective, but also well tolerated in clinical trials with a desirable bleeding profile and minimal impact on triglycerides, cholesterol, and glucose, as well as weight and endocrine markers.”

Nearly 10 million American women use short-acting combination contraceptives (estrogen and progestin). Of these contraceptives, more than 99% contain ethinyl estradiol (EE), a synthetic estrogen that binds widely to all estrogen receptors in the body.

NEXTSTELLIS is the **only** oral contraceptive to contain E4; E4 acts differently than other estrogens and is the first estrogen to be described as a NEST: A **N**ative **E**strogen with **S**elective actions in **T**issues. It has more selective activity in tissues, focusing on those needed to support contraceptive efficacy, cycle control and other beneficial effects of estrogen. NEXTSTELLIS pairs E4, which has a long half-life (24-28 hours), with the proven progestin drospirenone, specifically chosen due to its long half-life (~30 hours) and its anti-androgenic and anti-mineralocorticoid properties.

“The approval of NEXTSTELLIS represents an important milestone in providing women with another choice for their reproductive health,” said Scott Richards, CEO of Mayne Pharma. “We are delighted to be introducing a new estrogen and bringing to market this novel, safe and effective option for women to consider with their healthcare providers.”

The comprehensive NEXTSTELLIS clinical study program included a diverse patient population with women both starting and switching birth control as well as patients with a body mass index (BMI) of up to 35 kg/m<sup>2</sup>. According to phase 3 study findings, NEXTSTELLIS demonstrated contraceptive efficacy across all subgroups by age, BMI<sup>1</sup> and prior hormonal contraception use. NEXTSTELLIS was also associated with a favorable bleeding profile and low rates of breakthrough bleeding, including in cycle 1.

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<sup>1</sup> In females with BMI  $\geq$  30 kg/m<sup>2</sup>, decreasing effectiveness may be associated with increasing BMI.



NEXTSTELLIS was developed by Mayne Pharma's development and manufacturing partner, Mithra Pharmaceuticals, SA. The company anticipates the commercial launch of NEXTSTELLIS by the end of June 2021.

## About NEXTSTELLIS

NEXTSTELLIS is a novel, combined oral contraceptive pill containing 3 mg drospirenone (DRSP) and 14.2 mg estetrol (E4) indicated for use by females of reproductive age to prevent pregnancy. E4 is a naturally produced estrogen during pregnancy, which can now be made from a plant source. In two phase 3 clinical studies conducted in 3,725 women, NEXTSTELLIS was shown both safe and effective and met its primary efficacy endpoint of pregnancy prevention while also meeting a variety of secondary endpoints that demonstrated favorable cycle control, bleeding control, safety, and tolerability.

## IMPORTANT SAFETY INFORMATION

The following ISI is based on the highlights section of the U.S. Prescribing Information for NEXTSTELLIS. These highlights do not include all the information needed to use NEXTSTELLIS safely and effectively. Please consult the full Prescribing Information for all labelled safety information for NEXTSTELLIS.

**WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS**  
*See full prescribing information for complete boxed warning.*

- **Females over 35 years old who smoke should not use NEXTSTELLIS**
- **Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use.**

## INDICATIONS AND USAGE

NEXTSTELLIS is a combination of drospirenone, a progestin, and estetrol, an estrogen, indicated for use by females of reproductive potential to prevent pregnancy.

### Limitations of Use

NEXTSTELLIS may be less effective in females with a BMI  $\geq 30$  kg/m<sup>2</sup>. In females with BMI  $\geq 30$  kg/m<sup>2</sup>, decreasing effectiveness may be associated with increasing BMI.

## CONTRAINDICATIONS

NEXTSTELLIS is contraindicated and should not be used in women with a high risk of arterial or venous thrombotic diseases; current or history of a hormonally-sensitive malignancy (e.g., breast cancer); hepatic adenoma; hepatocellular carcinoma; acute hepatitis or decompensated cirrhosis; co-administration with hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir; abnormal uterine bleeding that has an undiagnosed etiology; renal impairment; adrenal insufficiency.

## WARNINGS AND PRECAUTIONS

- **Thromboembolic Disorders and Other Vascular Problems:**
- Stop NEXTSTELLIS if a thrombotic or thromboembolic event occurs. Start no earlier than 4 weeks after delivery. Consider all cardiovascular risk factors before initiating in any female, particularly in the presence of multiple risk factors.
- **Hyperkalemia:**
  - Check serum potassium concentration during the first NEXTSTELLIS treatment cycle in females on long-term treatment with medications that may increase serum potassium concentration.
- **Hypertension** - Monitor blood pressure periodically and stop use if blood pressure rises significantly.
- **Migraine** – Discontinue if new, recurrent, persistent, or severe migraines occur.
- **Hormonally-Sensitive Malignancy** - Discontinue NEXTSTELLIS if a hormonally-sensitive malignancy is diagnosed.
- **Liver Disease**-Withhold or permanently discontinue for persistent or significant elevation of liver enzymes.
- **Glucose Tolerance and Hypertriglyceridemia** -Monitor glucose in females with prediabetes or diabetes. Consider an alternate contraceptive method for females with hypertriglyceridemia.
- **Gallbladder Disease and Cholestasis:** Consider discontinuing NEXTSTELLIS in females with symptomatic gallbladder or cholestatic disease.
- **Bleeding Irregularities and Amenorrhea:** may cause irregular bleeding or amenorrhea. Evaluate for other causes if symptoms persist.

## ADVERSE REACTIONS

- The following most common adverse reactions occurred in  $\geq 2\%$  of women who received NEXTSTELLIS: bleeding irregularities, mood disturbance, headache, breast symptoms, dysmenorrhea, acne, weight increased, and libido decreased.

To report SUSPECTED ADVERSE REACTIONS, contact Mayne Pharma at 1-844-825-8500 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch)

## DRUG INTERACTIONS

- **CYP3A Inducers:** May lead to contraceptive failure and/or increase breakthrough bleeding. Avoid concomitant use. If concomitant use is unavoidable, use an alternative or back-up contraceptive method during co-administration and up to 28 days after discontinuation of the CYP3A inducer.
- See Full Prescribing Information for additional clinically significant drug interactions.



This is not a comprehensive list of safety information related to NEXTSTELLIS.

Please See Full Prescribing Information, including BOXED WARNING.

#### About Mayne Pharma

Mayne Pharma is focused on applying its track record of innovation and success in developing new oral drug delivery systems to commercialize branded and generic pharmaceuticals, offering patients better and more accessible medicines. The company has an extensive Women's Health portfolio focused on contraceptives, including its flagship birth control product, NEXTSTELLIS. Its parent company, Mayne Pharma Group Limited, is an ASX-listed specialty pharmaceutical company that also provides contract development and manufacturing services to more than 100 clients worldwide.

Mayne Pharma and Mayne Pharma Group Limited are based in Greenville, NC and Salisbury, Australia, respectively.

*NEXTSTELLIS® is a registered trademark of a third party.*

PM-US-NEX-0006