Estrogen matters so it's time to get SELECTIVE

nextstellis®
(drospirenone and estetrol tablets)
3 mg/14.2 mg

IMPORTANT SAFETY INFORMATION

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.

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.

Please see Important Safety Information in this document and full Prescribing Information enclosed

This information is also available at www.NEXTSTELLIS.com

NEXTSTELLIS – combined to be native, selective and effective[1-5]

- NEXTSTELLIS is the first ever oral contraceptive to combine estetrol (E4) with drospirenone (DRSP)[2]
  - DRSP has proven anti-androgenic and anti-mineralocorticoid properties[6]
  - Long half lives: E4: 24-28h;[7,8] DRSP ~30h[9]
- NEXTSTELLIS has been specifically designed to help overcome the issues associated with synthetic or modified estrogen-based COCs[10,11]

Native

- Estetrol (E4) is a native estrogen, circulating at high levels in mother and fetus during human pregnancy[3]
- E4 is produced from a plant source[4]

Selective

- E4 provides the usual estrogen benefits to the vascular system, bone, vagina, and brain[12-16]
- But unlike other contraceptive estrogens, E4 has uniquely selective action at the endometrium, liver and breast[1,5,17,18]

Effective

- NEXTSTELLIS has 98% contraceptive efficacy in preventing pregnancy (Pearl Index of 2.65) with a **24/4 monophasic regimen**[2,5]
- Proven in large, robust clinical trials involving 3,632 women observed for >26,000 cycles – with 22% of women having a BMI 30-35 kg/m^2 (Pearl Index of 2.94)[2,5]

LIMITATIONS OF USE

NEXTSTELLIS may be less effective in females with a BMI ≥30 kg/m^2. In females with BMI ≥30 kg/m^2, decreasing effectiveness may be associated with increasing BMI.

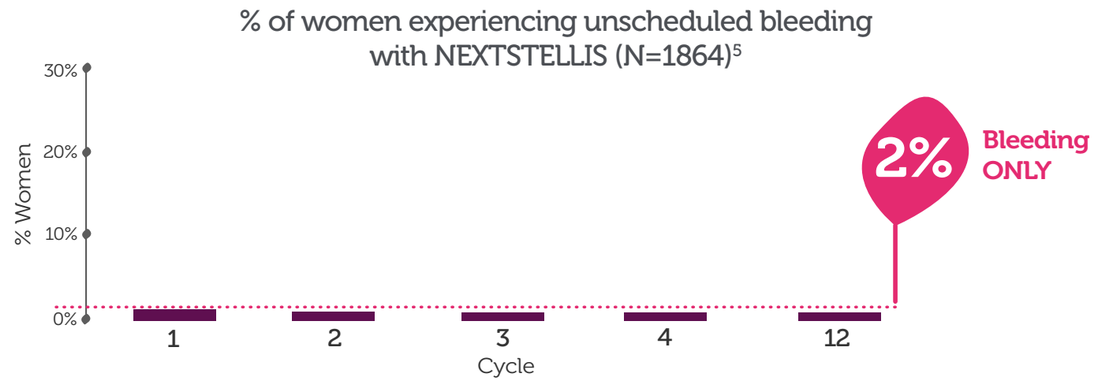
DOSAGE FORMS AND STRENGTHS

NEXTSTELLIS consists of 28 tablets in the following order:
- 24 pink active tablets each containing drospirenone 3 mg and estetrol 14.2 mg
- 4 white inert tablets

CONTRAINDICATIONS
- 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

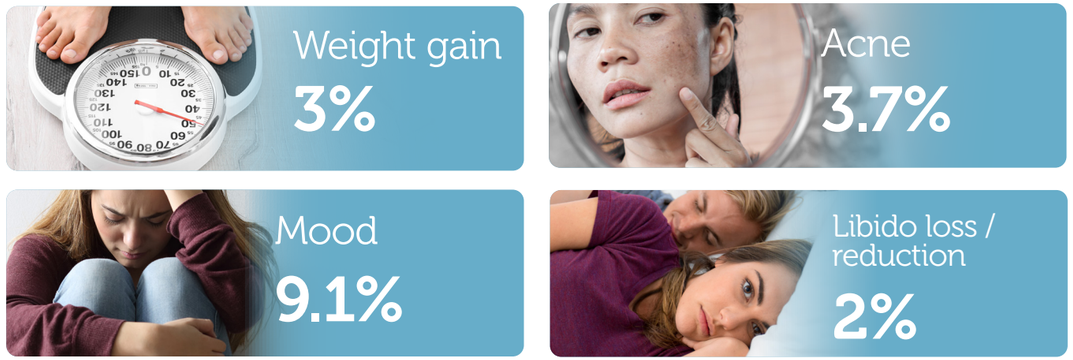
Please see Important Safety Information in this document, including Boxed Warning and full Prescribing Information enclosed

Which means women don't have to compromise between cycle control and tolerability[2,5]



- Less than **2%** of women experienced unscheduled bleeding[5]
- **The low rate of unscheduled bleeding starts at cycle 1** – with **<1 day** of unscheduled spotting or bleeding after cycle 1[5]
- Only **2.8%** of women withdrew from treatment due to bleeding irregularities[2]

Proven tolerability and safety in 2 Phase III studies with 3,632 patients studied over 26,455 cycles[2]



% women experiencing adverse events (N=3632)* *Any adverse reaction equals any adverse event >2% non-drug and drug-related[2]

- **ONE Venous thromboembolism (VTE)** in the phase 3 study program (One in the EU; zero in North America)[2]

Adverse events in women receiving NEXTSTELLIS

The most common adverse reactions (≥2%) in the studies were bleeding irregularities, mood disturbance, headache, breast symptoms, dysmenorrhea, acne, increased weight and decreased libido.

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NEXTSTELLIS safely and effectively. See full prescribing information for NEXTSTELLIS.

NEXTSTELLIS® (drospirenone and estetrol tablets), for oral use. Initial U.S. Approval: 2021

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 (4)
- Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. (4)

RECENT MAJOR CHANGES

Warnings and Precautions (5.5) 04/2022

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. (1)

Limitations of Use
NEXTSTELLIS may be less effective in females with a BMI ≥ 30 kg/m2. In females with BMI ≥ 30 kg/m2, decreasing effectiveness may be associated with increasing BMI (14).

DOSAGE AND ADMINISTRATION

- Take one tablet by mouth at the same time every day. (2.1)
- Take tablets in the order directed on the blister pack. (2.1)

DOSAGE FORMS AND STRENGTHS

NEXTSTELLIS consists of 28 tablets in the following order (3):
- 24 pink active tablets each containing drospirenone 3 mg and estetrol 14.2 mg
- 4 white inert tablets

CONTRAINDICATIONS

- A high risk of arterial or venous thrombotic diseases (4)
- Breast cancer or history of breast cancer (4)
- Hepatic adenoma, hepatocellular carcinoma, acute hepatitis or decompensated cirrhosis (4)
- Co-administration with hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir (4, 7.1)
- Abnormal uterine bleeding that has an undiagnosed etiology (4)
- Renal impairment (4)
- Adrenal insufficiency (4)

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. (5.1)
- 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. (5.2, 7.2)
- Hypertension: Monitor blood pressure periodically and stop use if blood pressure rises significantly. (5.3)
- Migraine: Discontinue if new, recurrent, persistent, or severe migraines occur. (5.4)
- Hormonally-Sensitive Malignancy: Discontinue NEXTSTELLIS if a hormonally-sensitive malignancy is diagnosed. (5.5)
- Liver Disease: Withhold or permanently discontinue for persistent or significant elevation of liver enzymes. (5.6)
- Glucose Tolerance and Hypertriglyceridemia: Monitor glucose in females with prediabetes or diabetes. Consider an alternate contraceptive method for females with hypertriglyceridemia. (5.8)
- Gallbladder Disease and Cholestasis: Consider discontinuing NEXTSTELLIS in females with symptomatic gallbladder or cholestatic disease. (5.9)
- Bleeding Irregularities and Amenorrhea: May cause irregular bleeding or amenorrhea. Evaluate for other causes if symptoms persist. (5.11)

ADVERSE REACTIONS

Most common adverse reactions (≥2%): bleeding irregularities, mood disturbance, headache, breast symptoms, dysmenorrhea, acne, weight increased, and libido decreased (6)
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

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. (7.1)
- See Full Prescribing Information for additional clinically significant drug interactions (7).

USE IN SPECIFIC POPULATIONS

- Pregnancy: Discontinue if pregnancy occurs. (8.1)
- Lactation: Advise postpartum females that NEXTSTELLIS can decrease milk production. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2022

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