

## CLINICAL UPDATE

<b>Brand Name</b>	Dolishale™
<b>Generic Name</b>	Levonorgestrel and ethinyl estradiol
<b>Drug Manufacturer</b>	Novast Labs

### Clinical Update

#### TYPE OF CLINICAL UPDATE

New brand

#### FDA APPROVAL DATE

October 22, 2020

#### LAUNCH DATE

N/A

#### REVIEW DESIGNATION

N/A

#### TYPE OF REVIEW

Abbreviated New Drug Application (ANDA): 091692

#### DISPENSING RESTRICTIONS

N/A

### Overview

#### INDICATION(S) FOR USE

Dolishale™ is indicated for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

#### MECHANISMS OF ACTION

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

#### DOSAGE FORM(S) AND STRENGTH(S)

Tablet: Levonorgestrel 90 mcg and ethinyl estradiol 20 mcg

#### DOSE & ADMINISTRATION

To achieve maximum contraceptive effectiveness, Dolishale™ (levonorgestrel and ethinyl estradiol tablets) must be taken exactly as directed and at intervals not exceeding 24 hours. The possibility of ovulation and conception prior to initiation of medication should be considered. Women who do not wish to become pregnant after discontinuation should be advised to immediately use another method of birth control. The dosage of Dolishale™ is one green tablet daily without any tablet-free interval.

It is recommended that Dolishale™ tablets be taken at the same time each day.

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Current contraceptive therapy	Dolishale start day	Nonhormonal back-up method of birth control needed when correctly starting Dolishale?
None	Day 1 of patient's menstrual cycle (during the first 24 hours of her period)	No
21-day COC regimen OR 28-day COC regimen	Day 1 of patient's withdrawal bleed, at the latest 7 days after her last active tablet.	No
Progestin-only pill	Day after taking a progestin-only pill	Yes, for the first 7 days of Dolishale tablet taking
Implant	Day of implant removal	Yes, for the first 7 days of Dolishale tablet taking
Injection	Day the next injection is due	Yes, for the first 7 days of Dolishale tablet taking

### EFFICACY

The efficacy and safety of levonorgestrel and ethinyl estradiol tablets were studied in 2 one-year clinical trials of subjects age 18 to 49. There were no exclusions for body mass index (BMI), weight, or bleeding history.

The primary efficacy and safety study (313-NA) was a one-year open-label clinical trial that treated 2,134 subjects in North America. Of these subjects 1,213 (56.8%) discontinued prematurely, including 102 (4.8%) discontinued by the Sponsor for early study closure. The mean weight of subjects in this study was 70.38 kg. The efficacy of levonorgestrel and ethinyl estradiol tablets was assessed by the number of pregnancies that occurred after the onset of treatment and within 14 days of the last dose. Among subjects 35 years or less, there were 23 pregnancies (4 of these occurred during the interval 1 to 14 days after the last day of pill use) during 12,572 28-day pill packs of use. The resulting total Pearl Index was 2.38 (95% CI: 1.51, 3.57) and the one-year life table pregnancy rate was 2.39 (95% CI: 1.57, 3.62). Pill pack cycles during which subjects used back-up contraception or were not sexually active were not included in these calculations. Among women 35 years or less who took the pills completely as directed, there were 15 pregnancies (method failures) resulting in a Pearl Index of 1.55 (95% CI: 0.87, 2.56) and the one-year life table pregnancy rate was 1.59 (95% CI: 0.95 to 2.67).

In a second supportive study conducted in Europe (315-EU), 641 subjects were randomized to levonorgestrel and ethinyl estradiol tablets (n=323) or the cyclic comparator of 100 mcg levonorgestrel and 20 mcg ethinyl estradiol (n=318). The mean weight of subjects in this study was 63.86 kg. The efficacy analysis among women 35 years or less included 2,756 levonorgestrel and ethinyl estradiol tablet pill packs and 2,886 cyclic comparator pill packs. There was one pregnancy in the levonorgestrel and ethinyl estradiol group that occurred within 14 days following the last dose. There were three pregnancies in the cyclic comparator group.

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