**NEXT CHOICE- levonorgestrel tablet**
**H.J. Harkins Company, Inc.**

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use Next Choice™ safely and effectively. See full prescribing information for Next Choice™.**
**Next Choice™ (levonorgestrel) Tablets, 0.75 mg, for oral use**
**Initial U.S. Approval: 1982**

**INDICATIONS AND USAGE**

Next Choice™ is a progestin-only emergency contraceptive, indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. Next Choice™ is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older. Next Choice™ is not intended for routine use as a contraceptive. (1)

**DOSAGE AND ADMINISTRATION**

The first tablet is taken orally as soon as possible within 72 hours after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Efficacy is better if Next Choice™ is taken as soon as possible after unprotected intercourse. (2)

**DOSAGE FORMS AND STRENGTHS**

A total of two 0.75 mg tablets taken 12 hours apart as a single course of treatment (3)

**CONTRAINDICATIONS**

Known or suspected pregnancy. (4)

**WARNINGS AND PRECAUTIONS**

- Ectopic Pregnancy: Women who become pregnant or complain of lower abdominal pain after taking Next Choice™ should be evaluated for ectopic pregnancy. (5.1)
- Next Choice™ is not effective in terminating an existing pregnancy. (5.2)
- Effect on menses: Next Choice™ may alter the next expected menses. If menses is delayed beyond 1 week, pregnancy should be considered. (5.3)
- STI/HIV: Next Choice™ do not protect against STI/HIV. (5.4)
- Contains FD&C Yellow #6 as a color additive.

**ADVERSE REACTIONS**

The most common adverse reactions (> 10%) in the clinical trial included menstrual changes (26%), nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), dizziness (11%), and breast tenderness (11%). (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Watson Laboratories, Inc. at 1-800-272-5525 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**DRUG INTERACTIONS**

Drugs or herbal products that induce certain enzymes, such as CYP3A4, may decrease the effectiveness of progestin-only pills. (7)

**USE IN SPECIFIC POPULATIONS**

- Nursing Mothers: Small amounts of progestin pass into the breast milk of nursing women taking progestin-only pills for long-term contraception, resulting in detectable steroid levels in infant plasma. (8.3)
- Next Choice™ is not intended for use in premenarcheal (8.4) or postmenopausal females (8.5).
- Clinical trials demonstrated a higher pregnancy rate in the Chinese population. (8.6)

**See 17 for PATIENT COUNSELING INFORMATION.**

**Revised: 10/2012**

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## FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Next Choice™ is a progestin-only emergency contraceptive indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet should be taken 12 hours later.

Next Choice™ is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older.

Next Choice™ is not indicated for routine use as a contraceptive.

### 2 DOSAGE AND ADMINISTRATION

Take one levonorgestrel tablet orally as soon as possible within 72 hours after unprotected intercourse

or a known or suspected contraceptive failure. Efficacy is better if the tablet is taken as soon as possible after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Next Choice™ can be used at any time during the menstrual cycle.

If vomiting occurs within two hours of taking either dose of medication, consideration should be given to repeating the dose.

## 3 DOSAGE FORMS AND STRENGTHS

Each Next Choice™ tablet is supplied as a peach, round, bevel edged, flat faced tablet containing 0.75 mg of levonorgestrel and is embossed with "475" on one side and "WATSON" on the other side.

## 4 CONTRAINDICATIONS

Next Choice™ is contraindicated for use in the case of known or suspected pregnancy.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of all reported pregnancies. Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic.

A history of ectopic pregnancy is not a contraindication to use of this emergency contraceptive method. Healthcare providers, however, should consider the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Next Choice™. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Next Choice™.

### 5.2 Existing Pregnancy

Next Choice™ is not effective in terminating an existing pregnancy.

### 5.3 Effects on Menses

Some women may experience spotting a few days after taking Next Choice™. Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and women using levonorgestrel for postcoital and emergency contraception. If there is a delay in the onset of expected menses beyond 1 week, consider the possibility of pregnancy.

### 5.4 STI/HIV

Next Choice™ does not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

### 5.5 Physical Examination and Follow-up

A physical examination is not required prior to prescribing Next Choice™. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Next Choice™.

### 5.6 Fertility Following Discontinuation

A rapid return of fertility is likely following treatment with Next Choice™ for emergency contraception; therefore, routine contraception should be continued or initiated as soon as possible following use of Next Choice™ to ensure ongoing prevention of pregnancy.

### 5.7 Presence of FD&C Yellow #6

Next Choice$^{TM}$ contains FD&C Yellow #6 as a color additive.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. A double-blind, controlled clinical trial in 1,955 evaluable women compared the efficacy and safety of levonorgestrel tablets (one 0.75 mg tablet of levonorgestrel taken within 72 hours of unprotected intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets each containing 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol, taken within 72 hours of intercourse, and two tablets taken 12 hours later).

The most common adverse events (>10%) in the clinical trial for women receiving levonorgestrel tablets included menstrual changes (26%), nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), dizziness (11%), and breast tenderness (11%). Table 1 lists those adverse events that were reported in >5% of levonorgestrel tablets users.

**Table 1: Adverse Events in >5% of Women, by % Frequency**

| Most Common Adverse Events | Levonorgestrel N=977 (%) |
|---|---|
| Nausea | 23.1 |
| Abdominal Pain | 17.6 |
| Fatigue | 16.9 |
| Headache | 16.8 |
| Heavier Menstrual Bleeding | 13.8 |
| Lighter Menstrual Bleeding | 12.5 |
| Dizziness | 11.2 |
| Breast Tenderness | 10.7 |
| Other complaints | 9.7 |
| Vomiting | 5.6 |
| Diarrhea | 5.0 |

### 6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Next Choice$^{TM}$. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

*Gastrointestinal Disorders*

Abdominal Pain, Nausea, Vomiting

*General Disorders and Administration Site Conditions*

Fatigue

*Nervous System Disorders*

Dizziness, Headache

*Reproductive System and Breast Disorders*

Dysmenorrhea, Irregular Menstruation, Oligomenorrhea, Pelvic Pain

## 7 DRUG INTERACTIONS

Drugs or herbal products that induce enzymes, including CYP3A4, that metabolize progestins may decrease the plasma concentrations of progestins, and may decrease the effectiveness of progestin-only pills. Some drugs or herbal products that may decrease the effectiveness of progestin-only pills include:

- barbiturates
- bosentan
- carbamazepine
- felbamate
- griseofulvin
- oxcarbazepine
- phenytoin
- rifampin
- St. John's wort
- topiramate

Significant changes (increase or decrease) in the plasma levels of the progestin have been noted in some cases of coadministration with HIV protease inhibitors or with non-nucleoside reverse transcriptase inhibitors.

Consult the labeling of all concurrently used drugs to obtain further information about interactions with progestin-only pills or the potential for enzyme alterations.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Many studies have found no harmful effects on fetal development associated with longterm use of contraceptive doses of oral progestins. The few studies of infant growth and development that have been conducted with progestin-only pills have not demonstrated significant adverse effects.

### 8.3 Nursing Mothers

In general, no adverse effects of progestin-only pills have been found on breastfeeding performance or on the health, growth or development of the infant. However, isolated post-marketing cases of decreased milk production have been reported. Small amounts of progestins pass into the breast milk of nursing mothers taking progestin-only pills for long-term contraception, resulting in detectable steroid levels in infant plasma.

### 8.4 Pediatric Use

Safety and efficacy of progestin-only pills for long-term contraception have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents less than 17 years and for users 17 years and older. Use of Next Choice$^{TM}$ emergency contraception before menarche is not indicated.

### 8.5 Geriatric Use

This product is not intended for use in postmenopausal women.

### 8.6 Race

No formal studies have evaluated the effect of race. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both levonorgestrel tablets and the Yuzpe regimen (another form of emergency contraception). The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown.

### 8.7 Hepatic Impairment

No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of levonorgestrel tablets.

### 8.8 Renal Impairment

No formal studies were conducted to evaluate the effect of renal disease on the disposition of levonorgestrel tablets.

## 9 DRUG ABUSE AND DEPENDENCE

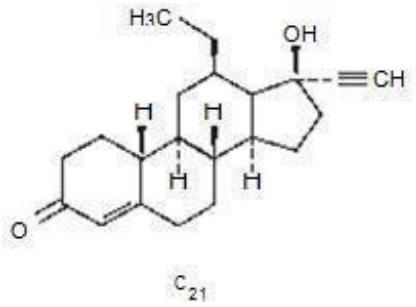
Levonorgestrel is not a controlled substance. There is no information about dependence associated with the use of Next Choice™.

## 10 OVERDOSAGE

There are no data on overdosage of levonorgestrel tablets, although the common adverse event of nausea and associated vomiting may be anticipated.

## 11 DESCRIPTION

Each Next Choice™ tablet contains 0.75 mg of a single active steroid ingredient, levonorgestrel [18,19-Dinorpregn-4-en-20-yn-3-one-13-ethyl-1 7-hydroxy-, (17α)-(-)-], a totally synthetic progestogen. The inactive ingredients present are colloidal silicon dioxide, corn starch, FD&C Yellow #6, magnesium stearate, povidone, and lactose monohydrate. Levonorgestrel has a molecular weight of 312.45, and the following structural and molecular formulas:

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## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Emergency contraceptive pills are not effective if a woman is already pregnant. Next Choice™ is believed to act as an emergency contraceptive principally by preventing ovulation or fertilization (by altering tubal transport of sperm and/or ova). In addition, they may inhibit implantation (by altering the endometrium). It is not effective once the process of implantation has begun.

### 12.3 Pharmacokinetics

#### Absorption

No specific investigation of the absolute bioavailability of levonorgestrel tablets in humans has been conducted. However, literature indicates that levonorgestrel is rapidly and completely absorbed after oral administration (bioavailability about 100%) and is not subject to first pass metabolism.

After a single dose of levonorgestrel tablets (0.75 mg) administered to 16 women under fasting

conditions, the mean maximum serum concentration of levonorgestrel was 14.1 ng/mL at an average of 1.6 hours. See Table 2.

**Table 2: Pharmacokinetic Parameter Values Following Single Dose Administration of Levonorgestrel Tablets 0.75 mg to Healthy Female Volunteers under Fasting Conditions**

| | Mean (± SD) | | | | | |
|---|---|---|---|---|---|---|
| | $C_{max}$ (ng/mL) | $T_{max}$ (h) | CL (L/h) | $V_d$ (L) | $t_{1/2}$ (h) | $AUC_{inf}$ (ng·hr/mL) |
| Levonorgestrel | 14.1 (7.7) | 1.6 (0.7) | 7.7 (2.7) | 260.0 | 24.4 (5.3) | 123.1 (50.1) |

$C_{max}$ = maximum concentration

$T_{max}$ = time to maximum concentration

CL = clearance

$V_d$ = volume of distribution

$t_{1/2}$ = elimination half life

$AUC_{inf}$ = area under the drug concentration curve from time 0 to infinity

Effect of Food: The effect of food on the rate and the extent of levonorgestrel absorption following single oral administration of levonorgestrel has not been evaluated.

**Distribution**

The apparent volume of distribution of levonorgestrel is reported to be approximately 1.8 L/kg. It is about 97.5 to 99% protein-bound, principally to sex hormone binding globulin (SHBG) and, to a lesser extent, serum albumin.

**Metabolism**

Following absorption, levonorgestrel is conjugated at the 17β-OH position to form sulfate conjugates and, to a lesser extent, glucuronide conjugates in plasma. Significant amounts of conjugated and unconjugated 3α, 5β-tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3α, 5α-tetrahydrolevonorgestrel and 16βhydroxylevonorgestrel. Levonorgestrel and its phase I metabolites are excreted primarily as glucuronide conjugates. Metabolic clearance rates may differ among individuals by several-fold, and this may account in part for the wide variation observed in levonorgestrel concentrations among users.

**Excretion**

About 45% of levonorgestrel and its metabolites are excreted in the urine and about 32% are excreted in feces, mostly as glucuronide conjugates.

**Specific Populations**

Pediatric: This product is not intended for use in the premenarcheal population, and pharmacokinetic data are not available for this population.

Geriatric: This product is not intended for use in postmenopausal women and pharmacokinetic data are not available for this population.

Race: No formal studies have evaluated the effect of race on pharmacokinetics of levonorgestrel tablets. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both levonorgestrel tablets and the Yuzpe regimen (another form of emergency contraception). The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown [see *USE IN SPECIFIC POPULATIONS (8.6)]*.

Hepatic Impairment: No formal studies were conducted to evaluate the effect of hepatic disease on the

disposition of levonorgestrel tablets.

Renal Impairment: No formal studies were conducted to evaluate the effect of renal disease on the disposition of levonorgestrel tablets.

**Drug-Drug Interactions**

No formal drug-drug interaction studies were conducted with levonorgestrel tablets [see *DRUG INTERACTIONS (7)]*.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity: There is no evidence of increased risk of cancer with short-term use of progestins. There was no increase in tumorgenicity following administration of levonorgestrel to rats for 2 years at approximately 5 µg/day, to dogs for 7 years at up to 0.125 mg/kg/day, or to rhesus monkeys for 10 years at up to 250 µg/kg/day. In another 7 year dog study, administration of levonorgestrel at 0.5 mg/kg/day did increase the number of mammary adenomas in treated dogs compared to controls. There were no malignancies.

Genotoxicity: Levonorgestrel was not found to be mutagenic or genotoxic in the Ames Assay, *in vitro* mammalian culture assays utilizing mouse lymphoma cells and Chinese hamster ovary cells, and in an *in vivo* micronucleus assay in mice.

Fertility: There are no irreversible effects on fertility following cessation of exposures to levonorgestrel or progestins in general.

## 14 CLINICAL STUDIES

A double-blind, randomized, multinational controlled clinical trial in 1,955 evaluable women (mean age 27) compared the efficacy and safety of levonorgestrel tablets (one 0.75 mg tablet of levonorgestrel taken within 72 hours of unprotected intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets each containing 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol, taken within 72 hours of intercourse, and two additional tablets taken 12 hours later). After a single act of intercourse occurring anytime during the menstrual cycle, the expected pregnancy rate of 8% (with no contraceptive use) was reduced to approximately 1% with levonorgestrel tablets.

Emergency contraceptives are not as effective as routine hormonal contraception since their failure rate, while low based on a single use, would accumulate over time with repeated use [see *INDICATIONS AND USAGE (1)]*.

At the time of expected menses, approximately 74% of women using levonorgestrel tablets had vaginal bleeding similar to their normal menses, 14% bled more than usual, and 12% bled less than usual. The majority of women (87%) had their next menstrual period at the expected time or within + 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

Next Choice™ (levonorgestrel) tablets, 0.75 mg, are available for a single course of treatment in PVC/aluminum foil blister packages of two tablets each. Each tablet is peach, round, bevel edged, and flat faced and embossed with “475” on one side and “WATSON” on the other side.

Available as: Unit-of-use NDC 52544-275-36

Store Next Choice™ tablets at 20° to 25°C (68° to 77°F) [see USP controlled room temperature].

## 17 PATIENT COUNSELING INFORMATION

### 17.1 Information for Patients

- Take Next Choice™ as soon as possible and not more than 72 hours after unprotected intercourse or a known or suspected contraceptive failure.
- If you vomit within two hours of taking either tablet, immediately contact your healthcare provider to discuss whether to take another tablet.
- Seek medical attention if you experience severe lower abdominal pain 3 to 5 weeks after taking Next Choice™, in order to be evaluated for an ectopic pregnancy.
- After taking Next Choice™, consider the possibility of pregnancy if your period is delayed more than one week beyond the date you expected your period.
- Do not use Next Choice™ as routine contraception.
- Next Choice™ is not effective in terminating an existing pregnancy.
- Next Choice™ does not protect against HIV-infection (AIDS) and other sexually transmitted diseases/infections.
- For women younger than age 17 years, Next Choice™ is available only by prescription.
- Next Choice™ contains FD&C Yellow #6 as a color additive.

Manufactured by: **Watson Laboratories, Inc.**

Corona, CA 92880 USA

Distributed by: **Watson Pharma, Inc.**

Corona, CA 92880 USA

Phone: 1 -866-9WATSON (1-866-992-8766)

www.mynextchoice.com

Issued: August 2009

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Repacked by:
H.J. Harkins Company, Inc.
Grover Beach, CA 93433

## PRINCIPAL DISPLAY PANEL

Next Choice™

(Levonorgestrel) tablets 0.75 mg

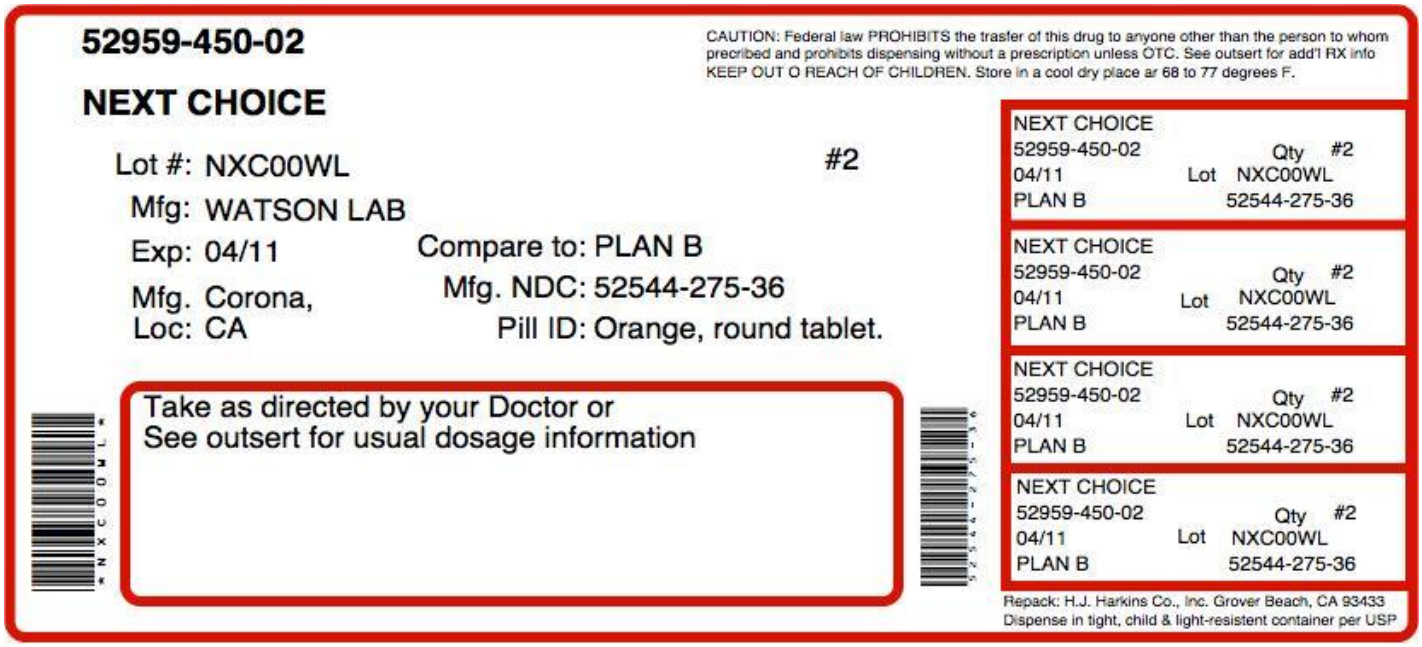
Emergency Contraceptive

*Reduces the chance of pregnancy after unprotected sex (if a regular birth control method fails or after sex without birth control).*

*Not for regular birth control.*

*Next Choice™ should be used only in emergencies.*

2 Levonorgestrel Tablets
0.75 mg each




# NEXT CHOICE

levonorgestrel tablet

| Product Information | | | |
|---|---|---|---|
| **Product Type** | HUMAN PRESCRIPTION DRUG | **Item Code (Source)** | NDC:52959-450(NDC:52544-275) |
| **Route of Administration** | ORAL | | |

| Active Ingredient/Active Moiety | | |
|---|---|---|
| **Ingredient Name** | **Basis of Strength** | **Strength** |
| **LEVONORGESTREL** (UNII: 5W7SIA7YZW) (LEVONORGESTREL - UNII:5W7SIA7YZW) | LEVONORGESTREL | 0.75 mg |

| Inactive Ingredients | |
|---|---|
| **Ingredient Name** | **Strength** |
| **SILICON DIOXIDE** (UNII: ETJ7Z6XBU4) | |
| **STARCH, CORN** (UNII: O8232NY3SJ) | |
| **FD&C YELLOW NO. 6** (UNII: H77VEI93A8) | |
| **MAGNESIUM STEARATE** (UNII: 70097M6I30) | |
| **POVIDONE** (UNII: FZ989GH94E) | |
| **LACTOSE MONOHYDRATE** (UNII: EWQ57Q8I5X) | |

| Product Characteristics | | | |
|---|---|---|---|
| **Color** | ORANGE (peach) | **Score** | no score |
| **Shape** | ROUND (bevel edged, flat faced) | **Size** | 6mm |
| **Flavor** | | **Imprint Code** | 475;WATSON |
| **Contains** | | | |

## Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|---|---|---|---|
| 1 | NDC:52959-450-02 | 2 in 1 BLISTER PACK | | |

## Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|---|---|---|---|
| ANDA | ANDA078665 | 09/04/2009 | |

## Labeler - H.J. Harkins Company, Inc. (147681894)

## Registrant - H.J. Harkins Company, Inc. (147681894)

## Establishment

| Name | Address | ID/FEI | Business Operations |
|---|---|---|---|
| H.J. Harkins Company, Inc. | | 147681894 | relabel(52959-450) , repack(52959-450) |

Revised: 10/2012 H.J. Harkins Company, Inc.