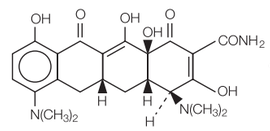
11 DESCRIPTION

Minocycline hydrochloride, a semi synthetic derivative of tetracycline, is [4S-(4α,4aα,5aα,12aα)]-4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide mono hydrochloride. The structural formula is represented below:



$C_{23}H_{27}N_3O_7$•HCl M. W. 493.95

SOLODYN Tablets for oral administration contain minocycline hydrochloride USP equivalent to 55 mg, 65 mg, 80 mg, 105 mg, or 115 mg of minocycline. In addition, 55 mg, 65 mg, 80 mg, 105 mg, and 115 mg tablets contain the following inactive ingredients: lactose monohydrate NF, hypromellose type 2910 USP, magnesium stearate NF, colloidal silicon dioxide NF, and carnauba wax NF. The 55 mg tablets also contain Opadry II Pink which contains: hypromellose type 2910 USP, titanium dioxide USP, lactose monohydrate NF, polyethylene glycol 3350 NF, triacetin USP, and FD&C Red #40. The 65 mg tablets also contain Opadry II Blue which contains: hypromellose type 2910 USP, lactose monohydrate NF, FD&C Blue #1, polyethylene glycol 3350 NF, FD&C Blue #2, titanium dioxide USP, triacetin USP, and D&C Yellow #10. The 80 mg tablets also contain Opadry II Gray which contains: hypromellose type 2910 USP, lactose monohydrate NF, polyethylene glycol 3350 NF, FD&C Blue #2, FD&C Red #40, titanium dioxide USP, triacetin USP, and FD&C Yellow #6. The 105 mg tablets also contain Opadry II Purple which contains: hypromellose type 2910 USP, lactose monohydrate NF, titanium dioxide USP, D&C Red #27, polyethylene glycol 3350 NF, triacetin USP, and FD&C Blue #1. The 115 mg tablets also contain Opadry II Green which contains: hypromellose type 2910 USP, lactose monohydrate NF, D&C Yellow #10, triacetin USP, FD&C Blue #1, titanium dioxide USP, and FD&C Blue #2.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of SOLODYN for the treatment of acne is unknown.

12.2 Pharmacodynamics

The pharmacodynamics of SOLODYN for the treatment of acne are unknown.

12.3 Pharmacokinetics

SOLODYN Tablets are not bioequivalent to non-modified release minocycline products. Based on pharmacokinetic studies in healthy adults, SOLODYN Tablets produce a delayed T_{max} at 3.5–4.0 hours as compared to a non-modified release reference minocycline product (T_{max} at 2.25–3 hours). At steady-state (Day 6), the mean AUC(0–24) and C_{max} were 33.32 µg×hr/mL and 2.63 µg/mL for SOLODYN Tablets and 46.35 µg×hr/mL and 2.92 µg/mL for Minocin® capsules, respectively. These parameters are based on dose adjusted to 135 mg per day for both products.

A single-dose, four-way crossover study demonstrated that SOLODYN Tablets used in the study (45 mg, 90 mg, 135 mg) exhibited dose-proportional pharmacokinetics. In another single-dose, five-way crossover pharmacokinetic study, SOLODYN Tablets 55 mg, 80 mg, and 105 mg were shown to be dose-proportional to SOLODYN Tablets 90 mg and 135 mg.

When SOLODYN Tablets were administered concomitantly with a meal that included dairy products, the extent and timing of absorption of minocycline did not differ from that of administration under fasting conditions.

Minocycline is lipid soluble and distributes into the skin and sebum.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis— In a carcinogenicity study in which minocycline HCl was orally administered to male and female rats once daily for up to 104 weeks at dosages up to 200 mg/kg/day, minocycline HCl was associated in both genders with follicular cell tumors of the thyroid gland, including increased incidences of adenomas, carcinomas and the combined incidence of adenomas and carcinomas in males, and adenomas and the combined incidence of adenomas and carcinomas in females. In a carcinogenicity study in which minocycline HCl was orally administered to male and female mice once daily for up to 104 weeks at dosages up to 150 mg/kg/day, exposure to minocycline HCl did not result in a significantly increased incidence of neoplasms in either males or females.

Mutagenesis—Minocycline was not mutagenic *in vitro* in a bacterial reverse mutation assay (Ames test) or CHO/HGPRT mammalian cell assay in the presence or absence of metabolic activation. Minocycline was not clastogenic *in vitro* using human peripheral blood lymphocytes or *in vivo* in a mouse micronucleus test.

Impairment of Fertility—Male and female reproductive performance in rats was unaffected by oral doses of minocycline of up to 300 mg/kg/day (which resulted in up to approximately 40 times the level of systemic exposure to minocycline observed in patients as a result of use of SOLODYN). However, oral administration of 100 or 300 mg/kg/day of minocycline to male rats (resulting in approximately 15 to 40 times the level of systemic exposure to minocycline observed in patients as a result of use of SOLODYN) adversely affected spermatogenesis. Effects observed at 300 mg/kg/day included a reduced number of sperm cells per gram of epididymis, an apparent reduction in the percentage of sperm that were motile, and (at 100 and 300 mg/kg/day) increased numbers of morphologically abnormal sperm cells. Morphological abnormalities observed in sperm samples included absent heads, misshapen heads, and abnormal flagella.

Limited human studies suggest that minocycline may have a deleterious effect on spermatogenesis.

SOLODYN should not be used by individuals of either gender who are attempting to conceive a child.

14 CLINICAL STUDIES

The safety and efficacy of SOLODYN in the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris was assessed in two 12-week, multi-center, randomized, double-blind, placebo-controlled, trials in subjects ≥ 12 years. The mean age of subjects was 20 years and subjects were from the following racial groups: White (73%), Hispanic (13%), Black (11%), Asian/Pacific Islander (2%), and Other (2%).

In two efficacy and safety trials, a total of 924 subjects with non-nodular moderate to severe acne vulgaris received SOLODYN or placebo for a total of 12 weeks, according to the following dose assignments.

Table 3: Clinical Studies Dosing Table

Subject's Weight (lbs.)	Subject's Weight (kg)	Available Tablet Strength (mg)	Actual mg/kg Dose
99 – 131	45 – 59	45	1 – 0.76
132 – 199	60 – 90	90	1.5 – 1
200 – 300	91 – 136	135	1.48 – 0.99

The two primary efficacy endpoints were:

1) Mean percent change in inflammatory lesion counts from Baseline to 12 weeks.
2) Percentage of subjects with an Evaluator's Global Severity Assessment (EGSA) of clear or almost clear at 12 weeks.

Efficacy results are presented in Table 4.

Table 4: Efficacy Results at Week 12

	Trial 1		Trial 2	
	SOLODYN (1 mg/kg) N = 300	**Placebo N = 151**	**SOLODYN (1 mg/kg) N = 315**	**Placebo N = 158**
Mean Percent Improvement in Inflammatory Lesions	43.1%	31.7%	45.8%	30.8%
No. (%) of Subjects Clear or Almost Clear on the EGSA*	52 (17.3%)	12 (7.9%)	50 (15.9%)	15 (9.5%)

*Evaluator's Global Severity Assessment

SOLODYN did not demonstrate any effect on non-inflammatory lesions (benefit or worsening).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

SOLODYN (minocycline HCl, USP) Extended Release Tablets are supplied as aqueous film coated tablets containing minocycline hydrochloride equivalent to 55 mg, 65 mg, 80 mg, 105 mg, or 115 mg minocycline, are supplied as follows.

The 55 mg extended release tablets are pink, unscored, coated, and debossed with "DYN-055" on one side. Each tablet contains minocycline hydrochloride equivalent to 55 mg minocycline, supplied as follows:

NDC 99207-465-30 Bottle of 30

The 65 mg extended release tablets are blue, unscored, coated, and debossed with "DYN-065" on one side. Each tablet contains minocycline hydrochloride equivalent to 65 mg minocycline, supplied as follows:

NDC 99207-463-30 Bottle of 30

The 80 mg extended release tablets are dark gray, unscored, coated, and debossed with "DYN-080" on one side. Each tablet contains minocycline hydrochloride equivalent to 80 mg minocycline, supplied as follows:

NDC 99207-466-30 Bottle of 30

The 105 mg extended release tablets are purple, unscored, coated, and debossed with "DYN-105" on one side. Each tablet contains minocycline hydrochloride equivalent to 105 mg minocycline, supplied as follows:

NDC 99207-467-30 Bottle of 30

The 115 mg extended release tablets are green, unscored, coated, and debossed with "DYN-115" on one side. Each tablet contains minocycline hydrochloride equivalent to 115 mg minocycline, supplied as follows:

NDC 99207-464-30 Bottle of 30

16.2 Storage

Store at 25ºC (77ºF); excursions are permitted to 15º-30ºC (59º-86ºF). [See USP Controlled Room Temperature].

16.3 Handling

Keep out of reach of children.

Protect from light, moisture, and excessive heat.

Dispense in tight, light-resistant container with child-resistant closure.

17 PATIENT COUNSELING INFORMATION

[See FDA-approved patient labeling (Patient Information)]

Patients taking SOLODYN (minocycline HCl, USP) Extended Release Tablets should receive the following information and instructions:

- SOLODYN should not be used by pregnant women or women attempting to conceive a child *[see Use in Specific Populations (8.1), Nonclinical Toxicology (13.1)]*.
- It is recommended that SOLODYN not be used by men who are attempting to father a child *[see Nonclinical Toxicology (13.1)]*.
- Patients should be advised that pseudomembranous colitis can occur with minocycline therapy. If patients develop watery or bloody stools, they should seek medical attention.
- Patients should be counseled about the possibility of hepatotoxicity. Patients should seek medical advice if they experience symptoms which can include loss of appetite, tiredness, diarrhea, skin turning yellow, bleeding easily, confusion, and sleepiness.
- Patients who experience central nervous system symptoms *[see Warnings and Precautions (5.5)]* should be cautioned about driving vehicles or using hazardous machinery while on minocycline therapy. Patients should seek medical help for persistent headaches or blurred vision.
- Concurrent use of tetracycline may render oral contraceptives less effective *[see Drug Interactions (7.5)]*.
- Autoimmune syndromes, including drug-induced lupus-like syndrome, autoimmune hepatitis, vasculitis and serum sickness have been observed with tetracycline-class drugs, including minocycline. Symptoms may be manifested by arthralgia, fever, rash and malaise. Patients who experience such symptoms should be cautioned to stop the drug immediately and seek medical help.
- Patients should be counseled about discoloration of skin, scars, teeth or gums that can arise from minocycline therapy.
- Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines, including minocycline. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using minocycline. If patients need to be outdoors while using minocycline, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. Treatment should be discontinued at the first evidence of skin erythema.
- SOLODYN should be taken exactly as directed. Skipping doses or not completing the full course of therapy may decrease the effectiveness of the current treatment course and increase the likelihood that bacteria will develop resistance and will not be treatable by other antibacterial drugs in the future.
- Patients should be advised to swallow SOLODYN Tablets whole and not to chew, crush, or split the tablets.

Patient Information
SOLODYN® (SO-lo-dĭn)
(minocycline HCl)
Extended Release Tablets

Read this Patient Information leaflet that comes with SOLODYN before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

What is SOLODYN?

SOLODYN is a tetracycline-class drug. SOLODYN is prescription medicine used to treat pimples and red bumps (non-nodular inflammatory lesions) that happen with moderate to severe acne vulgaris in people 12 years and older. SOLODYN is not effective for acne that is not red-looking (this means acne that is not inflammatory).

It is not known if SOLODYN is:

- safe for use longer than 12 weeks.
- safe and effective for the treatment of infections.
- safe and effective in children under the age of 12 years.

Who should not take SOLODYN?

Do not take SOLODYN if you are allergic to tetracycline-class drugs. Ask your doctor or pharmacist for a list of these medicines if you are not sure.

What should I tell my doctor before taking SOLODYN?

Before you take SOLODYN, tell your doctor if you:

- have kidney problems. Your doctor may prescribe a lower dose of medicine for you.
- have liver problems.
- have diarrhea or watery stools.
- have vision problems.
- plan to have surgery with general anesthesia.
- have any other medical conditions.
- are a male, and you and your female partner are trying to conceive a baby. You should not take SOLODYN.
- are pregnant or plan to become pregnant. SOLODYN may harm your unborn baby. Taking SOLODYN while you are pregnant may cause serious side effects on the growth of bone and teeth of your baby. Talk to your doctor before taking SOLODYN if you plan to become pregnant, **or** if you are already taking SOLODYN and plan to become pregnant. Stop taking SOLODYN and call your doctor right away if you become pregnant while taking SOLODYN.
- are breastfeeding or plan to breastfeed. SOLODYN passes into your milk and may harm your baby. You and your doctor should decide if you will take SOLODYN or breastfeed. You should not do both.

Tell your doctor about all the other medicines you take including prescription and nonprescription medicines, vitamins and herbal supplements. SOLODYN® may affect the way other medicines work, and other medicines may affect how SOLODYN® works.

Especially tell your doctor if you take:

- **birth control pills.** SOLODYN® may make your birth control pills less effective. You could become pregnant. You should use a second form of birth control while taking SOLODYN®.
- **a blood thinner medicine.**
- **a penicillin antibiotic medicine.** SOLODYN® and penicillins should not be used together.
- **antacids that contain aluminum, calcium, or magnesium or iron-containing products.**
- an acne medicine that contains **isotretinoin** (Amnesteem, Claravis, Sotret). SOLODYN® and isotretinoin should not be used together.

Ask your doctor or pharmacist if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist.

How should I take SOLODYN?

- Take SOLODYN exactly as your doctor tells you.
- Skipping doses or not taking all doses of SOLODYN may:
  - make the treatment not work as well.
  - increase the chance that the bacteria will become resistant to SOLODYN.
- **SOLODYN can be taken with or without food.** Taking SOLODYN with food may lower your chances of getting irritation or ulcers in your esophagus. Your esophagus is the tube that connects your mouth to your stomach.
- **Swallow SOLODYN Tablets whole. Do not chew, crush, or split the tablets.**

If you take too much SOLODYN, call your doctor or poison control center right away. Your doctor may do blood tests to check you for side effects during treatment with SOLODYN.

What should I avoid while taking SOLODYN?

- Avoid sunlight, sunlamps, and tanning beds. SOLODYN can make your skin sensitive to the sun and the light from sunlamps and tanning beds. You could get severe sunburn.
- Protect your skin while out in sunlight.
- You should not drive or operate dangerous machinery until you know how SOLODYN affects you. SOLODYN may cause you to feel dizzy or lightheaded, or have a spinning feeling (vertigo).

What are possible side effects of SOLODYN?

SOLODYN may cause serious side effects, including:

- **Harm to an unborn baby.** See "**What should I tell my doctor before taking SOLODYN?**"
- **Permanent teeth discoloration.** SOLODYN may permanently turn a baby or child's teeth yellow-grey-brown during tooth development. SOLODYN should not be used during tooth development. Tooth development happens in the last half of pregnancy, and from birth to 8 years of age. See "**What should I tell my doctor before taking SOLODYN?**"
- **Intestine infection** (pseudomembranous colitis). Pseudomembranous colitis can happen with most antibiotics, including SOLODYN. Call your doctor right away if you get watery diarrhea, diarrhea that does not go away, or bloody stools.
- **Serious liver problems.** Stop taking SOLODYN and call your doctor right away if you get any of the following symptoms of liver problems:
  - loss of appetite
  - tiredness
  - diarrhea
  - yellowing of your skin or the whites of your eyes
  - unexplained bleeding
  - confusion
  - sleepiness
- **Central nervous system effects.** See "**What should I avoid while taking SOLODYN?**" Central nervous system effects such as light headedness, dizziness, and a spinning feeling (vertigo) may go away during your treatment with SOLODYN or if treatment is stopped.
- **Benign intracranial hypertension, also called pseudotumor cerebri.** This is a condition where there is high pressure in the fluid around the brain. This swelling may lead to vision changes and permanent vision loss. Stop taking SOLODYN and tell your doctor right away if you have blurred vision, vision loss, or unusual headaches.
- **Immune system reactions including a lupus-like syndrome, hepatitis, and inflammation of blood or lymph vessels (vasculitis).** Using SOLODYN for a long time to treat acne may cause immune system reactions. Tell your doctor right away if you get a fever, rash, joint pain, or body weakness. Your doctor may do tests to check your blood for immune system reactions.
- **Serious rash and allergic reactions.** SOLODYN may cause a serious rash and allergic reactions that may affect parts of your body such as your liver, lungs, kidneys and heart. Sometimes these can lead to death.
- Stop taking SOLODYN and get medical help right away if you have any of these symptoms:
  - skin rash, hives, sores in your mouth, or your skin blisters and peels
  - swelling of your face, eyes, lips, tongue, or throat
  - trouble swallowing or breathing
  - blood in your urine
  - fever, yellowing of the skin or the whites of your eyes, dark colored urine
  - pain on the right side of the stomach area (abdominal pain)
  - chest pain or abnormal heartbeats
  - swelling in your legs, ankles, and feet
  - darkening of your nails, skin, eyes, scars, teeth, and gums

The most common side effects of SOLODYN include:

- headache
- tiredness
- dizziness or spinning feeling
- itching

Call your doctor if you have a side effect that bothers you or that does not go away. Your doctor may do tests to check you for side effects during treatment with SOLODYN.

These are not all the side effects with SOLODYN. Ask your doctor or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Valeant Pharmaceuticals North America LLC at 1-800-321-4576.

How should I store SOLODYN?

- Store SOLODYN between 59ºF to 86ºF (15ºC to 30ºC).
- Keep SOLODYN Tablets in the container that it comes in and keep the container tightly closed.
- Keep SOLODYN Tablets dry.

Keep SOLODYN and all medicines out of the reach of children.

General information about SOLODYN

Medicines are sometimes prescribed for purposes other than those listed in the Patient Information leaflet. Do not use SOLODYN for a condition for which it was not prescribed. Do not give SOLODYN to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about SOLODYN. If you would like more information, talk to your doctor. You can ask your doctor or pharmacist for information about SOLODYN that is written for health professionals.

For more information, call 1-800-321-4576.

What are the ingredients in SOLODYN?

Active ingredient: minocycline HCl.

Inactive ingredients: lactose monohydrate, hypromellose type 2910, magnesium stearate, colloidal silicon dioxide, and carnauba wax.

The 55 mg tablets also contain Opadry II Pink which contains: hypromellose type 2910, titanium dioxide, lactose monohydrate, polyethylene glycol 3350, triacetin, and FD&C Red #40.

The 65 mg tablets also contain Opadry II Blue which contains: hypromellose type 2910, lactose monohydrate, FD&C Blue #1, polyethylene glycol 3350, FD&C Blue #2, titanium dioxide, triacetin, and D&C Yellow #10.

The 80 mg tablets also contain Opadry II Gray which contains: hypromellose type 2910, lactose monohydrate, polyethylene glycol 3350, FD&C Blue #2, FD&C Red #40, titanium dioxide, triacetin, and FD&C Yellow #6.

The 105 mg tablets also contain Opadry II Purple which contains: hypromellose type 2910, lactose monohydrate, titanium dioxide, D&C Red #27, polyethylene glycol 3350, triacetin, and FD&C Blue #1.

The 115 mg tablets also contain Opadry II Green which contains: hypromellose type 2910, lactose monohydrate NF, D&C Yellow #10, triacetin, FD&C Blue #1, titanium dioxide, FD&C Blue #2.

SOLODYN® is manufactured by WellSpring Pharmaceutical Canada Corp. for Medicis, The Dermatology Company, Scottsdale, Arizona, 85256.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: 10/2013

Manufactured for:

Medicis, The Dermatology Company

Scottsdale, AZ 85256

Manufactured by:

WellSpring Pharmaceutical Canada Corp.

Oakville, Ontario, CANADA L6H 1M5

Product of Portugal

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