AT A GLANCE—ABSORPTION

ABSORICA LD™
isotretinoin capsules
8mg • 16mg • 24mg • 32mg

Relapse and retreatment of severe recalcitrant nodular acne may be due to inadequate absorption of prescribed doses.[1,2]

Adequate absorption is critical to reach a therapeutic dose.

Help your patients avoid relapse and retreatment.[3-5]*

Write DAW-1 for

↑2× more absorption in a fasted state*

Compared to ABSORICA® (isotretinoin) with a similar safety profile[3,4]

INDICATIONS AND USAGE

ABSORICA LD (isotretinoin) capsules are indicated for the treatment of severe recalcitrant nodular acne in non-pregnant patients 12 years of age and older with multiple inflammatory nodules with a diameter of 5 mm or greater. Because of significant adverse reactions associated with its use, ABSORICA LD is reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics.

Limitations of Use:
If a second course of ABSORICA LD therapy is needed, it is not recommended before a two-month waiting period because the patient's acne may continue to improve following a 15 to 20-week course of therapy

Please see additional Important Safety Information inside this brochure. For more information, please see enclosed full Prescribing Information for Boxed Warning, Contraindications, and other important Warnings and Precautions.

IMPORTANT SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY – CONTRAINDICATED IN PREGNANCY

ABSORICA LD can cause severe life-threatening birth defects and is contraindicated in pregnancy. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking any amount of ABSORICA LD even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining prenatally whether an exposed fetus has been affected. If pregnancy occurs, discontinue ABSORICA LD immediately and refer the patient to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Because of the risk of embryo-fetal toxicity, ABSORICA LD is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the iPLEDGE® REMS.

IMPORTANT SAFETY INFORMATION (CONTINUED)

CONTRAINDICATIONS

Pregnancy: ABSORICA LD is contraindicated in pregnancy

Hypersensitivity: ABSORICA LD is contraindicated in patients with hypersensitivity to isotretinoin (or Vitamin A, given the chemical similarity to isotretinoin) or to any of its components (anaphylaxis and other allergic reactions have occurred)

WARNINGS AND PRECAUTIONS

ABSORICA and ABSORICA LD are Not Substitutable: The bioavailability and the recommended dosage of ABSORICA and ABSORICA LD are different. For example, while ABSORICA and ABSORICA LD both have a 20 mg strength, these strengths have different bioavailability and are not substitutable.

Psychiatric Disorders: ABSORICA LD may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. Prior to and during therapy, assess for these conditions.

Patients should immediately stop ABSORICA LD and promptly contact their prescriber if they develop depression, mood disturbance, psychosis, or aggression. Discontinuation of ABSORICA LD may be insufficient; further evaluation may be necessary such as a referral to a mental healthcare professional.

Intracranial Hypertension (Pseudotumor Cerebri): Isotretinoin use has been associated with cases of intracranial hypertension (pseudotumor cerebri), some of which involved concomitant use of tetracyclines. Concomitant treatment with tetracyclines should therefore be avoided with ABSORICA LD use.

Serious Skin Reactions: There have been postmarketing reports of erythema multiforme and severe skin reactions [e.g., Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)] associated with isotretinoin use. These reactions may be serious and result in death, life-threatening events, hospitalization, or disability. Patients should be monitored closely for severe skin reactions, and ABSORICA LD should be discontinued if they occur.

Acute Pancreatitis: Acute pancreatitis has been reported with isotretinoin use in patients with either elevated or normal serum triglyceride levels. In rare instances, fatal hemorrhagic pancreatitis has been reported. If symptoms of pancreatitis occur, the patient should discontinue ABSORICA LD and seek medical attention.

Lipid Abnormalities: Elevations of serum triglycerides above 800 mg/dL have been reported with isotretinoin use. These lipid changes were reversible upon isotretinoin capsule cessation. Some patients have been able to reverse triglyceride elevation by reduction in weight and restriction of dietary fat and alcohol while continuing isotretinoin or through dosage reduction. The cardiovascular consequences of hypertriglyceridemia associated with isotretinoin are unknown.

Hearing Impairment: Impaired hearing has been reported in patients taking isotretinoin; in some cases, the impairment has been reported to persist after therapy has been discontinued. Mechanism(s) and causality for this reaction have not been established. Patients who experience tinnitus or hearing impairment should discontinue ABSORICA LD treatment and be referred for specialized care for further evaluation.

Hepatotoxicity: Clinical hepatitis has been reported with isotretinoin use. Additionally, mild to moderate elevations of liver enzymes have been observed in approximately 15% of individuals treated during clinical trials with isotretinoin capsules, some of which normalized with dosage reduction or continued administration of the drug. If normalization does not readily occur or if hepatitis is suspected during treatment, ABSORICA LD should be discontinued.

Inflammatory Bowel Disease: Isotretinoin has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. In some instances, symptoms have been reported to persist after isotretinoin treatment has been stopped. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue ABSORICA LD immediately**.**

Musculoskeletal Abnormalities: Effects of multiple courses of isotretinoin on the developing musculoskeletal system are unknown. There is some evidence that long-term, high-dose, or multiple courses of therapy with isotretinoin have more of an effect than a single course of therapy on the musculoskeletal system. It is important that ABSORICA LD be given at the recommended dose for no longer than the recommended duration.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Ocular Abnormalities: Visual problems should be carefully monitored. If visual difficulties occur, the patient should discontinue ABSORICA LD treatment and obtain an ophthalmological examination.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 5%) are: dry lips, dry skin, back pain, dry eye, arthralgia, epistaxis, headache, nasopharyngitis, chapped lips, dermatitis, increased creatine kinase, cheilitis, musculoskeletal discomfort, upper respiratory tract infection, reduced visual acuity.

DRUG INTERACTIONS

Vitamin A: ABSORICA LD is closely related to vitamin A. Therefore, the use of both vitamin A and ABSORICA LD at the same time may lead to vitamin A related adverse reactions. Patients treated with ABSORICA LD should be advised against taking supplements containing Vitamin A to avoid additive toxic effects.

Tetracyclines: Concomitant treatment with ABSORICA LD and tetracyclines should be avoided because isotretinoin use has been associated with a number of cases of intracranial hypertension (pseudotumor cerebri), some of which involved concomitant use of tetracyclines.

USE IN SPECIFIC POPULATIONS

There are no data on the presence of isotretinoin in either animal or human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions in nursing infants from isotretinoin, advise patients that breastfeeding is not recommended during treatment with ABSORICA LD, and for at least 8 days after the last dose of ABSORICA LD.

These are not all of the possible side effects of ABSORICA LD. Call your doctor for medical advice about side effects. You may report side effects to FDA at **1-800-FDA-1088** or Sun Pharmaceutical Industries, Inc. at **1-800-818-4555**.

Please see full Prescribing Information, for Boxed Warning, Contraindications, and other important Warnings and Precautions.

References: 1. Colburn WA, Gibson DM, Wiens RE, Hanigan JJ. Food increases the bioavailability of isotretinoin. *J Clin Pharmacol.* 1983;23:534-9. **2.** Del Rosso JQ. Face to face with oral isotretinoin: a closer look at the spectrum of therapeutic outcomes and why some patients need repeated courses. *J Clin Aesthet Dermatol.* 2012;5(11)17-24. **3.** ABSORICA/ABSORICA LD Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc: October 2019. **4.** Madan S, Kumar S, Segal J. Comparative pharmacokinetic profiles of a novel low-dose micronized-isotretinoin 32 mg formulation and lidose-isotretinoin 40 mg in fed and fasted conditions: two open-label, randomized, crossover studies in healthy adult participants. *Acta Derm Venereol.* 2020;100(1-4):1-7. **5.** Del Rosso JQ, Gold LS, Segal J, Zaenglein AL. An open-label, phase IV study evaluating lidose-isotretinoin administered without food in patients with severe recalcitrant nodular acne: low relapse rates observed over the 104-week post-treatment period. *J Clin Aesth Dermatol.* 2019;12(11):13-18. **6.** Webster GF, Leyden JJ, Gross JA. Comparative pharmacokinetic profiles of a novel isotretinoin formulation (isotretinoin-Lidose) and the innovator isotretinoin formulation: a randomized, 4-treatment, crossover study. *J Am Acad Dermatol.* 2013;69(5):762-7.

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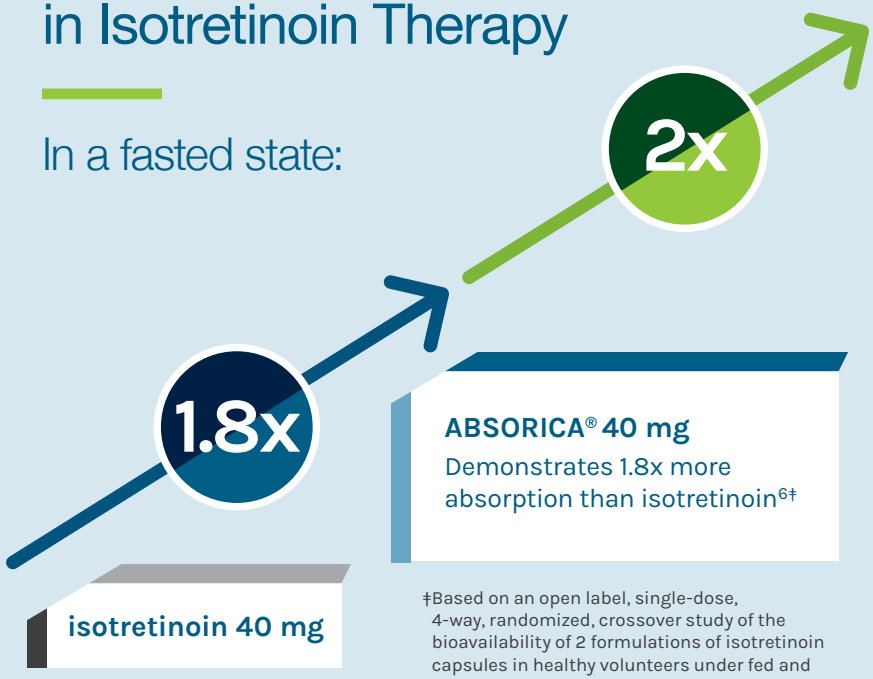
Absorption Advancements in Isotretinoin Therapy

In a fasted state:



‡Based on an open label, single-dose, 4-way, randomized, crossover study of the bioavailability of 2 formulations of isotretinoin capsules in healthy volunteers under fed and fasting conditions (n=57).[6]

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ABSORICA LD™ 32 mg offers 2x more absorption than ABSORICA®3,4†

†Based on 2 open-label, randomized, crossover studies, plasma concentrations with ABSORICA LD were demonstrated to be 2X as bioavailable as ABSORICA in a fasted state. When administered in a fed state, plasma concentrations were bioequivalent between ABSORICA and ABSORICA LD (n=18).[4]

Dose Strengths[3]

Other isotretinoins	10 mg	20 mg	30 mg	40 mg
ABSORICA LD™	8 mg	16 mg	24 mg	32 mg

Delivers **greater isotretinoin absorption** and therapeutic serum levels **at a lower dose.***[3,4]

*ABSORICA®/ABSORICA LD™ clinical statement

The effectiveness of ABSORICA/ABSORICA LD for the treatment of severe recalcitrant nodular acne in patients 12 years of age and older has been established and is based on a double-blind, randomized, parallel group trial in subjects with severe recalcitrant nodular acne who received ABSORICA or another isotretinoin capsule product under fed conditions. A total of 925 subjects were randomized 1:1 to receive ABSORICA or another isotretinoin capsule product. Study subjects ranged from 12 to 54 years of age (including 397 pediatric subjects aged 12 to 17 years); 60% were male, 40% were female; and the racial groups included 87% White, 4% Black, 6% Asian, and 3% Other. Enrolled subjects had a weight of 40 kg to 110 kg and had at least 10 nodular lesions on the face and/or trunk. Subjects were treated with an initial dose of 0.5 mg/kg/day in two divided doses for the first 4 weeks, followed by 1 mg/kg/day in two divided doses for the following 16 weeks.[3] ABSORICA was the active drug in all clinical studies claimed in this piece.

A NOTE about the iPLEDGE® Program

The goal of the iPLEDGE® Program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin. This is because there is a very high chance of birth defects if an unborn baby's mother takes isotretinoin. The iPLEDGE® Program requires 2 forms of birth control for female patients who can get pregnant for at least 1 month before, during, and 1 month after stopping treatment and pregnancy tests before, during, and after treatment. Both male and female patients must enroll and follow the requirements of the iPLEDGE® Program.

For more information on the iPLEDGE® Program, please visit ABSORICALD-hcp.com.

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SUN DERMATOLOGY

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