HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ABSORICA/ABSORICA LD safely and effectively. See full prescribing information for ABSORICA/ABSORICA LD.

ABSORICA® (isotretinoin) capsules, for oral use
ABSORICA LD® (isotretinoin) capsules, for oral use
Initial U.S. Approval: 1982

WARNING: EMBRYO-FETAL TOXICITY - CONTRAINDICATED IN PREGNANCY
See full prescribing information for complete boxed warning.

- **ABSORICA/ABSORICA LD can cause life-threatening birth defects and is contraindicated in pregnancy. There is an extremely high risk that life-threatening birth defects will result if pregnancy occurs while taking ABSORICA/ABSORICA LD in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected. (4, 5.1, 8.1)**
- **ABSORICA/ABSORICA LD are available only through a restricted program called the iPLEDGE® REMS. (5.2)**

----------INDICATIONS AND USAGE----------
ABSORICA and ABSORICA LD are retinoids 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 and ABSORICA LD are reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. (1)

Limitations of Use:
If a second course of ABSORICA/ABSORICA LD treatment is needed, it is not recommended before a 2-month waiting period because the patient's acne may continue to improve following a 15 to 20-week course of treatment. (1)

----------DOSAGE AND ADMINISTRATION----------
- Evaluations Prior To Prescribing and Use of ABSORICA/ABSORICA LD:
  - In patients who can get pregnant, only prescribe ABSORICA/ABSORICA LD after verification and documentation that they are not pregnant. See the Full Prescribing Information for the detailed requirements prior to prescribing ABSORICA/ABSORICA LD (2.1, 8.3)
  - Complete the following laboratory tests in all patients: fasting lipid profile and liver function tests. (2.1)
- ABSORICA is not substitutable with ABSORICA LD because of different bioavailability and recommended dosage. (221, 5.3)
- Recommended dosage for (2.2):
  - **ABSORICA is 0.5 to 1 mg/kg/day** given in two divided doses without regard to meals for 15 to 20 weeks
  - **ABSORICA LD is 0.4 to 0.8 mg/kg/day** given in two divided doses without regard to meals for 15 to 20 weeks
- Adult patients with very severe disease (scarring, trunk involvement) may increase dosage to 2 mg/kg/day of ABSORICA (1.6 mg/kg/day of ABSORICA LD) in divided doses. (2.2)
- Once daily dosing is not recommended. (2.2)
- If a dose of ABSORICA/ABSORICA LD is missed, just skip that dose. Do not take two doses of ABSORICA/ABSORICA LD at the same time. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
ABSORICA Capsules: 10 mg, 20 mg, 25 mg, 30 mg, 35 mg and 40 mg (3)
ABSORICA LD Capsules: 8 mg, 16 mg, 20 mg, 24 mg, 28 mg and 32 mg (3)

----------CONTRAINDICATIONS----------
ABSORICA/ABSORICA LD is contraindicated in:
- Pregnancy (4, 8.1)
- Patients with hypersensitivity to isotretinoin (or Vitamin A) or any of its components (4, 5.14)

----------WARNINGS AND PRECAUTIONS----------
- Psychiatric Disorders (depression, psychosis, suicidal thoughts and behavior, and aggressive and/or violent behaviors): Prior to and during treatment assess for these conditions; stop if these conditions occur on treatment (5.4)
- Intracranial Hypertension (Pseudotumor Cerebri): Avoid concomitant use with tetracyclines (5.5)
- Serious Skin Reactions: Monitor for Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and other serious skin reactions and discontinue treatment if they occur (5.6)
- Acute Pancreatitis: If pancreatitis symptoms occur, discontinue treatment (5.7)
- Lipid Abnormalities (hypertriglyceridemia, low HDL, and elevation of cholesterol): Monitor lipid levels at regular intervals; stop if hypertriglyceridemia cannot be controlled (5.8)
- Hearing Impairment: Discontinue and refer to specialized care (5.9)
- Hepatotoxicity: Monitor liver function tests prior to and during treatment (5.10, 5.15)
- Inflammatory Bowel Disease: Discontinue for abdominal pain, rectal bleeding, or severe diarrhea (5.11)
- Musculoskeletal Abnormalities: Arthralgias, back pain, decreases in bone mineral density and premature epiphyseal closure (5.12)
- Ocular Abnormalities e.g., corneal opacities, decreased night vision: If visual symptoms occur, discontinue and refer for an ophthalmological exam (5.13)

----------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. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sun Pharmaceutical Industries, Inc. at 1-800-818-4555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or iPLEDGE at (1-866-495-0654).

----------DRUG INTERACTIONS----------
- Vitamin A: avoid concomitant use (7.1)
- Tetracyclines: avoid concomitant use (7.2)

----------USE IN SPECIFIC POPULATIONS----------
- Lactation: Breastfeeding not recommended (8.2).
- In Patients Who Can Get Pregnant: Pregnancy testing is required prior to, during, and after ABSORICA/ABSORICA LD treatment. See the Full Prescribing Information for the detailed pregnancy test and contraception requirements. (8.3).

See Section 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 6/2026

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FULL PRESCRIBING INFORMATION

WARNING: EMBRYO-FETAL TOXICITY – CONTRAINDICATED IN PREGNANCY

ABSORICA/ABSORICA LD can cause life-threatening birth defects and is contraindicated in pregnancy. There is an extremely high risk that life-threatening birth defects will result if pregnancy occurs while taking any amount of ABSORICA/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/ABSORICA LD immediately and refer the patient to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling *[see Contraindications (4), Warnings and Precautions (5.1), and Use in Specific Populations (8.1)]*.

Because of the risk of embryo-fetal toxicity, ABSORICA and ABSORICA LD are available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the iPLEDGE REMS *[see Warnings and Precautions (5.2)].*

1 INDICATIONS AND USAGE

ABSORICA and ABSORICA LD 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 and ABSORICA LD are 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/ABSORICA LD treatment is needed, it is not recommended before a 2-month waiting period because the patient's acne may continue to improve following a 15 to 20-week course of treatment *[see Dosage and Administration (2.2)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Evaluations Prior To Prescribing and Use of ABSORICA/ABSORICA LD

In patients who can get pregnant, only prescribe ABSORICA/ABSORICA LD after verification and documentation that they are not pregnant *[see Contraindications (4) and Warnings and Precautions (5.1, 5.2)]*. For the detailed requirements prior to prescribing ABSORICA/ABSORICA LD, *see Use in Specific Populations (8.3)*.

Prior to ABSORICA/ABSORICA LD use in all patients, complete the following laboratory testing:

- A fasting lipid profile including triglycerides *[see Warnings and Precautions (5.8, 5.15)]*.
- Liver function tests *[see Warnings and Precautions (5.10, 5.15)]*.

2.2 Recommended Dosage

ABSORICA is not substitutable with ABSORICA LD *[see Warnings and Precautions (5.3)]*. The recommended dosage of:

- **ABSORICA is 0.5 to 1 mg/kg/day** given in two divided doses with or without meals for 15 to 20 weeks (see Table 1).
- **ABSORICA LD is 0.4 to 0.8 mg/kg/day** given in two divided doses with or without meals for 15 to 20 weeks (see Table 2).

To decrease the risk of esophageal irritation, instruct patients to swallow the capsules with a full glass of liquid. Swallow capsules whole. Do not split, crush, chew, or suck on the capsules.

During treatment, the dosage may be adjusted according to response of the disease and/or adverse reactions, some of which may be dose-related. Adult patients whose disease is very severe with scarring or is primarily manifested on the trunk may require dosage adjustments up to **2 mg/kg/day for ABSORICA (1.6 mg/kg/day for ABSORICA LD)** in divided doses, as tolerated.

The safety and effectiveness of once daily dosing with ABSORICA/ABSORICA LD has not been established and is not recommended.

If a dose of ABSORICA/ABSORICA LD is missed, just skip that dose. Do not take two doses of ABSORICA/ ABSORICA LD at the same time.

Table 1: ABSORICA Daily Dosage by Body Weight[1]

Body Weight	Total Daily Dosage (mg)[1]		
	0.5 mg/kg	1 mg/kg	2 mg/kg
40 kg	20	40	80
50 kg	25	50	100
60 kg	30	60	120
70 kg	35	70	140
80 kg	40	80	160
90 kg	45	90	180
100 kg	50	100	200

[1] Administer in two divided doses with or without meals

Table 2: ABSORICA LD Daily Dosage by Body Weight[1]

Body Weight	Total Daily Dosage (mg)[1]		
	0.4 mg/kg	0.8 mg/kg	1.6 mg/kg
40 kg	16	32	64
50 kg	20	40	80
60 kg	24	48	96
70 kg	28	56	112
80 kg	32	64	128
90 kg	36	72	144
100 kg	40	80	160

[1] Administer in two divided doses with or without meals

2.3 Duration of Use

A normal course of treatment is 15 to 20 weeks. If the total nodule count has been reduced by more than 70% prior to completing 15 to 20 weeks of treatment, may discontinue ABSORICA/ABSORICA LD.

After a period of 2 months or more off treatment, and if warranted by persistent or recurring severe nodular acne, may initiate a second course of ABSORICA/ABSORICA LD in patients who have completed skeletal growth. The use of another course of ABSORICA/ABSORICA LD treatment is not recommended before a 2-month waiting period because the patient's acne may continue to improve after a 15 to 20-week course of treatment. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth.

Long-term use of ABSORICA/ABSORICA LD, even in low dosages, has not been studied, and is not recommended. The effect of long-term use of ABSORICA/ABSORICA LD on bone loss is unknown *[see Warnings and Precautions (5.12)]*.

3 DOSAGE FORMS AND STRENGTHS

ABSORICA and ABSORICA LD have different dosage regimens *[see Dosage and Administration (2.1)]*. Although ABSORICA and ABSORICA LD have a 20 mg strength, these strengths have different bioavailability and are not substitutable.

ABSORICA is available in 10 mg, 20 mg, 25 mg, 30 mg, 35 mg and 40 mg capsules.

- **10 mg:** Dark yellow, opaque, capsule imprinted with black ink "**G240**" on cap and "**10**" on the body
- **20 mg:** Red, opaque, capsule imprinted with black ink "**G241**" on cap and "**20**" on the body
- **25 mg:** Green, opaque, capsule imprinted with white ink "**G342**" on cap and "**25**" on the body
- **30 mg:** Brown, opaque, capsule imprinted with white ink "**G242**" on cap and "**30**" on the body
- **35 mg:** Dark blue, opaque, capsule imprinted with white ink "**G343**" on cap and "**35**" on the body
- **40 mg:** Brown and red, capsule imprinted with white ink "**G325**" on cap and "**40**" on the body

ABSORICA LD is available in 8 mg, 16 mg, 20 mg, 24 mg, 28 mg and 32 mg opaque-printed, hard-gelatin capsules.

- **8 mg:** A size 3, light green with a colorless band (the cap is printed in white with "**RL29**" and the body is printed in white with "**RL29**").
- **16 mg:** A size 2, dark blue with a colorless band (the cap is printed in white with "**RL30**" and the body is printed in white with "**RL30**").
- **20 mg**: A size 1, dark pink with a colorless band (the cap is printed in black with "**RL33**"and the body is printed in black with "**RL33**").
- **24 mg:** A size 1, yellow with a colorless band (the cap is printed in white with "**RL31**" and the body is printed in white with "**RL31**").
- **28 mg:** A size 0, light blue, with a colorless band (the cap is printed in black with "**RL34**" and the body is printed in black with "**RL34**").
- **32 mg:** A size 0, caramel with a colorless band (the cap is printed in white with "**RL32**" and the body is printed in white with "**RL32**").

4 CONTRAINDICATIONS

ABSORICA/ABSORICA LD is contraindicated in:

- Pregnancy *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)]*.
- 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) *[see Warnings and Precautions (5.14)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

ABSORICA/ABSORICA LD is contraindicated in pregnancy *[see Contraindications (4.1)]*. Based on human data, ABSORICA/ABSORICA LD can cause fetal harm when administered to a pregnant patient. There is an extremely high risk that life-threatening birth defects will result if pregnancy occurs while taking any amount of ABSORICA/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. Major congenital malformations, spontaneous abortions, and premature births have been documented following exposure to isotretinoin during pregnancy *[see Use in Specific Populations (8.1)]*.

If a pregnancy occurs during ABSORICA/ABSORICA LD treatment, immediately discontinue ABSORICA/ABSORICA LD and refer the patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. Immediately report any suspected fetal exposure during or 1 month after ABSORICA/ABSORICA LD treatment to the FDA via the MedWatch telephone number 1-800-FDA-1088, and also to the iPLEDGE pregnancy registry at 1-866-495-0654 or via the internet (www.ipledgeprogram.com).

Inform patients not to donate blood during ABSORICA/ABSORICA LD treatment and for 1 month following discontinuation because the blood might be given to a pregnant patient whose fetus must not be exposed to isotretinoin.

ABSORICA/ABSORICA LD is available only through a restricted program under a REMS *[see Warnings and Precautions (5.2)]*.

5.2 iPLEDGE REMS

Because of the risk of embryo-fetal toxicity, ABSORICA/ABSORICA LD are available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the iPLEDGE REMS *[see Warnings and Precautions (5.1)]*.

Notable requirements of the iPLEDGE REMS include the following:

- Prescribers must be certified in the REMS and comply with the REMS requirements, including the following:
  - Assess the reproductive status of all patients prior to initiating treatment and during treatment.
  - Counsel patients who cannot get pregnant on the risk and REMS requirements prior to initiating treatment.
  - Counsel patients who can get pregnant on the risk and REMS requirements prior to and during treatment.
  - Counsel patients who can get pregnant on pregnancy prevention requirements prior to and during treatment, or refer patients who can get pregnant to an expert for such counseling.
  - Comply with the pregnancy testing requirements.
  - Assess the pregnancy status for patients who can get pregnant by reviewing pregnancy tests and documenting a negative result prior to each prescription.
  - Report all pregnancies to the REMS.

- Patients who can get pregnant must be enrolled in the REMS and must comply with the REMS requirements, including the following
  - Comply with the pregnancy testing and pregnancy prevention requirements *[see Use in Specific Populations (8.3)]*.
  - Demonstrate comprehension of the risk and REMS requirements before each prescription is dispensed.
  - Obtain the prescription within the 7-day prescription window (i.e., within 7 days of the pregnancy test collection).

- Patients who cannot get pregnant must be enrolled in the REMS and must comply with the REMS requirements, including to not share isotretinoin and not donate blood.

- Pharmacies that dispense ABSORICA/ABSORICA LD must be certified in the REMS and must comply with the REMS requirements, including the following:
  - Obtain authorization to dispense and only dispense to patients who are authorized to receive ABSORICA/ABSORICA LD.
  - Dispense a maximum of a 30-day supply with a Medication Guide.
  - Do not dispense refills.

- Wholesalers and distributors must be registered in the REMS and must only distribute to certified pharmacies.

Further information, including a list of qualified pharmacies and distributors, is available at www.ipledgeprogram.com or 1-866-495-0654.

5.3 ABSORICA and ABSORICA LD are Not Substitutable

Given that the bioavailability and the recommended dosage of ABSORICA and ABSORICA LD are different, ABSORICA and ABSORICA LD are not substitutable on a mg per mg basis. For example, ABSORICA and ABSORICA LD have a 20 mg strength; however, these strengths have different bioavailability and are not substitutable.

5.4 Psychiatric Disorders

ABSORICA/ABSORICA LD may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors *[see Adverse Reactions (6)]*.

Be alert to the warning signs of psychiatric disorders to help ensure patients receive the help they need (Prescribers should read the REMS educational material on recognizing psychiatric disorders*)*. Prior to initiation of ABSORICA/ABSORICA LD treatment, ask patients and family members about any history of psychiatric disorder, and at each visit during treatment assess patients for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation is necessary.

If a patient develops depression, mood disturbance, psychosis, or aggression, instruct patients (or caregivers) to immediately stop ABSORICA/ABSORICA LD and promptly contact their health care provider. Discontinuation of

ABSORICA/ABSORICA LD may be insufficient; further evaluation may be necessary such as a referral to a mental healthcare professional.

5.5 Intracranial Hypertension (Pseudotumor Cerebri)

Isotretinoin use has been associated with cases of intracranial hypertension (pseudotumor cerebri), some of which involved concomitant use of tetracyclines. Avoid concomitant use of ABSORICA/ABSORICA LD with tetracyclines*[see Drug Interactions (7.2)]*. Early signs and symptoms of intracranial hypertension include papilledema, headache, nausea and vomiting, and visual disturbances. Screen patients with these symptoms for papilledema and, if present, immediately discontinue ABSORICA/ABSORICA LD and refer the patient to a neurologist for further diagnosis and care *[see Adverse Reactions (6)]*.

5.6 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. Monitor patients closely for severe skin reactions and discontinue ABSORICA/ABSORICA LD if they occur.

5.7 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, discontinue ABSORICA/ABSORICA LD and instruct patients to seek medical attention.

5.8 Lipid Abnormalities

Elevations of serum triglycerides above 800 mg/dL have been reported with isotretinoin use. In clinical trials, marked elevations of serum triglycerides, decreases in high-density lipoproteins (HDL), and increases in cholesterol levels were reported in 25%, 15%, and 7% of subjects treated with isotretinoin capsules, respectively. 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.

Perform fasting lipid tests before ABSORICA/ABSORICA LD treatment and then at intervals until the lipid response to ABSORICA/ABSORICA LD is known, which usually occurs within 4 weeks. Carefully consider the risk/benefit of ABSORICA/ABSORICA LD in patients who are at higher risk of hypertriglyceridemia (e.g., patients with diabetes, obesity, increased alcohol intake, lipid metabolism disorder or familial history of lipid metabolism disorder). If ABSORICA/ABSORICA LD treatment is instituted in such patients, more frequent checks of serum values for lipids are recommended *[see Warnings and Precautions (5.15)]*. Discontinue ABSORICA/ABSORICA LD if hypertriglyceridemia cannot be controlled.

5.9 Hearing Impairment

Impaired hearing has been reported in patients taking isotretinoin; in some cases, the hearing impairment has been reported to persist after treatment has been discontinued. Mechanism(s) and causality for this reaction have not been established. Discontinue ABSORICA/ABSORICA LD treatment in patients who experience tinnitus or hearing impairment and refer them for specialized care for further evaluation.

5.10 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. Discontinue ABSORICA/ABSORICA LD if normalization does not readily occur or if hepatitis is suspected during treatment.

5.11 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. Discontinue ABSORICA/ABSORICA LD immediately if patients experience abdominal pain, rectal bleeding or severe diarrhea *[see Adverse Reactions (6)]*.

5.12 Musculoskeletal Abnormalities

Bone Mineral Density Changes, Osteoporosis, and Fractures

Isotretinoin may have a negative effect on bone mineral density (BMD) in some patients. In a clinical trial of ABSORICA and another isotretinoin capsule product, 27/306 (9%) of pediatric subjects 12 years of age and older had BMD declines, defined as ≥ 4% lumbar spine or total hip, or ≥ 5% femoral neck, during the 20-week treatment period. Repeat scans conducted within 2 to 3 months after the post-treatment scan showed no recovery of BMD. Long-term data at 4 to 11 months showed that 3 out of 7 subjects had total hip and femoral neck BMD below pre-treatment baseline, and 2 others did not show the increase in BMD above baseline expected in this pediatric population. Therefore, healthcare providers should use caution when prescribing ABSORICA/ABSORICA LD to patients with a history of childhood osteoporosis conditions, osteomalacia, or other disorders of bone metabolism or patients diagnosed with anorexia nervosa *[see Use in Specific Populations (8.4)]*.

There have been spontaneous reports of osteoporosis, osteopenia, fractures and/or delayed healing of fractures in patients while on treatment with isotretinoin or following cessation of treatment with isotretinoin.

Patients in early and late adolescence who participate in sports with repetitive impact may be at an increased risk of spondylolisthesis with and without pars fractures, and hip growth plate injuries have been reported.

Musculoskeletal Abnormalities

Approximately 16% of subjects treated with isotretinoin capsules in a clinical trial developed musculoskeletal symptoms (including arthralgia) during treatment. In general, these symptoms were mild to moderate, but occasionally required discontinuation of isotretinoin.

In a trial of pediatric subjects treated with isotretinoin capsules, approximately 29% (104/358) developed back pain. Back pain was severe in 14% (14/104) of the cases and occurred at a higher frequency in female subjects than male subjects. Arthralgias were experienced in 22% (79/358) of pediatric subjects. Arthralgias were severe in 8% (6/79) of subjects. Evaluate the musculoskeletal system of patients who present with these symptoms during or after a course of ABSORICA/ABSORICA LD. Consider discontinuing ABSORICA/ABSORICA LD if any significant abnormality is found.

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 treatment with isotretinoin have more of an effect than a single course of treatment on the musculoskeletal system. It is important to administer ABSORICA/ABSORICA LD at the recommended dose for no longer than the recommended duration.

Hyperostosis

A high prevalence of skeletal hyperostosis was noted in clinical trials for disorders of keratinization with a mean dose of 2.24 mg/kg/day of isotretinoin capsules (approximately 1.1 times the maximum recommended daily dosage). Additionally, skeletal hyperostosis was noted in 6 of 8 patients in a prospective trial of disorders of keratinization. Minimal skeletal hyperostosis and calcification of ligaments and tendons have also been observed by x-ray in prospective trials of nodular acne patients treated with a single course of treatment at recommended doses. The skeletal effects of multiple isotretinoin treatment courses for acne are unknown.

In a clinical trial of 217 pediatric subjects 12 years of age and older with severe recalcitrant nodular acne, hyperostosis was not observed after 16 to 20 weeks of treatment with approximately 1 mg/kg/day of isotretinoin capsules given in two divided doses. Hyperostosis may require a longer time frame to appear. The clinical course and significance remain unknown.

Premature Epiphyseal Closure

There are spontaneous literature reports of premature epiphyseal closure in acne patients receiving recommended doses of isotretinoin capsules. The effect of multiple courses of isotretinoin on epiphyseal closure is unknown.

In a 20-week clinical trial that included 289 pediatric subjects 12 years of age and older on ABSORICA or another isotretinoin capsule product who had hand radiographs taken to assess bone age, a total of 9 (3%) subjects had bone age changes that were clinically significant and for which a drug-related effect cannot be excluded.

5.13 Ocular Abnormalities

Carefully monitor for visual problems. If visual difficulties occur, discontinue ABSORICA/ABSORICA LD treatment and obtain an ophthalmological examination *[see Adverse Reactions (6)]*.

Corneal Opacities

Corneal opacities have occurred in patients receiving isotretinoin capsules and more frequently when higher drug dosages were used in patients with disorders of keratinization. The corneal opacities that have been observed in clinical trial subjects treated with isotretinoin capsules have either completely resolved or were resolving at follow-up 6 to 7 weeks after discontinuation of isotretinoin *[see Adverse Reactions (6)]*.

Decreased Night Vision

Decreased night vision has been reported during isotretinoin use and in some instances the event has persisted after treatment was discontinued. Because the onset in some patients was sudden, advise patients of this potential problem and warn patients to be cautious when driving or operating any vehicle at night.

Dry Eyes

Dry eyes has been reported in patients during isotretinoin use. Patients who wear contact lenses may have trouble wearing them while on ABSORICA/ABSORICA LD treatment and afterwards.

5.14 Hypersensitivity Reactions

Anaphylactic reactions and other allergic reactions have been reported with isotretinoin use. Cutaneous allergic reactions and serious cases of allergic vasculitis, often with purpura (bruises and red patches) of the extremities and extracutaneous involvement (including renal) have been reported. If a severe allergic reaction occurs, discontinue ABSORICA/ABSORICA LD treatment and initiate appropriate medical management.

Allergic Reactions Due to the Inactive Ingredient (FD&C Yellow No. 5) in the 25 mg ABSORICA Capsule

The 25 mg ABSORICA capsule contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of tartrazine sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity. The 10 mg, 20 mg, 30 mg, 35 mg, and 40 mg ABSORICA capsules do not contain FD&C Yellow No. 5 and all of the ABSORICA LD capsules do not contain FD&C Yellow No. 5. Thus, in patients with allergic reactions to tartrazine, avoid using the 25 mg ABSORICA capsules.

5.15 Laboratory Abnormalities and Laboratory Monitoring for Adverse Reactions

Laboratory Monitoring

Pregnancy Testing: Obtain a screening and confirmatory pregnancy test **prior to treatment initiation.** Repeat a pregnancy test prior to each prescription, at the end of the entire course of ABSORICA/ABSORICA LD treatment, and 1 month after the discontinuation of ABSORICA/ABSORICA LD *[see Use in Specific Populations (8.3)]*.

Lipid Tests: Obtain pretreatment and follow-up fasting lipid tests under fasting conditions. Wait 36 hours after consumption of alcohol before testing is performed. It is recommended that these tests be performed periodically until the lipid response to ABSORICA/ABSORICA LD is known. The incidence of hypertriglyceridemia is 25% in patients treated with isotretinoin capsules *[see Warnings and Precautions (5.8)]*.

Liver Function Tests: As elevations of liver enzymes have been observed during clinical trials, and hepatitis has been reported in patients on isotretinoin capsules, perform pretreatment and follow-up liver function tests periodically until the response to ABSORICA/ABSORICA LD is known *[see Warnings and Precautions (5.10)]*.

Additional Laboratory Abnormalities

Glucose: With isotretinoin use, some patients have experienced problems in the control of their blood sugar. In addition, new cases of diabetes have been diagnosed during isotretinoin use.

CPK: Some patients undergoing vigorous physical activity while taking isotretinoin have experienced elevated CPK levels; however, the clinical significance is unknown. There have been rare postmarketing reports of rhabdomyolysis with isotretinoin use, some associated with strenuous physical activity. In a clinical trial of 924 subjects, marked elevations in CPK (≥350 U/L) were observed in approximately 24% of subjects treated with isotretinoin capsules.

In another clinical trial of 217 pediatric subjects 12 years of age and older elevations in CPK were observed in 12% of subjects, including those undergoing strenuous physical activity in association with reported musculoskeletal adverse events such as back pain, arthralgia, limb injury, or muscle sprain. In these subjects, approximately half of the CPK elevations returned to normal within 2 weeks and half returned to normal within 4 weeks. No cases of rhabdomyolysis were reported in this clinical trial.

6 ADVERSE REACTIONS

The following adverse reactions with ABSORICA/ABSORICA LD or other isotretinoin capsule products are described in more detail in other sections of the labeling:

- Embryo-Fetal Toxicity *[see Warnings and Precautions (5.1)]*
- Psychiatric Disorders *[see Warnings and Precautions (5.4)]*
- Intracranial Hypertension (Pseudotumor Cerebri) *[see Warnings and Precautions (5.5)]*
- Serious Skin Reactions *[see Warnings and Precautions (5.6)]*
- Pancreatitis *[see Warnings and Precautions (5.7)]*
- Lipid Abnormalities *[see Warnings and Precautions (5.8)]*
- Hearing Impairment *[see Warnings and Precautions (5.9)]*
- Hepatotoxicity *[see Warnings and Precautions (5.10)]*
- Inflammatory Bowel Disease *[see Warnings and Precautions (5.11)]*
- Musculoskeletal Abnormalities *[see Warnings and Precautions (5.12)]*
- Ocular Abnormalities *[see Warnings and Precautions (5.13)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.14)]*

The following adverse reactions associated with the use of isotretinoin capsules were identified in clinical trials or postmarketing reports. Because some of these reactions were 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.

Dose Relationship
Cheilitis and hypertriglyceridemia were dose related.

Body as a Whole
Fatigue, irritability, pain, allergic reactions, systemic hypersensitivity, edema, lymphadenopathy, weight loss.

Cardiovascular
Vascular thrombotic disease, stroke, palpitation, tachycardia.

Endocrine/Metabolism and Nutritional
Decreased appetite, weight fluctuation, alterations in blood sugar.

Gastrointestinal
Dry lips, chapped lips, cheilitis, nausea, constipation, diarrhea, abdominal pain, vomiting, inflammatory bowel disease, hepatitis, pancreatitis, bleeding and inflammation of the gums, colitis, esophagitis, esophageal ulceration, ileitis.

Hematologic
Anemia and decreased RBC parameters, thrombocytopenia, increased platelet counts, decreased WBC counts, severe neutropenia, rare reports of agranulocytosis.

Infections and Infestations
Nasopharyngitis, hordeolum, infections (including disseminated herpes simplex and upper respiratory tract infection).

Laboratory Abnormalities
The following lab tests were increased: creatine phosphokinase (CPK), triglycerides, alanine aminotransferase (SGPT), aspartate aminotransferase (SGOT), gamma-glutamyltransferase (GGTP), cholesterol, low density lipoprotein (LDL), alkaline phosphatase, bilirubin, LDH, fasting blood glucose, uric acid, and sedimentation rate. However, high density lipoprotein (HDL) was decreased. Urine findings included increased white cells, proteinuria, microscopic or gross hematuria.

Musculoskeletal and Connective Tissue
Decreases in bone mineral density, musculoskeletal symptoms (sometimes severe) including back pain, arthralgia, musculoskeletal pain, neck pain, extremity pain, myalgia, musculoskeletal stiffness *[see Warnings and Precautions (5.12)]*, skeletal hyperostosis, calcification of tendons and ligaments, premature epiphyseal closure, tendonitis, arthritis, transient chest pain, and rare reports of rhabdomyolysis.

Neurological
Headache, syncope, intracranial hypertension (pseudotumor cerebri), dizziness, drowsiness, lethargy, malaise, nervousness, paresthesia, seizures, stroke, weakness.

Psychiatric
Suicidal ideation, insomnia, anxiety, depression, irritability, panic attack, anger, violent behaviors, emotional instability, suicide attempts, suicide, aggression, psychosis and auditory hallucinations. Of the patients reporting depression, some reported that the depression subsided with discontinuation of treatment and recurred with reinstitution of treatment.

Reproductive System
Abnormal menses and sexual dysfunction, including erectile dysfunction, decreased libido, decreased vaginal lubrication, and vaginal dryness.

Respiratory
Epistaxis, nasal dryness, bronchospasm (with or without a history of asthma), respiratory infection, voice alteration.

Skin and Subcutaneous Tissue
Dry skin, dermatitis, eczema, rash, contact dermatitis, alopecia, pruritus, sunburn, erythema, acne fulminans, alopecia (which in some cases persisted), bruising, dry nose, eruptive xanthomas, erythema multiforme, flushing, skin fragility, hair abnormalities, hirsutism, hyperpigmentation and hypopigmentation, nail dystrophy, paronychia, peeling of palms and soles, photoallergic/photosensitizing reactions, pruritus, pyogenic granuloma, rash (including facial erythema, seborrhea, and eczema), Stevens-Johnson syndrome, increased sunburn susceptibility, sweating, toxic epidermal necrolysis, urticaria, vasculitis (including granulomatosis with polyangiitis), abnormal wound healing (delayed healing or exuberant granulation tissue with crusting).

Senses
Hearing: tinnitus and hearing impairment.

Ocular: dry eyes, reduced visual acuity, blurred vision, eye pruritis, eye irritation, asthenopia, decreased night vision, ocular hyperemia, increased lacrimation, conjunctivitis, corneal opacities, decreased night vision which may persist, cataracts, color vision disorder, conjunctivitis, eyelid inflammation, keratitis, optic neuritis, photophobia, visual disturbances.

Renal and Urinary
Glomerulonephritis.

7 DRUG INTERACTIONS

7.1 Vitamin A
Avoid concomitant use of ABSORICA/ABSORICA LD with supplements containing vitamin A.

ABSORICA/ABSORICA LD is closely related to vitamin A. Therefore, concomitant use of ABSORICA/ABSORICA LD with vitamin A may lead to ABSORICA/ABSORICA LD-associated adverse reactions.

7.2 Tetracyclines
Avoid concomitant use of ABSORICA/ABSORICA LD with tetracyclines because isotretinoin use has been associated with a number of cases of intracranial hypertension (pseudotumor cerebri), some of which involved concomitant use of tetracyclines *[see Warnings and Precautions (5.5)]*.

7.3 Oral Contraceptives
Isotretinoin Capsules did not result in clinically significant changes in the pharmacokinetics of norethindrone and ethinyl estradiol when used concomitantly with a norethindrone and ethinyl estradiol oral contraceptive *[see Clinical Pharmacology (12.3)]*. It is not known if there is an interaction with the concomitant use of ABSORICA/ABSORICA LD with other oral contraceptives.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that documents pregnancies in patients exposed to isotretinoin during pregnancy. Report any suspected fetal exposure during or 1 month after ABSORICA/ABSORICA LD treatment immediately to the FDA via the MedWatch telephone number 1-800-FDA-1088 and also to the iPLEDGE pregnancy registry at 1-866-495-0654 or via the internet (www.ipledgeprogram.com).

Risk Summary

ABSORICA/ABSORICA LD are contraindicated during pregnancy because isotretinoin can cause fetal harm when administered to a pregnant patient. There is an increased risk of major congenital malformations, spontaneous abortions, and premature births following isotretinoin exposure during pregnancy in humans. If ABSORICA/ABSORICA LD is used during pregnancy, or if the patient becomes pregnant while taking ABSORICA/ABSORICA LD, apprise the patient of the potential hazard to a fetus. If pregnancy occurs during treatment of a patient who is taking ABSORICA/ABSORICA LD, immediately discontinue ABSORICA/ABSORICA LD and refer the patient to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Data

Human Data: Major congenital malformations that have been documented following isotretinoin exposure include malformations of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. External malformations include: skull; ear (including anotia, micropinna, small or absent external auditory canals); eye (including microphthalmia); facial dysmorphia and cleft palate. Internal abnormalities include: central nervous system (including cerebral and cerebellar malformations, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular; thymus gland; parathyroid hormone deficiency. In some cases, death has occurred as a result of the malformations.

Cases of IQ scores less than 85 with or without other abnormalities have been reported in children exposed in utero to isotretinoin. An increased risk of spontaneous abortion and premature births have been reported with isotretinoin exposure during pregnancy.

8.2 Lactation

Risk Summary

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/ABSORICA LD, and for at least 8 days after the last dose of ABSORICA/ABSORICA LD.

8.3 Females and Males of Reproductive Potential

All patients who can get pregnant must comply with the iPLEDGE REMS requirements *[see Warnings and Precautions (5.2)]*.

Pregnancy Testing

In patients who can get pregnant, pregnancy testing is required prior to, during, and after ABSORICA/ABSORICA LD treatment.

Pregnancy Testing Prior to Prescribing ABSORICA/ABSORICA LD: In patients who can get pregnant, only prescribe ABSORICA/ABSORICA LD after verification and documentation that they are not pregnant:

(1) Complete the **first urine or serum pregnancy test (screening test)** in a medical setting (e.g., prescriber's office, clinic, laboratory) and verify and document that the test is negative, AND
(2) For patients with:
- *Regular menstrual cycles,* complete the **second urine or serum pregnancy test (confirmatory test)** in a medical setting (1) at least 30 days after the screening test and during the first five days of their menstrual period immediately preceding the beginning of ABSORICA/ABSORICA LD treatment, AND (2) after the patient has used their chosen pregnancy prevention methods (i.e., two forms of contraception or committed to abstinence) for at least 30 days. Verify and document that the confirmatory test is negative, OR

- *Amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding*, complete the **second urine or serum pregnancy test (confirmatory test)** in a medical setting (1) at least 30 days after the screening test and immediately preceding the beginning of ABSORICA/ABSORICA LD treatment, AND (2) after the patient has used their chosen pregnancy prevention methods (i.e., two forms of contraception or committed to abstinence) for at least 30 days. Verify and document that the confirmatory test is negative.

If a patient who can get pregnant has had negative screening and confirmatory pregnancy tests but they missed the 7-day prescription window (the patient has not obtained their ABSORICA/ABSORICA LD prescription within 7 days of the pregnancy test collection) and has not started ABSORICA/ABSORICA LD treatment, repeat the urine or serum pregnancy test in a medical setting and verify and document that this repeat test is negative prior to prescribing ABSORICA/ABSORICA LD. The confirmatory pregnancy test must be repeated, as needed, until the patient receives ABSORICA/ABSORICA LD.

Pregnancy Testing During Treatment with ABSORICA/ABSORICA LD: In patients who can get pregnant who are being treated with ABSORICA/ABSORICA LD, within 7 days before each prescription, obtain a urine or serum pregnancy test in a medical setting (e.g., prescriber's office, laboratory, clinic) or instruct patients to use a home pregnancy test.

If the patient who can get pregnant missed the 7-day prescription window (the patient has not obtained their ABSORICA/ABSORICA LD prescription within 7 days of the pregnancy test collection), repeat the urine or serum pregnancy test within 7 days before the next prescription in a medical setting or instruct patients to use a home pregnancy test. Verify and document the negative pregnancy test result prior to prescribing additional ABSORICA/ABSORICA LD treatment.

Pregnancy Testing in Patients Who Have Completed ABSORICA/ABSORICA LD Treatment: In patients who can get pregnant who have completed ABSORICA/ABSORICA LD treatment, complete a urine or serum pregnancy test in a medical setting (e.g., prescriber's office, laboratory, clinic) or instruct patients to use a home pregnancy test:

- At the end of the entire course of ABSORICA/ABSORICA LD treatment, AND
- 1 month after the discontinuation of ABSORICA/ABSORICA LD.

Contraception

Patients who can get pregnant must use 2 forms of contraception simultaneously, at least 1 of which must be a primary form, for at least 1 month prior to initiation of ABSORICA/ABSORICA LD treatment, during ABSORICA/ABSORICA LD treatment, and for 1 month after discontinuing ABSORICA/ABSORICA LD treatment. However, 2 forms of contraception is not required if the patient commits to continuous abstinence from not having any sexual contact with a partner which may result in pregnancy, has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Micro-dosed progesterone preparations ("minipills" that do not contain an estrogen) are an inadequate form of contraception during ABSORICA/ABSORICA LD treatment. Any birth control method can fail. There have been reports of pregnancy from patients who have used combination oral contraceptives, as well as contraceptive vaginal systems, vaginal inserts, transdermal systems, and injections; these pregnancies occurred while taking isotretinoin capsules. These reports are more frequent for patients who use only a single method of contraception. Therefore, it is critically important that patients who can get pregnant use two forms of contraception simultaneously.

Primary forms	**Secondary forms**
• Tubal sterilization • Male partner vasectomy • Intrauterine device • Hormonal (combination oral contraceptives, vaginal systems, vaginal inserts, transdermal systems, injections, or implants)	Barrier: • male latex condom with or without spermicide • diaphragm with spermicide • cervical cap with spermicide Other: • Vaginal sponge (contains spermicide)

If the patient has unprotected sexual contact with a partner that could result in pregnancy at any time 1 month before, during, or 1 month after treatment, the patient must:

a. Stop taking ABSORICA/ABSORICA LD immediately, if on treatment

b. Have a pregnancy test at least 19 days after the last act of unprotected sexual contact with a partner that could result in pregnancy
c. Start using 2 forms of contraception simultaneously again for 1 month before resuming ABSORICA/ABSORICA LD treatment
d. Have a second pregnancy test after using 2 forms of contraception for 1 month.

Infertility

In a trial of female acne patients (n = 79) receiving another isotretinoin capsule product, the mean total ovarian volume, the total antral follicle count and mean anti-Mullerian hormone decreased at the end of the treatment (6th month). However, the values returned to normal at the 18th month (12 months after the end of treatment). There were no statistically significant changes in terms of follicle-stimulating hormone and luteinizing hormone, both at the end of the treatment and 12 months after the end of treatment. Although the results suggest that possible deteriorative effects of isotretinoin on ovarian reserve may be reversible, the study has important methodological limitations, including a small sample size, lack of a control group, and lack of generalizability.

Sperm Study: In trials of 66 men, 30 of whom were patients with nodular acne under treatment with oral isotretinoin, no significant changes were noted in the count or motility of spermatozoa in the ejaculate. In a study of 50 men (ages 17 to 32 years) receiving isotretinoin treatment for nodular acne, no significant effects were seen on ejaculate volume, sperm count, total sperm motility, morphology or seminal plasma fructose.

8.4 Pediatric Use

The safety and effectiveness of ABSORICA/ABSORICA LD for the treatment of severe recalcitrant nodular acne have been established in non-pregnant pediatric patients 12 years of age and older with multiple inflammatory nodules with a diameter of 5 mm or greater who are unresponsive to conventional therapy, including systemic antibiotics. Use of ABSORICA/ABSORICA LD in this age group for this indication is supported by evidence from a clinical trial (Study 1) that compared the use ABSORICA to another isotretinoin capsule product in 397 pediatric subjects 12 years of age and older *[see Clinical Studies (14)]* and pharmacokinetic data in pediatric subjects *[see Clinical Pharmacology (12.3)]*.

The safety and effectiveness of ABSORICA/ABSORICA LD in pediatric patients less than 12 years of age have not been established.

Adverse Reactions in Pediatric Subjects

In trials with isotretinoin capsules, adverse reactions reported in pediatric subjects 12 years of age and older were similar to those described in adults except for the increased incidence of back pain and arthralgia (both of which were sometimes severe) and myalgia in pediatric subjects. In a trial of pediatric subjects 12 years of age and older treated with isotretinoin capsules, approximately 29% (104/358) developed back pain. Back pain was severe in 14% (14/104) of the cases and occurred at a higher frequency in female subjects than male subjects. Arthralgias were experienced in 22% (79/358) of pediatric subjects including severe arthralgias in 8% (6/79) of subjects. Evaluate the musculoskeletal system of pediatric patients who present with these symptoms during or after a course of ABSORICA/ABSORICA LD. Consider discontinuing ABSORICA/ABSORICA LD if any significant abnormality is found.

Effects on Bone Mineral Density in Pediatric Subjects

The effect on bone mineral density (BMD) of a 20-week course of treatment with ABSORICA or another isotretinoin capsule product was evaluated in a double-blind, randomized clinical trial involving 396 pediatric subjects with severe recalcitrant nodular acne (mean age 15.4 years old, range 12 to 17 years old, 80% males). Given that there were no statistically significant differences between the two isotretinoin capsule groups following 20 weeks of treatment, the results are presented for the pooled treatment groups. The mean changes in BMD from baseline for the overall trial population were 1.8% for lumbar spine, -0.1% for total hip and -0.3% for femoral neck. Mean BMD Z-scores declined from baseline at each of these sites (-0.053, -0.109 and -0.104 respectively). Out of 306 pediatric subjects, 27 (9%) had clinically significant BMD declines defined as ≥4% lumbar spine or total hip, or ≥5% femoral neck, including 2 subjects for lumbar spine, 17 for total hip and 20 for femoral neck. Repeat DXA scans within 2 to 3 months after the post treatment scan showed no recovery of BMD. Long-term follow-up at 4 to 11 months showed that 3 out of 7 subjects had total hip and femoral neck BMD below pre-treatment baseline, and 2 others did not show the increase in BMD above baseline expected in this adolescent population. The significance of these changes in regard to long-term bone health and future fracture risk is unknown *[see Warnings and Precautions (5.12)]*.

In an open-label clinical trial (N=217) of a single course of treatment with isotretinoin capsules for pediatric subjects 12 years of age and older with severe recalcitrant nodular acne, BMD at several skeletal sites were not significantly decreased (lumbar spine change >-4% and total hip change >-5%) or were increased in the majority of subjects. One subject had a decrease in lumbar spine BMD >4% based on unadjusted data. Sixteen (8%) subjects had decreases in lumbar spine BMD >4%, and all the other subjects (92%) did not have significant decreases or had increases (adjusted for body mass index). Nine subjects (5%) had a decrease in total hip BMD >5% based on unadjusted data. Twenty-one (11%) subjects had decreases in total hip BMD >5%, and all the other subjects (89%) did not have significant decreases or had increases (adjusted for body mass index). Follow-up trials performed in 8 of the subjects with decreased BMD for up to 11 months thereafter demonstrated increasing BMD in 5 subjects at the lumbar spine, while the other 3 subjects had lumbar spine BMD measurements below baseline values. Total hip BMD remained below baseline (range −1.6% to −7.6%) in 5 of 8 subjects (63%).

In a separate open-label extension trial of 10 pediatric subjects including those 13 years of age and older, who started a second course of isotretinoin capsules 4 months after the first course, two subjects showed a decrease in mean lumbar spine BMD up to 3.3%.

Epiphyseal Closure

There are reports of premature epiphyseal closure in acne patients who used isotretinoin at recommended doses. The effect of multiple courses of isotretinoin on epiphyseal closure is unknown. In a 20-week clinical trial that included 289 pediatric subjects 12 years of age and older who had hand radiographs taken to assess bone age, a total of 9 subjects had bone age changes that were clinically significant and for which an isotretinoin-related effect cannot be excluded *[see Warnings and Precautions (5.12)]*.

8.5 Geriatric Use

Clinical studies of ABSORICA/ABSORICA LD did not include sufficient numbers of geriatric subjects (subjects aged 65 years of age and older) to determine whether they respond differently from younger adult subjects. The effects of aging may increase some risks associated with ABSORICA/ABSORICA LD treatment.

10 OVERDOSAGE

Isotretinoin overdosage has been associated with vomiting, facial flushing, cheilosis, abdominal pain, headache, dizziness, and ataxia. These symptoms quickly resolved without apparent residual effects.

Evaluate patients who can become pregnant who present with an ABSORICA/ABSORICA LD overdosage for pregnancy. Because an overdosage would be expected to result in higher levels of isotretinoin in semen than found during a normal treatment course, instruct male patients treated with ABSORICA/ABSORICA LD to use a condom, or avoid reproductive sexual activity with a patient who is or might become pregnant, for 1 month after the overdose.

Instruct all patients with ABSORICA/ABSORICA LD overdose to not donate blood for at least 1 month. If an overdose occurs, consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

ABSORICA

ABSORICA (isotretinoin) capsules contain 10 mg, 20 mg, 25 mg, 30 mg, 35 mg or 40 mg of isotretinoin (a retinoid) in hard gelatin capsules for oral administration. In addition to the active ingredient, isotretinoin, each capsule contains the following inactive ingredients: propyl gallate, sorbitan monooleate, soybean oil and stearoyl polyoxylglycerides. The gelatin capsules contain the following dye systems:

- 10 mg – iron oxide (yellow) and titanium dioxide;
- 20 mg – iron oxide (red), and titanium dioxide;
- 25 mg – FD&C Blue #1, FD&C Yellow #5 *[see Warnings and Precautions (5.14)],* FD&C Yellow #6 and titanium dioxide;
- 30 mg – iron oxide (black, red and yellow) and titanium dioxide;
- 35 mg – FD&C Blue #2, iron oxide (black, red and yellow) and titanium dioxide;
- 40 mg – iron oxide (black, red and yellow) and titanium dioxide.

ABSORICA LD

ABSORICA LD (isotretinoin) capsules contain 8 mg, 16 mg, 20 mg, 24 mg, 28 mg and 32 mg of micronized isotretinoin (a retinoid) in suspension filled in hard gelatin capsules for oral administration. In addition to the active ingredient, isotretinoin, USP each capsule contains the following inactive ingredients: butylated hydroxy anisole, gelatin, hard gelatin capsule shell, polysorbate 80 and soybean oil. The gelatin capsules contain the following dye systems:

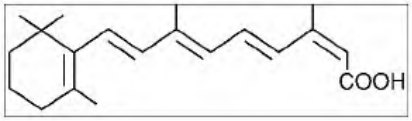
- 8 mg – D&C Yellow #10, FD&C Blue #1, FD&C Red #40 and titanium dioxide
- 16 mg – FD&C Blue #1, FD&C Red #40, and titanium dioxide
- 20 mg – FD&C Blue #1, FD&C Red #40, and titanium dioxide
- 24 mg – D&C Yellow #10, FD&C Yellow #6 and titanium dioxide
- 28 mg – FD&C Blue #1, FD&C Red #40, and titanium dioxide
- 32 mg – ferrosoferric oxide, ferric oxide (red and yellow) and titanium dioxide

The imprinting ink of 8 mg, 16 mg, 24 mg and 32 mg capsules contain the following ingredients: potassium hydroxide, propylene glycol, shellac and titanium dioxide.

The imprinting ink of 20 mg and 28 mg capsules contain the following ingredients: ferrosoferric oxide, propylene glycol and shellac glaze.

Isotretinoin

Chemically, isotretinoin is 13-*cis*-retinoic acid and is related to both retinoic acid and retinol (vitamin A). It is a yellow to orange crystalline powder with a molecular weight of 300.44. It is practically insoluble in water, soluble in chloroform and sparingly soluble in alcohol and in isopropyl alcohol. The structural formula is:



ABSORICA meets USP Dissolution Test 3.
For ABSORICA LD, FDA approved dissolution test differs from the USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The exact mechanism of action of ABSORICA/ABSORICA LD in 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 who are unresponsive to conventional therapy, including systemic antibiotics is unknown.

ABSORICA/ABSORICA LD is a retinoid, which inhibits sebaceous gland function and keratinization. Clinical improvement in nodular acne patients occurs in association with a reduction in sebum secretion. The decrease in sebum secretion is temporary and reflects a reduction in sebaceous gland size and an inhibition of sebaceous gland differentiation.

12.2 Pharmacodynamics

Decreased sebum secretion is related to the dose and duration of treatment with ABSORICA/ABSORICA LD.

12.3 Pharmacokinetics

No clinically significant differences in the pharmacokinetics of isotretinoin between patients with nodular acne and healthy subjects without acne were reported in published literature.

Absorption Following ABSORICA Administration

The ABSORICA mean T_{max} was 6.4 hours under fed conditions and 2.9 hours under fasting conditions following administration of a single 40 mg dose.

Effect on Food

No clinically significant differences in ABSORICA pharmacokinetics were observed following administration with a modified high-fat, high-calorie meal (123.2 calories from protein, 265.6 calories from carbohydrates, and 468 calories from fat; total calories 857 calories) with reduced vitamin A content. The mean AUC_{0-t} and C_{max} of isotretinoin were 6095 ng*hr/mL and 369 ng/mL, respectively, following administration of a single 40 mg ABSORICA dose under fed conditions; which were approximately 50% and 26% higher, respectively, compared to fasting conditions. However, ABSORICA may be given with or without meals *[see Dosage and Administration (2.1)]*.

Absorption Following ABSORICA LD Administration

The ABSORICA LD median T_{max} was 5 hours under fed conditions and 3.5 hours under fasting conditions following administration of a single 32 mg dose.

Effect on Food: No clinically significant differences in ABSORICA LD pharmacokinetics were observed following administration with a high-fat, high-calorie meal (150 calories from protein, 250 calories from carbohydrates, and 500 calories from fat; total calories 900 calories). The mean AUC_{0-t} and C_{max} of isotretinoin were 10209 ng*hr/mL and 646 ng/mL, respectively, following administration of a single 32 mg ABSORICA LD dose under fed conditions; which were approximately 20% and 6% higher, respectively, compared to fasting conditions. However, ABSORICA LD may be given with or without meals *[see Dosage and Administration (2.1)]*.

Distribution

Isotretinoin is more than 99.9% bound to plasma proteins, primarily albumin.

Elimination

The mean elimination half-lives of isotretinoin and its 4-oxo-isotretinoin metabolite were:

- 18 hours and 38 hours, respectively, after a single oral ABSORICA 40 mg dose.
- Approximately 24 hours and 38 hours, respectively, after a single oral ABSORICA LD 32 mg dose.

Metabolism: Isotretinoin is primarily metabolized by CYP2C8, 2C9, 3A4, and 2B6 in vitro. Isotretinoin and its metabolites are further metabolized into conjugates.

Following oral administration of isotretinoin capsules, at least three metabolites (4-oxo-isotretinoin, retinoic acid (tretinoin), and 4-oxo-retinoic acid (4-oxo-tretinoin)) have been identified in human plasma. The extent of formation of all metabolites was higher under fed conditions. All of these metabolites possess retinoid activity in vitro. The clinical significance is unknown.

Excretion: Following oral administration of an 80 mg dose of radiolabeled-isotretinoin as a liquid suspension, the metabolites of isotretinoin were excreted in feces and urine in relatively equal amounts (total of 65% to 83%).

Specific Populations

Pediatric Patients: No clinically significant differences in the pharmacokinetics of isotretinoin were observed based on age (12 to 15 years (n=38), and ≥18 years (n=19)). In both age groups, 4-*oxo*-isotretinoin was the major metabolite; tretinoin and 4-*oxo*-tretinoin were also observed *[see Use in Specific Populations (8.4)]*.

Drug Interaction Studies

Phenytoin: No clinically significant differences in the pharmacokinetics of phenytoin (CYP2C9 substrate) were observed when used concomitantly with isotretinoin.

Norethindrone and Ethinyl Estradiol: There were no clinically significant differences in the pharmacokinetics of norethindrone and ethinyl estradiol after the concomitant use of Isotretinoin Capsules 1 mg/kg/day with an oral contraceptive in premenopausal female patients with severe recalcitrant nodular acne. Additionally, there were no clinically significant differences in the serum levels of progesterone, follicle-stimulating hormone and luteinizing hormone in the serum levels of progesterone, follicle-stimulating hormone and luteinizing hormone in these patients.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility

Carcinogenesis

In male and female Fischer 344 rats given oral isotretinoin at dosages of 8 or 32 mg/kg/day (1.3 or 5.3 times the recommended clinical ABSORICA dosage of 1 mg/kg/day or the recommended clinical ABSORICA LD dosage of 0.8 mg/kg/day, respectively, after normalization for total body surface area) for greater than 18 months, there was a dose-related increased incidence of pheochromocytoma relative to controls. The incidence of adrenal medullary hyperplasia was also increased at the higher dosage in both sexes. The relatively high level of spontaneous pheochromocytomas occurring in the male Fischer 344 rat makes it an equivocal model for study of this tumor; therefore, the relevance of this tumor to humans is uncertain.

Mutagenesis

The Ames test was conducted with isotretinoin in two laboratories. The results of the tests in one laboratory were negative, while in the second laboratory, a weakly positive response (less than 1.6 times background) was noted in *S. typhimurium* TA100 when the assay was conducted with metabolic activation. No dose response effect was seen, and all other strains were negative. Additionally, other tests designed to assess genotoxicity (Chinese hamster cell assay, mouse micronucleus test, *S. cerevisiae* D7 assay, in vitro clastogenesis assay with human-derived lymphocytes, and unscheduled DNA synthesis assay) were all negative.

Impairment of Fertility

In rats, no adverse effects on gonadal function, fertility, conception rate, gestation or parturition were observed at oral dosages of isotretinoin of 2, 8, or 32 mg/kg/day (0.3, 1.3, or 5.3 times the recommended clinical ABSORICA dosage of 1 mg/kg/day or the recommended clinical ABSORICA LD dosage of 0.8 mg/kg/day, respectively, after normalization for total body surface area).

In dogs, testicular atrophy was noted after treatment with oral isotretinoin for approximately 30 weeks at dosages of 20 or 60 mg/kg/day (10 or 30 times the recommended clinical ABSORICA dosage of 1 mg/kg/day or the recommended clinical ABSORICA LD dosage of 0.8 mg/kg/day, respectively, after normalization for total body surface area). In general, there was microscopic evidence for appreciable depression of spermatogenesis, but some sperm were observed in all testes examined, and in no instance were completely atrophic tubules seen.

13.2 Animal Toxicology and/or Pharmacology

In rats given 8 or 32 mg/kg/day of isotretinoin (1.3 or 5.3 times the recommended clinical ABSORICA dosage of 1 mg/kg/day or the recommended clinical ABSORICA LD dosage of 0.8 mg/kg/day, respectively, after normalization for total body surface area) for 18 months or longer, the incidences of focal calcification, fibrosis and inflammation of the myocardium, calcification of coronary, pulmonary and mesenteric arteries, and metastatic calcification of the gastric mucosa were greater than in control rats of similar age. Focal endocardial and myocardial calcifications associated with calcification of the coronary arteries were observed in two dogs after approximately 6 to 7 months of treatment with isotretinoin at a dosage of 60 to 120 mg/kg/day (30 to 60 times the recommended clinical ABSORICA dosage of 1 mg/kg/day or the recommended clinical ABSORICA LD dosage of 0.8 mg/kg/day, respectively, after normalization for total body surface area).

14 CLINICAL STUDIES

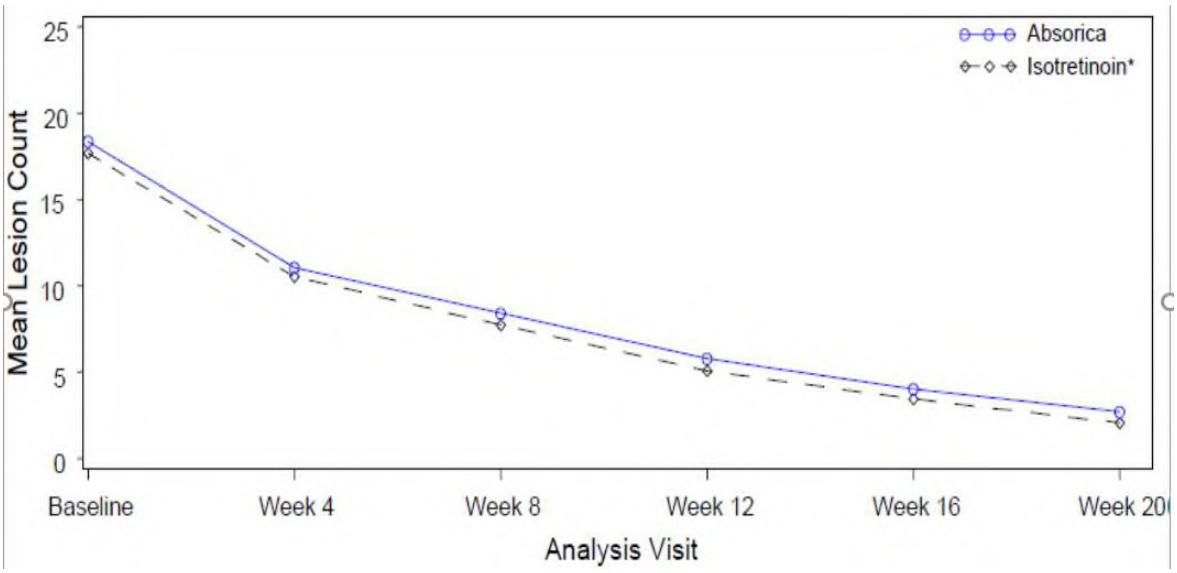
The effectiveness of ABSORICA/ABSORICA LD for the treatment of severe recalcitrant nodular acne in non-pregnant patients 12 years of age and older has been established and is based on a double-blind, randomized, parallel group trial (Study 1) in subjects with severe recalcitrant nodular acne who received 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 12 years of age and older); 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 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.

Change from baseline to Week 20 in total nodular lesion count and proportion of subjects with at least a 90% reduction in total nodular lesion count from baseline to Week 20 are presented in Table 3. Total nodular lesion counts by visit are presented in Figure 1. A single course of ABSORICA and another isotretinoin capsule product treatment for 15 to 20 weeks has been shown to result in complete and prolonged remission of acne in many patients.

Table 3: Efficacy Results in Subjects with Severe Recalcitrant Nodular Acne at Week 20 (Study 1)

	ABSORICA N=464	**Another Isotretinoin Capsule Product* N=461**
Nodular Lesions		
Mean Baseline Count	18.4	17.7
Mean Reduction	-15.68	-15.62
Subjects Achieving 90% Reduction, n (%)	324 (70%)	344 (75%)

Figure 1: Total Nodular (Facial and Truncal) Lesion Count in Subjects with Severe Recalcitrant Nodular Acne by Visit in Study 1



* Another isotretinoin capsule product.

16 HOW SUPPLIED/STORAGE AND HANDLING

ABSORICA and ABSORICA LD have different dosage regimens. Although ABSORICA and ABSORICA LD have a 20 mg strength, these strengths have different bioavailability and are not substitutable *[see Dosage and Administration (2.1)]*.

ABSORICA
ABSORICA (isotretinoin) Capsules (opaque) are supplied as follows:

- 10 mg: Dark yellow, capsule imprinted with black ink “G240” on cap and “10” on the body
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-115-31
- 20 mg: Red, capsule imprinted with black ink “G241” on cap and “20” on the body
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-116-31
- 25 mg: Green, capsule imprinted with white ink “G342” on cap and “25” on the body
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-133-31

- 30 mg: Brown, capsule imprinted with white ink “G242” on cap and “30” on the body
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-117-31
- 35 mg: Dark blue, capsule imprinted with white ink “G343” on cap and “35” on the body
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-134-31
- 40 mg: Brown and red, capsule imprinted with white ink “G325” on cap and “40” on the body
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-118-31

ABSORICA LD
ABSORICA LD (isotretinoin) Capsules (opaque-printed, hard-gelatin) are supplied as follows:

- 8 mg: A size 3, light green, capsules banded with a colorless band. The cap is printed in white with “RL29” and the body is printed in white with “RL29”.
  Box of 30 capsules (3 x 10 Prescription Packs) NDC 10631-002-31
- 16 mg: A size 2, dark blue, capsules banded with a colorless band. The cap is printed in white with “RL30” and the body is printed in white with “RL30”.
  Box of 30 capsules (3 x 10 Prescription Packs) NDC 10631-003-31
- 20 mg: A size 1, dark pink, capsules banded with a colorless band. The cap is printed in black with “RL33”and the body is printed in black with “RL33”.
  Box of 30 capsules (3 x 10 Prescription Packs) NDC 10631-004-31
- 24 mg: A size 1, yellow, capsules banded with a colorless band. The cap is printed in white with “RL31” and the body is printed in white with “RL31”.
  Box of 30 capsules (3 x 10 Prescription Packs) NDC 10631-005-31
- 28 mg: A size 0, light blue, capsules banded with a colorless band. The cap is printed in black with “RL34” and the body is printed in black with “RL34”.
  Box of 30 capsules (3 x 10 Prescription Packs) NDC 10631-006-31
- 32 mg: A size 0, caramel, capsules banded with a colorless band. The cap is printed in white with “RL32” and the body is printed in white with “RL32”.
  Box of 30 capsules (3 x 10 Prescription Packs): NDC 10631-007-31

Storage and Handling of ABSORICA and ABSORICA LD
Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Protect from light.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Embryo-Fetal Toxicity
There is an extremely high risk of life-threatening birth defects when ABSORICA/ABSORICA LD is used in pregnancy *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)]*. Instruct patients who can become pregnant that they must not be pregnant during or up to 1 month after ABSORICA/ABSORICA LD treatment. Instruct patients to not donate blood during ABSORICA/ABSORICA LD treatment and for 1 month following discontinuation to avoid blood donation to a pregnant patient.

iPLEDGE REMS
ABSORICA and ABSORICA LD are available only through a restricted program called the iPLEDGE REMS *[see Warnings and Precautions (5.2)]*. Inform patients who can get pregnant of the following notable requirements. These patients must:

- Enroll in the REMS
- Comply with REMS requirements including:
  - Comply with the pregnancy testing and pregnancy prevention requirements *[see Use in Specific Populations (8.3)]*.
  - Demonstrate comprehension of the risk and REMS requirements prior to each prescription.
  - Obtain the prescription within the 7-day prescription window (i.e., within 7 days of the pregnancy test collection).

- Inform their prescriber if they get pregnant and stop treatment.

Inform patients who cannot get pregnant of the following notable requirements. These patients must enroll in the REMS and comply with the REMS requirements.

ABSORICA/ABSORICA LD is available only from certified pharmacies participating in the REMS. Therefore, provide patients with the telephone number and website for information on how to obtain ABSORICA/ABSORICA LD *[see Warnings and Precautions (5.2)]*.

Lactation
Because of the potential for serious adverse reactions in nursing infants from isotretinoin, advise patients that breastfeeding is not recommended during treatment with ABSORICA/ABSORICA LD, and for at least 8 days after the last dose of ABSORICA/ABSORICA LD *[see Use in Specific Populations (8.2)]*.

Psychiatric Disorders
Instruct patients and/or their caregivers/families that ABSORICA/ABSORICA LD may cause depression, psychosis, suicidal ideation, suicide attempts, and aggressive or violent behavior. Instruct patients to stop ABSORICA/ABSORICA LD and to contact a healthcare provider if they develop any of these signs or symptoms *[see Warnings and Precautions (5.4)]*.

Important Administration Instructions
To decrease the risk of esophageal irritation, instruct patients to swallow the capsules with a full glass of liquid *[see Dosage and Administration (2.1)]*.

Intracranial Hypertension (Pseudotumor Cerebri)
Advise patients that intracranial hypertension (pseudotumor cerebri) has occurred with ABSORICA/ABSORICA LD use including concomitant use with tetracyclines. Thus, advise patients to avoid concomitant use with tetracyclines and to discontinue ABSORICA/ABSORICA LD immediately if they have symptoms of intracranial hypertension *[see Warnings and Precautions (5.5)]*.

Serious Skin Reactions
Advise patients that severe skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis) have been reported in patients treated with isotretinoin and to discontinue ABSORICA/ABSORICA LD if clinically significant skin reactions occur *[see Warnings and Precautions (5.6)]*.

Inflammatory Bowel Disease
Advise patients that inflammatory bowel disease (including regional ileitis) have occurred with isotretinoin use including those without a prior history of IBD and if they experience IBD symptoms, to discontinue ABSORICA/ABSORICA LD immediately *[see Warnings and Precautions (5.11)]*.

Musculoskeletal Abnormalities
Inform patients that:

- There have been reports of osteoporosis and fractures and that isotretinoin may have a negative effect on bone mineral density *[see Warnings and Precautions (5.12)]*.
- Isotretinoin use has been associated with musculoskeletal abnormalities (e.g., arthralgia, back pain) *[see Warnings and Precautions (5.12)]*.

Inform pediatric patients and their families that isotretinoin use in pediatric patients who participated in sports with repetitive impact increased their risk of spondylolisthesis or hip growth plate injuries *[see Warnings and Precautions (5.12)]*.

Inform pediatric patients and their caregivers that pediatric patients treated with isotretinoin capsules developed back pain including severe back pain, and arthralgias including severe arthralgias *[see Use in Specific Populations (8.4)]*.

Ocular Abnormalities

Inform patients that they may experience dry eyes, corneal opacities, and decreased night vision and contact lens wearers may experience decreased tolerance to contact lenses during and after treatment *[see Warnings and Precautions (5.13)]*.

Rhabdomyolysis

Inform patients there have been rare postmarketing reports of rhabdomyolysis in patients treated with isotretinoin capsules, some associated with strenuous physical activity *[see Warnings and Precautions (5.15)]*.

Hypersensitivity Reactions

Given that anaphylactic reactions and other allergic reactions have been reported in patients treated with isotretinoin capsules, instruct the patient to discontinue ABSORICA/ABSORICA LD and contact their healthcare provider if they have a severe allergic reaction *[see Warnings and Precautions (5.14)]*.

Lipid Abnormalities

Instruct patients that hypertriglyceridemia, decreased HDL, and increased cholesterol levels were reported in patients treated with isotretinoin capsules *[see Warnings and Precautions (5.8)]*.

Additional Instructions

Inform patients:

- To not share ABSORICA/ABSORICA LD with anyone else because of the risk of birth defects and other serious adverse reactions.
- That transient exacerbation (flare) of acne has been seen, generally during the initial period of treatment.
- To avoid wax epilation and skin resurfacing procedures (such as dermabrasion, laser) during ABSORICA/ABSORICA LD treatment and for at least 6 months thereafter due to the possibility of scarring.
- To avoid prolonged exposure to UV rays or sunlight.

Manufactured by:
ABSORICA
Galephar Pharmaceutical Research, Inc., Humacao, PR 00792

ABSORICA LD
Ohm Laboratories Inc., New Brunswick, NJ 08901

Distributed by:
Sun Pharmaceutical Industries, Inc., Cranbury, NJ 08512

ABSORICA and ABSORICA LD are registered trademarks of Sun Pharmaceutical Industries, Inc. All other trademarks are property of their respective owners.

ABSORICA LD 8 mg, 16 mg, 20 mg, 24 mg, 28 mg and 32 mg are protected by US Patent No. US 9,700,535 and US 9,750,711.

MEDICATION GUIDE

ABSORICA® (ab-sore-i-kah)
(isotretinoin)
capsules, for oral use

ABSORICA (ab-sore-i-kah) LD®
(isotretinoin)
capsules, for oral use

Important: ABSORICA LD is not the same as ABSORICA or other isotretinoin products. **Do not** change between ABSORICA LD and ABSORICA or other isotretinoin products.

Read the Medication Guide that comes with ABSORICA or ABSORICA LD before you start taking it and each time you get a prescription. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about ABSORICA and ABSORICA LD?
ABSORICA and ABSORICA LD can cause serious side effects, including:

- **ABSORICA and ABSORICA LD can harm your unborn baby, including birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.**
  Patients who are pregnant or who plan to become pregnant must not take ABSORICA or ABSORICA LD.
  - Because of the risk of birth defects, ABSORICA and ABSORICA LD are only available through a special program called the iPLEDGE Risk Evaluation and Mitigation Strategy (REMS).
  - Your healthcare provider must be enrolled in the iPLEDGE REMS for you to be prescribed ABSORICA or ABSORICA LD.
  - Before you start treatment with ABSORICA or ABSORICA LD, you must enroll in the iPLEDGE REMS.
  - You must understand and agree to do everything required in the iPLEDGE REMS.

  Patients must not get pregnant:
  - for 1 month before starting ABSORICA or ABSORICA LD
  - during treatment with ABSORICA or ABSORICA LD
  - for 1 month after stopping ABSORICA or ABSORICA LD

  If you get pregnant during treatment with ABSORICA or ABSORICA LD, stop taking it right away and tell your healthcare provider. Healthcare providers and patients should report all cases of pregnancy that happen during treatment or 1 month after stopping treatment to:
  - FDA MedWatch at 1-800-FDA-1088, and
  - the iPLEDGE® Pregnancy Registry at 1-866-495-0654 or www.ipledgeprogram.com

  If you have any questions about the iPLEDGE REMS, ask your healthcare provider, or go to www.ipledgeprogram.com, or call 1-866-495-0654.
- **Serious mental health problems**, **including:**
  - **depression**
  - **psychosis** (seeing or hearing things that are not real)
  - **suicide.** Some patients taking ABSORICA or ABSORICA LD have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. Some people have ended their own lives.

  Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you or a family member notices that you get any of the following signs and symptoms of depression or psychosis:
  - start to feel sad or have crying spells
  - lose interest in activities you once enjoyed
  - sleep too much or have trouble sleeping
  - become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence
  - have a change in your appetite or body weight
  - suicide attempts
  - have trouble concentrating
  - withdraw from your friends or family
  - feel like you have no energy
  - have feelings of worthlessness or guilt
  - start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
  - start acting on dangerous impulses
  - start seeing or hearing things that are not real

  Your healthcare provider may tell you to see a mental healthcare professional if you get any of these symptoms.

See "**What are the possible side effects of ABSORICA and ABSORICA LD?"** for more information about side effects.

What are ABSORICA and ABSORICA LD?
ABSORICA and ABSORICA LD are prescription medicines used in patients 12 years of age and older, who are not pregnant, for the treatment of severe acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. ABSORICA and ABSORICA LD can cause serious side effects (see **"What is the most important information I should know about ABSORICA and ABSORICA LD?"**).

ABSORICA and ABSORICA LD can only be:
- prescribed by healthcare providers that are enrolled in the iPLEDGE REMS.
- dispensed by a pharmacy that is enrolled in the iPLEDGE REMS.
- given to patients who are enrolled in the iPLEDGE REMS and agree to do everything required in the program.

It is not known if ABSORICA and ABSORICA LD are safe and effective in children less than 12 years of age.

Who should not take ABSORICA or ABSORICA LD?

Do not take ABSORICA or ABSORICA LD if you:

- **are pregnant, plan to become pregnant, or become pregnant during ABSORICA and ABSORICA LD treatment.** ABSORICA and ABSORICA LD can cause life-threatening birth defects. See **"What is the most important information I should know about ABSORICA and ABSORICA LD?"**
- **are allergic to isotretinoin, vitamin A, or any of the ingredients in ABSORICA and ABSORICA LD.** See the end of this Medication Guide for a complete list of ingredients in ABSORICA and ABSORICA LD.

Before taking ABSORICA or ABSORICA LD, tell your healthcare provider if you or a family member has any of the following health conditions:

- mental health problems
- asthma
- liver problems
- diabetes
- heart disease
- increased blood fat levels (cholesterol and triglycerides)
- bone loss (osteoporosis), weak bones or any other bone problems
- an eating problem called anorexia nervosa (where people eat too little)
- bowel or digestion problems
- food or medicine allergies, including aspirin or FD&C Yellow No. 5 (tartrazine)

Tell your healthcare provider if you are pregnant or breastfeeding. Do not breastfeed during treatment or for at least 8 days after the last dose of ABSORICA or ABSORICA LD.

Tell your healthcare provider about all of the medicines you take including prescription and over-the-counter medicines, vitamins and herbal supplements, including St. John's wort. ABSORICA and ABSORICA LD and certain other medicines can affect each other, sometimes causing serious side effects.

Do not take the following medicines during treatment with ABSORICA or ABSORICA LD:

- vitamin A supplements
- tetracycline antibiotics

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist. Do not take any new medicine without talking with your healthcare provider.

You will not be prescribed ABSORICA or ABSORICA LD if you cannot agree to or follow all the instructions of the iPLEDGE REMS.

- You will get no more than a 30-day supply of ABSORICA or ABSORICA LD at a time. This is to make sure you are following the ABSORICA and ABSORICA LD iPLEDGE REMS.

How should I take ABSORICA or ABSORICA LD?

You must take ABSORICA or ABSORICA LD exactly as prescribed. You must also follow all the instructions of the iPLEDGE REMS. Before prescribing ABSORICA or ABSORICA LD, your healthcare provider will:

- explain the iPLEDGE REMS to you.
- have you sign the Patient Informed Consent form (for all patients). Patients who can get pregnant must also sign another consent form.
- give you pregnancy tests to make sure you are not pregnant before you start ABSORICA or ABSORICA LD. You will receive 2 pregnancy tests at least 30 days apart before starting treatment.
- The amount of ABSORICA or ABSORICA LD you take has been specially chosen for you. It is based on your body weight and may change during treatment.
- Take ABSORICA or ABSORICA LD 2 times a day with or without meals, unless your healthcare provider tells you otherwise.
- **Swallow ABSORICA or ABSORICA LD capsules whole with a full glass of liquid. Do not split, crush, chew, or suck on the capsules.** ABSORICA and ABSORICA LD can hurt the tube that connects your mouth to your stomach (esophagus) if not swallowed whole.
- Your healthcare provider will tell you how long you will receive treatment with ABSORICA or ABSORICA LD.
- If you miss a dose, just skip that dose. **Do not** take 2 doses at the same time.
- If you take too much ABSORICA or ABSORICA LD, call your healthcare provider or Poison Help line at 1-800-222-1222 right away.
- Your acne may get worse when you first start taking ABSORICA or ABSORICA LD. This should last only a short while. Talk with your healthcare provider if this is a concern for you. Your acne may continue to improve after treatment.
- You must return to your healthcare provider as directed to make sure you don't have signs of serious side effects. Your healthcare provider may do blood tests to check for serious side effects from ABSORICA or ABSORICA LD and may stop treatment if you get certain side effects.

- Patients who can get pregnant will get a pregnancy test before each prescription is given during treatment with ABSORICA or ABSORICA LD, when you stop treatment, and 1 month after you stop treatment.
- You must get your prescription within 7 days of receiving your pregnancy test.
- Patients who can get pregnant must:
  - Talk about birth control options with your healthcare provider or go for a free visit to talk about birth control with another healthcare provider or family planning expert. Your healthcare provider can arrange this free visit, which will be paid for by the company that makes ABSORICA and ABSORICA LD.
  - Use your chosen pregnancy prevention methods. **You must choose to use 2 separate forms of birth control at the same time or commit to not having sexual contact with a partner that could result in pregnancy** for at least 1 month before treatment, during treatment, and for 1 month after treatment with ABSORICA or ABSORICA LD.
  - **Access the iPLEDGE REMS system to answer questions about the REMS requirements and enter your chosen pregnancy prevention methods (2 separate forms of birth control or commitment to not having sexual contact with a partner that could result in pregnancy).** To access the iPLEDGE REMS system, go to www.ipledgeprogram.com or call 1-866-495-0654.

If you have sex at any time without using 2 forms of birth control 1 month before, during, or 1 month after treatment, get pregnant, or miss your expected period, stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away.

What should I avoid while taking ABSORICA or ABSORICA LD?

- **Do not give blood** during treatment with ABSORICA or ABSORICA LD and for 1 month after stopping ABSORICA or ABSORICA LD. If someone who is pregnant gets your donated blood, ABSORICA/ABSORICA LD may cause miscarriage, premature birth, birth defects or death of the baby.
- **Do not take other medicines or herbal products during treatment** with ABSORICA or ABSORICA LD unless you talk to your healthcare provider. See **"Before taking ABSORICA or ABSORICA LD"**
- **Do not drive at night until you know if ABSORICA or ABSORICA LD affect your vision.** ABSORICA and ABSORICA LD may decrease your ability to see in the dark.
- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, during treatment with ABSORICA or ABSORICA LD and for at least 6 months after you stop.** ABSORICA and ABSORICA LD can increase your chance of scarring from these procedures. Check with your healthcare provider for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. ABSORICA and ABSORICA LD may make your skin more sensitive to light.
- **Do not share ABSORICA or ABSORICA LD with other people**. ABSORICA and ABSORICA LD can cause life-threatening birth defects and other serious health problems.

What are the possible side effects of ABSORICA and ABSORICA LD?
ABSORICA and ABSORICA LD can cause serious side effects, including:

- See "**What is the most important information I should know about ABSORICA and ABSORICA LD?"**
- **increased pressure in the brain (intracranial hypertension).** ABSORICA and ABSORICA LD can increase the pressure in your brain. This can lead to permanent loss of eyesight, and in rare cases, death. Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you get any of these signs of increased brain pressure:
  - bad headache
  - blurred vision or other vision problems
  - dizziness
  - nausea or vomiting
  - seizures (convulsions)
  - stroke
- **serious skin problems.** Skin rash can happen in patients taking ABSORICA or ABSORICA LD. Sometimes rash can be severe and may be life-threatening and lead to hospitalization or death. Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you get:
  - conjunctivitis (red or inflamed eyes, like "pink eye")
  - rash with fever
  - blisters on legs, arms, or face
  - sores in your mouth, throat, nose or eyes
  - peeling of your skin
- **inflammation of your pancreas (pancreatitis)** can happen in patients who take ABSORICA or ABSORICA LD and can lead to death. Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you get any of the following symptoms of pancreatitis:
  - severe upper stomach (abdomen) pain
  - swelling of your stomach
  - nausea and vomiting
  - fever
- **increased blood fat (lipid) levels.** ABSORICA and ABSORICA LD can raise blood fat levels (cholesterol and triglycerides). Your healthcare provider will do blood tests to check your lipids before and during treatment. These problems usually go away when ABSORICA or ABSORICA LD treatment is finished.
- **hearing problems.** Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **liver problems, including hepatitis.** Your healthcare provider will do tests to check your liver before and during

treatment with ABSORICA or ABSORICA LD. Tell your healthcare provider if you get:

- yellowing of your skin or the whites of your eyes
- pain on the right side of your stomach area (abdomen)
- dark urine
- bleeding or bruising more easily than normal

- **inflammation of your digestive tract (inflammatory bowel disease).** Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you get:
  - severe stomach, chest or bowel pain
  - nausea or vomiting
  - trouble swallowing or painful swallowing
  - new or worsening heartburn
  - diarrhea
  - rectal bleeding
- **bone and muscle problems.**
  - **bone problems** including softening or thinning of bones which may lead to fractures. ABSORICA and ABSORICA LD may stop long bone growth in teenagers who are still growing. Teenagers who participate in sports with hard physical activity and repeated actions during treatment with ABSORICA or ABSORICA LD may have a higher risk of bone fractures or injuries. Tell all your healthcare providers if you get:
    - bone pain
    - back pain
    - a broken bone (fracture)
  - **muscle problems.** Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you have muscle or joint pain or weakness. **Muscle weakness with or without pain can be a sign of serious muscle damage.**
- **vision problems.** Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider right away if you have any vision changes. ABSORICA and ABSORICA LD may affect your ability to see in the dark. This usually goes away after you stop taking ABSORICA or ABSORICA LD, but it may be permanent. Some patients get dry eyes during treatment. If you wear contact lenses, you may have trouble wearing them during and after you stop treatment with ABSORICA or ABSORICA LD.
- **serious allergic reactions.** Stop taking ABSORICA or ABSORICA LD and get emergency medical help right away if you get hives, a swollen face or mouth, or have trouble breathing. Stop taking ABSORICA or ABSORICA LD and tell your healthcare provider if you get a fever, rash, or red patches or bruises on your legs.
- **blood sugar problems, including diabetes**. Tell your healthcare provider if you are very thirsty or urinate more than usual.

The most common side effects of ABSORICA and ABSORICA LD include:

- dry lips
- dry skin
- back pain
- dry eyes
- joint pain
- nose bleeds
- headache
- upper respiratory tract infection (common cold)
- chapped lips or swelling of the lips
- skin reactions
- muscle problems
- eye problems, including decreased vision

These are not all of the possible side effects of ABSORICA and 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.

How should I store ABSORICA and ABSORICA LD?

- Store ABSORICA and ABSORICA LD at room temperature, 68°F to 77°F (20°C to 25°C).
- Protect from light.

Keep ABSORICA and ABSORICA LD and all medicines out of the reach of children.

General information about the safe and effective use of ABSORICA and ABSORICA LD.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ABSORICA or ABSORICA LD for a condition for which it was not prescribed. Do not give ABSORICA or ABSORICA LD to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about ABSORICA and ABSORICA LD that is written for health professionals.

You can also call iPLEDGE REMS at 1-866-495-0654 or visit www.ipledgeprogram.com.

What are the ingredients in ABSORICA and ABSORICA LD?

Active ingredient: isotretinoin

Inactive ingredients in ABSORICA: propyl gallate, sorbitan monooleate, soybean oil and stearoyl polyoxylglycerides. The gelatin capsules contain the following dye systems:

- 10 mg – iron oxide (yellow) and titanium dioxide
- 20 mg – iron oxide (red), and titanium dioxide
- 25 mg – FD&C Blue #1, FD&C Yellow #5, FD&C Yellow #6 and titanium dioxide
- 30 mg – iron oxide (black, red and yellow) and titanium dioxide
- 35 mg – FD&C Blue #2, iron oxide (black, red and yellow) and titanium dioxide
- 40 mg – iron oxide (black, red and yellow) and titanium dioxide

Inactive ingredients in ABSORICA LD: butylated hydroxy anisole, gelatin, hard gelatin capsule shell, polysorbate 80, and soybean oil. The gelatin capsules contain the following dye systems:

- 8 mg – D&C Yellow #10, FD&C Blue #1, FD&C Red #40 and titanium dioxide
- 16 mg – FD&C Blue #1, FD&C Red #40, and titanium dioxide
- 20 mg – FD&C Blue #1, FD&C Red #40, and titanium dioxide
- 24 mg – D&C Yellow #10, FD&C Yellow #6 and titanium dioxide
- 28 mg – FD&C Blue #1, FD&C Red #40, and titanium dioxide
- 32 mg – ferrosoferric oxide, ferric oxide (red and yellow) and titanium dioxide

The imprinting ink of 8 mg, 16 mg, 24 mg and 32 mg capsules contain the following ingredients: potassium hydroxide, propylene glycol, shellac and titanium dioxide.

The imprinting ink of 20 mg and 28 mg capsules contain the following ingredients: ferrosoferric oxide, propylene glycol and shellac glaze.

ABSORICA LD 8 mg, 16 mg, 20 mg, 24 mg, 28 mg and 32 mg is protected by US Patent No. US 9,700,535 and US 9,750,711.

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ABSORICA
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