MDWISE PRIOR AUTHORIZATION CRITERIA

AMNESTEEM® (isotretinoin) Caps: 10mg, 20mg, 40mg  
CLARAVIS® (isotretinoin) Capsules: 10mg, 20mg, 30mg, 40mg  
SOTRET® (isotretinoin) Capsule: 20mg

FORMULARY STATUS: Preferred (generic)

PA CRITERIA FOR APPROVAL

- Diagnosis of severe recalcitrant nodular acne.
- Documented treatment with a therapeutic trial and failure or intolerance to oral antibiotic therapy first line therapy (e.g. doxycycline, minocycline, tetracycline, erythromycin) for at least 4 weeks (28 days) of therapy in the previous 60 days.

If the above conditions are met, the request will be approved for up to a 6 month duration with generic medication.

FDA INDICATIONS

Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those females who are not pregnant because isotretinoin can cause severe birth defects.

DOSAGE AND ADMINISTRATION

Dosage is adjusted and individualized according to side effects and disease response. Recommended course of therapy: Initial dose is 0.5 to 1 mg/kg/day (range is 0.5 to 2 mg/kg/day) divided into 2 doses with food, for 15 to 20 weeks. Failure to take isotretinoin with food will significantly decrease absorption. The safety of once daily dosing has not been established. Once-daily dosing is not recommended. Patients whose disease is very severe or is primarily manifested on the body may require up to the maximum dose. If the total nodule count decreases by > 70% prior to 15 weeks the drug may be discontinued. After a period of > 2 months off therapy, and if warranted by persistent or recurring severe nodular acne, a second course of therapy may be initiated.

BLACK BOX WARNING

Isotretinoin must not be used by females who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin 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.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality, ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an obstetrician-gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Because of isotretinoin’s teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE™. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE. Meeting the requirements for a female patient of childbearing potential signifies that she:
To receive isotretinoin all patients must meet all of the following conditions:

- Has been counseled and has signed a patient information/informed consent about birth defects form that contains warnings about the risk of potential birth defects if the fetus is exposed to isotretinoin. The patient must sign the informed consent form before starting treatment and patient counseling must also be done at that time and on a monthly basis thereafter.
- Has had two negative urine or serum pregnancy tests with a sensitivity of at least 25mIU/mL before receiving the initial isotretinoin prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue qualification of the patient for isotretinoin. The second pregnancy test (a confirmation test) must be done in a CLIA-certified laboratory. The interval between the two tests should be at least 19 days.
  - For patients with regular menstrual cycles, the second pregnancy test should be done during the first 5 days of the menstrual period and within 7 days of the office visit, immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for one month.
  - For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done within 7 days following the office visit, immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for one month.
- Has had a negative result from a urine or serum pregnancy test in a CLIA-certified laboratory before receiving each subsequent course of isotretinoin. A pregnancy test must be repeated every month, in a CLIA-certified laboratory, prior to the female patient receiving each prescription.
- Has selected and has committed to use 2 forms of effective contraception simultaneously, at least one of which must be a primary form, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use two effective forms of contraception for at least one month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for one month after discontinuing isotretinoin therapy. Counseling about contraception and behaviors associated with an increased risk of pregnancy must be repeated on a monthly basis.

Primary contraception includes: tubal sterilization; partner’s vasectomy; intrauterine device; hormonal (combination oral contraceptives, transdermal patch, injectables, implantables, or vaginal ring). Secondary forms include latex condoms, diaphragms, cervical caps, and vaginal sponges all of which must be used with spermicide. Any birth control method can fail. There have been reports of pregnancy from female patients who have used oral contraceptives, as well as transdermal patch/injectable/implantable/vaginal ring hormonal birth control products; these pregnancies occurred while these patients were taking isotretinoin. These reports are more frequent for female patients who use only a single method of contraception. There for it is critically important that female patients of childbearing potential use 2 effective forms of contraception simultaneously. Patients must receive written warnings about the rates of possible contraception failure. If a pregnancy does occur during isotretinoin treatment, isotretinoin must be discontinued immediately. The patient should be referred to an obstetrician-gynecologist experienced in reproductive toxicity for further evaluation and counseling. Any suspected fetal exposure during or one month after isotretinoin therapy must be reported immediately to the FDA via the MedWatch number 1-800-FDA-1088 and also to the iPLEDGE pregnancy registry at 1-866-495-0654 or via the internet (www.ipledgeprogram.com)
- Patients should be prospectively cautioned not to self-medicate with the herbal supplement St. John’s Wort because a possible interaction has been suggested with hormonal contraceptives based on reports of breakthrough bleeding on oral contraceptives shortly after starting St. John’s Wort. Pregnancies have been reported by users of combined hormonal contraceptives who also used some form of St. John’s Wort

To receive isotretinoin all patients must meet all of the following conditions:

- Must be registered with the iPLEDGE program by the prescriber
- Must understand that severe birth defects can occur with the use of isotretinoin by female patients
- Must be reliable in understanding and carrying out instructions
- Must sign a patient information/informed consent (for all patients) form that contains warnings about the potential risks associated with isotretinoin
- Must fill the prescription within 7 days of the office visit
- Must not donate blood while on isotretinoin and for one month after treatment has ended
- Must not share isotretinoin with anyone, even someone who has similar symptoms
In addition to the requirements for all patients described above, female patients of childbearing potential must meet the following conditions:

- Must not be pregnant or breast-feeding
- Must comply with the required pregnancy testing at a CLIA-certified laboratory
- Must be capable of complying with the mandatory contraceptive measures required for isotretinoin therapy, or commit to continuous abstinence from heterosexual intercourse, and understand behaviors associated with an increased risk of pregnancy
- Must understand that it is her responsibility to avoid pregnancy one month before, during, and one month after isotretinoin therapy
- Must have signed an additional patient information/informed consent about birth defects form before starting isotretinoin that contains warnings about the risk of potential birth defects if the fetus is exposed to isotretinoin
- Must access the iPLEDGE program via the internet or telephone before starting isotretinoin, on a monthly basis during therapy, and one month after the last dose to answer questions on the program requirements and to enter the patient’s two chosen forms of contraception
- Must have been informed of the purpose and importance of providing information to the iPLEDGE program should she become pregnant while taking isotretinoin or within one month of the last dose

To dispense isotretinoin, pharmacies must be registered and activated with the pregnancy risk management program iPLEDGE. To dispense isotretinoin, the pharmacist must:

- Obtain authorization from iPLEDGE via the internet or telephone for every isotretinoin prescription. Authorization signifies that the patient has met all program requirements and is qualified to receive isotretinoin
- Write the Risk Management Authorization (RMA) number on the prescription.
- Isotretinoin must only be dispensed:
  - In no more than a 30-day supply
  - With an isotretinoin Medication Guide
  - After authorization from the iPLEDGE program
  - Prior to the "do not dispense to patient after" date provided by the iPLEDGE system
  - With a new prescription for refills and another authorization from the iPLEDGE program

Psychiatric disorders: Isotretinoin may cause depression, psychosis, and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. No mechanism of action had been established for these events. Health care providers should read the brochure, Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide for Prescribers of Isotretinoin. Health care providers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin therapy, physicians should ask patients and family members about any history of psychiatric disorder, and at each visit during therapy, assess patients for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary.

REFERENCES
1. Is accutane really dangerous? Med Lett Drugs Ther 2002 Sep 16;44(1139):82

Revision/Review Date: MAC 10/12/2010
Associated Policy: Prior Authorization of Medications 236.200