



**GUIDELINES FOR ISOTRETINOIN (ACCUTANE)
USE FOR THE TREATMENT OF ACNE**

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1. GUIDELINES FOR ISOTRETINOIN (ACUTANE) USE FOR THE TREATMENT OF ACNE

Indications for which Accutane may be considered:

1. Patients with extensive nodulocystic acne should receive Accutane to minimize scarring.

2. Patients with moderate acne who have less than 50% improvement after three consecutive courses of antibiotics.

These patients should undergo trial of oral antibiotic treatment plus a topical agent for three months. If response is poor patients should receive an alternative antibiotic for another three months. If the outcome remains unsatisfactory a third antibiotic should be administered. Commonly used antibiotics include:

- Tetracycline
- Erythromycin
- Minocycline
- Doxycycline
- Trimethoprim-sulfamethoxazole

3. Patients who scar. Most patients with acne have the potential to develop scarring which may be atrophic, hypertrophic, or keloid forming and may vary in location, severity and discoloration. Scarring has both clinical and psychological implications so these patients should be considered for Accutane therapy sooner rather than later.

4. Seborrheic patients. Patients with a high sebum excretion rate respond less well to conventional antibiotics. Inadequate responders should be given Accutane early.

5. Severely depressed or dysmorphic patients. Some patients with acne are depressed and even suicidal. It is important to assess the psychological status of the patient. Even those with mild acne may be candidates for oral antibiotics or Accutane.

6. Special Note for Provider: Providers must register on website ipledgeprogram.com before prescribing Accutane. Prescriptions have to be entered on the website in addition to giving the patient a written prescription. The patient has a limited amount of time in which to fill the prescription, and the pharmacy is required to verify everything on the website before dispensing the drug to the patient.

Contraindications for Accutane use

Accutane is teratogenic. It must not be used by females who are pregnant or who may become pregnant while undergoing treatment. Women of childbearing potential should meet the following conditions before being started on Accutane.

- Have severe, disfiguring, cystic acne that is recalcitrant to standard therapies.
- Be reliable and capable of understanding the physician's instructions on the use of Accutane, the risks involved, and be willing to comply with these instructions.
- Be capable of complying with effective contraceptive measures (which may include abstinence) for at least one month prior to, throughout, and one month after treatment.
- Have received both oral and written warnings of the hazards of taking Accutane during pregnancy and exposing the fetus to the drug.
- Have received both oral and written warnings of the risk of possible contraceptive failure and of the need for two reliable forms of contraception simultaneously, unless abstinence is the chosen method, or the patient has undergone hysterectomy and has acknowledged in writing her understanding of these warnings and of the need for using dual contraceptive methods.

- Have had a negative serum or urine pregnancy test with a sensitivity of at least 50 mIU/ml within one week prior to beginning therapy.
- Will begin therapy only on the second or third day of the next normal menstrual period.

Warning

- Because of the relationship between Accutane and vitamin A, patients should be advised against taking vitamin supplements containing vitamin A to avoid toxic effects.
- Patients should be informed that transient exacerbation of acne may occur, often during initial period of therapy.
- Patients should be informed that they may experience decreased tolerance to contact lenses during and after therapy.
- It is recommended that patients not donate blood during therapy and for 1 month following discontinuation of the drug.
- Women should not take Accutane while breastfeeding.
- Accutane interferes with healing. Accutane should be stopped if patient is to undergo major surgery or has a severe injury.
- Accutane may cause depression, psychosis and rarely suicidal ideation, suicide attempts and suicide. The mechanism of action is unclear.
- Possible contraindications include patients with pancreatitis, liver failure, coronary artery disease, and elevated triglycerides.

Side effects

- The most severe side effects are the risks to the fetus of exposure to Accutane. These include: CNS abnormalities (e.g. cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); skull abnormality; external ear abnormalities (e.g. anotia, micropinna, small or absent external auditory canals); eye abnormalities (e.g. microphthalmia); cardiovascular abnormalities; facial dysmorphism; cleft palate; thymus gland abnormality; parathyroid hormone deficiency. Spontaneous abortions and premature births have also been reported.
- About 10-20% patients will have an exacerbation of their acne during the initial phase of treatment.
- With the exception of teratogenicity, the side effects of Accutane are dose dependent and may be modified by a reduction in dose.
- The most common mucocutaneous side effects necessitating dose reduction are severe cheilitis, severe facial dermatitis, vestibulitis, blepharoconjunctivitis, photosensitivity and epistaxis. The use of lip salves, moisturizers, artificial tears, sunscreen and application of bacitracin to the nasal mucosa may control these side effects. However, if the cutaneous side effects are extensive, secondary colonization with *S. aureus* is likely.
- Other common side effects include arthralgias, myalgias, and headaches. These usually respond to NSAIDs or Tylenol. Hair loss is also common, but usually resolves once treatment is completed.
- Biochemical side effects include elevated total cholesterol, hypertriglyceridemia, reduced HDL, and abnormal liver function tests and hematologic parameters. Lab monitoring is recommended initially during treatment. Patients may be advised to modify their dietary fat intake, and alcohol and cigarette use.
- Rare side effects include:
 - Decreased night vision. This usually resolves after the drug is stopped. Advise patients to be cautious when driving at night
 - Corneal opacities. This has been associated with higher doses and usually resolves after the drug is discontinued.
 - Pseudotumor cerebri. This is more common in patients taking minocycline or tetracycline.

Patients should be instructed to call the doctor if they have severe or persistent headache, visual disturbances or nausea and vomiting. Patients with these complaints should be screened for papilledema and referred to a neurologist.

- Pancreatitis may occur due to elevated triglycerides
- Depression, suicidal thoughts
- Exacerbation of inflammatory bowel disease
- Skeletal hyperostosis has been observed on X-ray. The significance is unknown
- Pyogenic granuloma lesions
- Diarrhea

Recommended dosage

- Initially: 0.5-1mg/kg/day in 2 divided doses; max 2mg/kg/day
- Maintenance: 0.5-2mg/kg/day in 2 divided doses
- Duration: 16-20 weeks. May stop sooner if nodule count decreased by 70%.
- Cumulative dose is important; better long-term remission is significantly associated with a cumulative dose greater than 120mg/kg. This can be achieved by a dose of 1mg/kg/day for 4 months.
- Higher doses are associated with more side effects, but these are dose dependent and can be reduced by reducing the dose.
- If necessary repeat treatment after two months or more off drug.

Patient Management

- Establish need for treatment with Accutane
- Make sure patient is adequately informed on all side effects and has read the patient information brochure. A written informed consent must be signed by the patient and by the physician or third party witness and, in the case of a minor patient, by the patient's legal guardian. A copy of the signed form should be given to the patient, or guardian. The original consent should be maintained in the chart.
- If the patient is a sexually active female, highly effective contraception must be ensured. Determine if the patient has ever become pregnant while seemingly on adequate contraception.
- Obtain baseline labs:
 - Fasting lipid profile
 - Liver function tests
 - CBC
 - Blood or urine pregnancy test within one week prior to starting therapy.
- Follow patient at 2nd and 4th week and monthly thereafter.
- Follow-up labs:
 - Pregnancy test every month
 - Liver function tests and Fasting Lipid Profile at 2nd and 4th week to determine response to Accutane. Reduce dose and continue to monitor or discontinue if necessary.
- Give prescription for one month (6 weeks max). A prescription for Accutane must not be given until the pregnancy test is reported as negative. Therapy should begin on day two or three after the next normal menstrual period.
- Treat for 16-20 weeks. Aim for a cumulative dose of 100-120mg/kg.

Accutane Follow Up Form

Date Accutane Started: _____
 Total Weeks Completed: _____
 Target Cumulative Dose: _____ mg/kg

Name: _____
 Date: _____

How many pills a day are you taking? _____ Dose: _____mg/kg/day
 Cumulative dose to date _____mg/kg
 How has the acne been? Better Worse No Change
 Has the location of the breakouts changed? Yes No
 Are you getting any large painful cysts? _____ Where? _____

Other Medications:

Review of Symptoms:

Yes	No

Headache
 Nausea, Vomiting
 Visual Changes
 Blurred or double vision
 Dryness/Redness in eyes
 Abdominal pain
 Diarrhea
 Pain in muscles, joints, or bones

Yes	No

Depression
 Skin Changes
 Dry Lips
 Dry skin/cracking/Bleeding
 Sores that won't heal
 Rashes or growths on skin
 Periods regular
 Any concerns could be pregnant

EXAM:

General:
 Neuro/Psych:

Skin: Circle involved areas and indicate type of lesion (Comedones, Papules, Pustules, Cysts, Scars, Excoriations, Post Inflammatory Hyperpigmentation)

Scalp RUE
 Face LUE
 Neck RLE
 Chest LLE
 Back Groin
 Abdomen Buttocks

ENT:
 Eyes:
 Extremities:

Labs: Date done: _____ Result _____

A/P: Acne Vulgaris: Improved/Well-Controlled/Resolving/Resolved/Inadequately controlled/
 Worsening/No change

RX: Accutane _____ Length of course _____

Additional Recommendations:

Follow-Up: _____ wks Labs _____

Physician: _____

Patient Information and Consent

This guideline is designed for general use for most patients but may need to be adapted to meet the special needs of a specific patient as determined by the patient's provider.

All patients must read this section and sign at the bottom of the next page

Accutane is effective in treating severe acne, which has not responded to conventional treatment including oral antibiotics. The exact mode of action is unknown, but it causes a decrease in oil (sebum) excretion through a reduction in the size and activity of sebum producing glands. It also causes a reduction in the number of bacteria on the skin that are involved in acne. The average length of treatment is 16-20 weeks. In most patients the acne will resolve and they will have long term remissions. Some patients will need re-treatment. About 10-20% patients will have an exacerbation of their acne during the initial phase of treatment. Most will see improvement within one to two months and will have cleared significantly by the end of treatment. Continued improvement is seen even after the drug is stopped.

Absolute contraindications to Accutane are Pregnancy and Nursing mothers.

Accutane causes severe birth defects when taken by pregnant women. You must avoid intercourse or be using two forms of birth control for at least one month prior to beginning Accutane and for six weeks after Accutane is discontinued. If you miss a period or you think you are pregnant while taking Accutane, inform your doctor immediately. A pregnancy test will be done every month

Possible contraindications include: 1) Pancreatic disease. 2) Liver disease. 3) Coronary artery disease. 4) Elevated blood cholesterol and triglycerides

Common Side effects

<u>Side effect</u>	<u>Incidence</u>	<u>Treatment</u>
Dry chapped lips and cracks at corner of mouth	90-100%	Apply Vaseline, Carmex or A&D ointment to lips
Dry red skin on face arms and hands	40%	Apply moisturizer
Dry, irritated eyes (this is worse in contact wearers)	40	Avoid wearing contacts. Use artificial tears frequently. If severe, use Lacrilube ointment at bedtime
Nose crusting and nose bleeds	30%	Bedroom humidifier. Ocean Spray nose drops if mild dryness. For nosebleeds apply Bacitracin Ointment with Q-tip at bedtime.
Headaches, muscle pain and joint stiffness	15-20%	Usually mild, may need to reduce physical activity. Oral Tylenol or Ibuprofen is helpful.
Thinning hair	10%	Hair loss usually returns to normal after treatment.
Sunburn	5%	Avoid excessive sun exposure. Wear #15 sunscreen.

Other rare side effects:

- 1) Pseudotumor cerebri. Increased pressure and fluid in the brain. This is very rare. It is more common in patients taking Accutane with Minocin or tetracycline. Call your doctor if you have severe or persistent headache, visual changes, dizziness, or nausea and vomiting.
- 2) Decreased night vision. This usually resolves once treatment is completed. Be careful or avoid driving at night.
- 3) Cataracts. This is very rare and usually resolves once treatment is completed. Report any visual changes to your doctor.
- 4) Lab abnormalities. Blood tests will be done prior to treatment and 2 and 4 weeks after starting treatment. Inform your doctor if you develop abdominal pain, yellowing of the skin or eyes and dark urine.
- 5) Depression. Call your doctor if you get depressed or have suicidal thoughts or tendencies
- 6) Dry anus, mild rectal bleeding and dry vagina
- 7) Gout. Pain in the joints due to elevated serum uric acid
- 8) Persistent red, dry skin
- 9) Diarrhea
- 10) Blood in the urine.
- 11) Pyogenic granuloma lesions. Swelling, crusting and scarring at sites of acne lesions
- 12) Bone spurs. Thickening of surface layer of bone, seen on Xray. Significance is unknown.

This section for women to read and sign

My treatment with Accutane has been personally explained to me by Dr._____. The following points of information, among others, have been specifically discussed and made clear:

1. I, _____(Patient's Name) understand that Accutane is a very powerful medicine used to treat severe nodular acne that did not get better with other treatments including oral antibiotics. INITIALS_____

2. I understand that I must not take Accutane if I am pregnant or may become pregnant during treatment. INITIALS_____

3. I understand that severe birth defects have occurred in babies of females who took Accutane during pregnancy. I have been warned by my doctor that there is an extremely high risk of severe damage to my unborn baby if I am pregnant or become pregnant while taking Accutane. INITIALS_____

4. I have been told by my doctor that effective birth control (contraception) must be used for at least 1 month before starting Accutane, all during Accutane therapy and for 1 month after Accutane treatment has stopped. My doctor has told me that I must either abstain from sexual intercourse or use two reliable kinds of birth control at the same time. I have also been told that any method of birth control can fail. I must use two forms of reliable birth control simultaneously even if I think I cannot become pregnant, unless I abstain from sexual intercourse or have had a hysterectomy. INITIALS_____

5. I know that I must have a blood or urine test done by my doctor that shows I am not pregnant within 1 week before starting Accutane, and I understand that I must wait until the second or third day of my next normal menstrual period before starting Accutane. INITIALS_____

6. I also know that I must immediately stop taking Accutane if I become pregnant while taking the drug and immediately contact my doctor to discuss the desirability of continuing the pregnancy. I also know that I must immediately contact my doctor if I become pregnant during the month after stopping Accutane. INITIALS_____

7. I have carefully read the Accutane patient brochure, "Important information concerning your treatment with Accutane," given to me by my doctor. I understand all of its contents and have talked over any questions I have with my doctor: INITIALS_____

8. I am not now pregnant, nor do I plan to become pregnant for 1 month after I have completely finished taking Accutane. INITIALS_____

I have read and understand the above side effects and have been given a chance to ask questions regarding the side effects by my doctor. I now authorize Dr._____ to begin my treatment with Accutane.

Patient, Parent or Guardian Date

I have fully explained to the patient, _____the nature and purpose of the treatment described above and the risks to females of childbearing potential. I have asked the patient if she has any questions regarding her treatment with Accutane and have answered those questions to the best of my ability.

Physician Date