Soriatane (acitretin) Flowsheet

Patient Name:_____ **Start Date:** _____

Indication: Severe psoriasis in adults: ___*generalized pustular* ___*erythrodermic* ___*severe recalcitrant* ___*severe plaque*

Off Label uses: ___Darier's ___PRP ___Lupus ___chemoprevention of malignancies Other: _____

Contraindications: ***Absolute***: ___ Pregnancy or a woman who is likely to become pregnant or who intend to become pregnant within 3 years following cessation of treatment with acitretin.
___Females who cannot use reliable contraception while undergoing treatment and for at least 3 years after d/c of acitretin
___ Noncompliance with contraception
___ Nursing mothers
___Concurrent use of methotrexate (increased liver toxicity) or tetracyclines (pseudotumor cerebri)
___Hypersensitivity

Relative: ___Leukopenia
___Moderate to severe chol or trig elevation
___Sig. hepatic dysfunction
___Sig. renal dysfunction

Precautions: ___Alcohol consumption will cause acitretin (half-life 2 days) to be metabolized to etretinate (half-life 120days and has been found in serum up to 4 years & 4 months- after d/c).

Supplied as: 10 and 25mg capsules.

Dosing: Not based on body weight. Start at 25mg/day and increase. Psoriasis clears faster at higher initial starting doses, but hair loss and paronychia occur more frequently. For psoriasis: 20-50mg/d maintenance dose recommended.

	Baseline	**1 mo**	**2 mo**	**3 mo**	**6 mo**	**9 mo**	**12 mo**	**15 mo**	**18 mo**	**21 mo**	**24 mo**
CBC	____	____	____	____	____	____	____	____	____	____	____
LFT's* : AST	____	____	____	____	____	____	____	____	____	____	____
ALT	____	____	____	____	____	____	____	____	____	____	____
T. chol	____	____	____	____	____	____	____	____	____	____	____
HDL	____						____				____
LDL	____						____				____
Trig	____	____	____	____	____	____	____	____	____	____	____
BUN/Creat	____	____	____	____	____	____	____	____	____	____	____
U/A**	_____	____	_____	_____	_____	_____	_____	_____	_____	_____	_____
Opthal exam***	_____										
Baseline x-rays****	_____						_____				_____
Signed consent	_____										

Female patients	**Baseline**	**1 mo**	**2 mo**	**3 mo**	**4 mo**	**5 mo**	**6 mo**	**7 mo**	**8 mo**	**9 mo**	**10 mo**	**11 mo**	**12 mo**
Serum HCG*****	____	____	____	____	____	____	____	____	____	____	____	____	____

13 mo	**14 mo**	**15 mo**	**16 mo**	**17 mo**	**18 mo**	**19 mo**	**20 mo**	**21 mo**	**22 mo**	**23 mo**	**24 mo**
____	____	____	____	____	____	____	____	____	____	____	____

2 forms of contraception: 1. _____2._____*****

BC counseling done: Y N *******

*Transaminase elevation >3x upper limit of normal: d/c; 2-3x: d/c until returns to normal, then resume at lower dose. <2x: will usually decrease with continued tx.
**Optional; for patients with renal dz, proteinuria, diabetes, or htn
***Consider for patients with hx of cataracts or retinopathy
****Consider wrists, ankles, thoracic spine x-rays if long-term therapy planned. Consider yearly.
*****Must have 2 neg serum or urine preg tests (sensitivity of at least 25mIU/ml). 2nd confirmatory test should be done during menses immediately preceding start.
******Must have selected 2 forms to be used simultaneously, at least one of which is a primary form. Primary: tubal ligation, vasectomy (of partner), BCP's, injectable/implantable/insertable/topical birth control. Exceptions are absolute abstinence (have pt sign agreement), pts with a hysterectomy or clearly postmenopausal. products. Secondary forms: diaphragms, latex condoms, cervical caps, all used with spermacide. Do not use microdosed "minipill" progestin preparations.
*******A Soriatane Patient Referral Form is available for free counseling.

Acitretin Information Sheet

What is it: a second-generation synthetic retinoid. A metabolite of etretinate.
MOA: package insert says unknown, but probably induces cellular differentiation, antiproliferation, antiinflammation, antikeratinization and inhibits neutrophil chemotaxis.
Absorption: enhanced with food, especially fatty foods, however patients should be warned not to consume an excessively fatty diet. 60% bioavailable. 99.9% protein bound.
Metabolism: mainly in the liver. 34-54% excreted in feces and 16-53% in urine. Not removed by hemodialysis.
Pregnancy category: X
Pediatric use: Safety and effectiveness "not established". There is some concern with retinoids about premature epiphyseal closure, ossification of tendons and ligaments, skeletal hyperostosis, and decreases in bone mineral density.
Steady state: 3 weeks.
Distribution: water soluble so there is little lipid deposition however if alcohol is consumed, acitretin is reesterified to etretinate, which is 50 times more water soluble, which results in increased storage in adipose tissue.

Half-life: 98% of acitretin is eliminated w/in 2 months (assuming a mean elimination half-life of 49 hours). If reesterfication occurs (i.e. when alcohol is consumed with acitretin), 98% is eliminated in 2 –3 years (assuming a half-life of 120-163 days). One patient (with a sporadic intake of alcohol) had etretinate found in plasma and SQ fat after 52 months.

Interactions:
Microdosed "minipill" progestin contraceptives: Acitretin interferes with their contraceptive effect. It is not known whether other progestational contraceptives such as implants and injectables, are adequate methods of contraception during acitretin therapy. Also, it has not been established if there is a pharmacokinetic interaction between acitretin and other BCP's.
St. John's Wort: interacts with hormonal contraceptives (reports of breakthrough bleeding and pregnancies).
Ethanol: causes acitretin to be reesterified to etretinate, which has a much longer half-life.
Vit. A: concomitant Vit. A should be limited to < 5000 IU Vit. A/day (Wolverton), however package insert says NO Vit. A.
Glibenclamide (a sulfonylurea): potentiated its glucose lowering effect in 3/7 pts studied.
Methotrexate: increased risk of hepatitis. Don't use concurrently.
Phenytoin: protein binding of phenytoin may be reduced.
Tetracyclines: increased risk of pseudotumor cerebri. Don't use concurrently.
No interactions with cimetidine, digoxin, glyburide coumadin/warfarin.

What to expect: ***Psoriasis***: generalized pustular and erythrodermic: most responsive. Localized pustular also responds well with retinoids as monotherapy. Plaque-type: partial improvement. More effective if combined with PUVA or UVB. Response rates for generalized pustular psoriasis: retinoids: 84%; MTX: 76%; cyclosporine: 71%; PUVA: 46%. Acitretin 50-75mg/day much more effective than 10-25mg/day. ***Psoriatic arthritis***: 60% improve with etretinate. ***HIV psoriasis***: effective. Not immunosuppressive. Optimal results with 75mg/day. ***Darier's***: responds to both isotretinoin and acitretin. More effective in widespread, hyperkeratotic forms. ***PRP***: isotretinoin at 1-1.5mg/kg/day . Acitretin use has not been reported but is assumed effective because etretinate is effective. About 70% respond. ***Ichthyosis***: responds well to acitretin. For IV and x-linked icthyosis-usually not severe enough to use systemic retinoids. For epidermolytic hyperkeratosis: may have an initial increase in bullae. Bullous flare less likely if started at 0.25mg/kg/d and increased gradually. ***Keratodermas***- the following respond well: palmoplantar hyperkeratosis of recessive hidrotic ectodermal dysplasia, pachonychia congenital tarda, Unna-Thost, punctuate forms, recessive forms with transgriediens such as Papillon-Lefevre and mal de Meleda, and Vohwinkel's. ***Pre-malignant diseases***- the following are retinoid responsive: oral leukoplakia, actinic keratosis, arsenical keratosis, Bowen's disease, keratoacanthomas, bowenoid papulosis, PUVA-induced keratosis. ***Malignancy syndromes***: retinoid responsive syndromes include basal cell nevus syndrome, paraneoplastic acrokeratosis (Basex's), xeroderma pigmentosus, Muir-Torre, epidermodysplasia veruciformis. Isotretinoin 1.5mg/kg/d demonstrated a marked reduction in new BCC's at an average maintenance dose of 1.5mg/kg/d in patients w/o basal cell nevus syndrome. ***Transplant patients***: acitretin 30mg/day in 44 renal transplant patients reduced significantly keratosis (13% vs 28%) and SCC's (11% vs 47%) compared with placebo. ***Lupus***: good response in hyperkeratotic variety of DLE. Generalized lupus (without hyperkeratosis) and CSLE also respond. Acitretin 50mg/day was about as effective as hydroxychloroquine 400mg/d in cutaneous LE, but had more side effects with acitretin. ***Lichen Planus***: mediocre results with isotretinoin and etretinate. Acitretin at 30mg/d showed a 64% response rate in 8 weeks. May be best for widespread, hypertrophic types or oral erosive types. May be best to combine with a systemic corticosteroid. ***Vulvar LS & A***: moderate to significant improvement with etretinate. Reduced pruritis and burning symptoms as early as 2 weeks. 93-95% response rate. Acitretin 20-30mg/day produced a 64% response rate. ***GVH disease***: for chronic GVHD with sclerodermatous skin changes, etretinate produced a significant response rate after 3 months (74%). Softened skin, flattened cutaneous lesions and increased range of motion. ***HPV infections***: etretinate reported effective for extensive warts.

Combination TX: ***Acitretin plus PUVA***: response rate 75-96% with clearance time of 40-57 days.
Acitretin plus UVB: response rate of 60-95% with clearance time of 44-48 days
Acitretin alone: response rate of 23-75%.
UVB alone: response rate of 24-63%
PUVA alone: response rate of 60-80%.
Other combination treatments have not yet been reported.

Side Effects

>75%: cheilitis
50-75%: alopecia, skin peeling
25-50%: rhinitis, dry skin, pruritis, nail disorder
10-25%: rigors, xeropthalmia, dry mouth, epistaxis, arthralgia, spinal hyperostosis (progression of existing lesions), erythematous rash, paresthesia, paronychia, skin atrophy, sticky skin

Elevated LFTS: 1/3 patients (AST,ALT,LDH). Slight to moderate. Usually return to normal during continuation of tx or cessation. 10-25%: increased alk phos, GGTP, direct bili.
Elevated cholesterol: 33% of pts.
Elevated triglycerides: 66% of pts.
10-25% of pts: increased uric acid
FBS: decreased in 10-25%, increased FBS in 25-50%
May increase or decrease: Mg, WBC count, Ca, Cl, lymphs, neuts, HCT, Hgb, PLTs, RBCs, alb, iron, phos, K, Na
1-10% of pts: increased bands, basophils, eos, monos, T. bili, T. protein, BUN, creat.

Hepatotoxicity: 2/1289 pts in European trial developed biopsy confirmed toxic hepatitis. 2/525 pts in US trial had clinical jaundice, and increased LFTs considered related to Soriatane. Returned to nl after d/c of Soriatane. 1/63 Canadian pts had a 3 fold increase in transaminases. Returned to normal after d/c of Soriatane. LFT changes usually occur 2-8 weeks after starting tx. Pts at risk for liver toxicity include those with DM, obesity, prior or concurrent methotrexate use, excess alcohol consumption, infectious hepatitis, and abnormal baseline LFTs.
Hyperostosis: 10-25% of pts have progression of pre-existing spinal hyperostosis. 3/380 pts showed formation of new (de novo) small spurs. Knee and ankle spurs: no de novo spurs, but 5/6 pts with pre-existing spurs had progression. Clinical complaints did not predict radiographic changes. Patients are often asymptomatic at sites where there are calcifications. Periodic radiography is only warranted in the presence of symptoms or long-term use of Soriatane. There are no official guidelines for monitoring bone-related adverse effects. Yearly screening x-rays (lateral thoracic spine and ankle films) are optional but should be considered for patients with known pretreatment radiologic abnormalities, with prominent musculoskeletal symptoms, and with prolonged high-dose therapy. The height of children should be recorded before and during retinoid therapy.
Premature epiphyseal closure: to date, 5 cases have been reported in children involving isotretinoin and etretinate. The epiphyseal closure is generally partial, associated with prolonged and very high dose retinoid therapy, and accompanied by other confounding factors such as concomitant or prior use of Vitamin A.
Hyperlipidemia: High carbohydrate, low fat diets exacerbate hypertriglyceridemia. Alcohol worsens this also. Oat bran diet can lower triglyceride levels. High risk pts for hyperlipidemia are pts with DM, obesity, excessive alcohol intake, pts with a high saturated fat, high cholesterol diet. The highest lipid elevations are seen in those with baseline hyperlipidemia.
Ophthal: 23%: dry eyes. 9%: irritation of eyes. 5%; brow and lash loss. <5%: decreased night vision, photophobia, recurrent sties, itchy eyes or eyelids, cataracts, conjunctivitis, blepharitis, blurred vision.
Pancreatitis: rare reports in the absence of hypertriglyceridemia. The lowest triglyceride level that resulted in pancreatitis was 770mg/dl. Most pts with pancreatitis will have triglyceride elevations well over 1000mg/dl.
Pseudotumor cerebri: only one pt reported with Soriatane use alone. The rest were taking tetracyclines.
Psych: Depressive feelings or feelings of aggression have been reported by some patients. It is not known if they are related to Soriatane.
Retinoid induced granulations tissue: particularly in nail sulci, healing cystic acne lesions and traumatic wounds. Can be treated with occlusive topical steroids, IL steroids, pulsed systemic steroids, curettage, chemical cautery or pulsed dye laser.

Soriatane (acitretin) Consent Form (all patients)

Soriatane (acitretin) is a drug that may help your medical condition. Like any other drug, it may have unwanted side effects. The following is a list of some of the side effects that Soriatane may have in addition to some important information you need to know while taking this medication. It is important that you read this information and ask any questions you may have before starting Soriatane. Do not sign this consent and do not take Soriatane if there is anything that you do not understand.

Initials

Common Side Effects

_____1. Chapped lips; peeling fingertips, palms and soles; itching; scaly skin all over; weak nails; sticky or fragile (weak) skin; runny or dry nose, or nosebleeds. Moisturizers for your lips, skin and Vaseline (petrolatum) for your nose (nostrils) will help with these effects.
_____2. Dry mouth.
_____3. Joint pain.
_____4. Tight muscles.
_____5. Hair loss. Most patients will have some degree of hair loss, but this condition varies among patients, No one can tell if you will lose hair, how much hair you may lose or if and when it may grow back.
_____6. Dry eyes. Wearing contact lenses may be uncomfortable during and after treatment with Soriatane because of the dry feeling in your eyes. If this happens, remove your contact lenses and call your prescriber.
_____7. Rise in blood fats (lipids). Soriatane can cause your blood fats (lipids) to rise. Most of the time, this is not serious. But sometimes the increase can become a serious problem. You should have blood tests as directed by your physician to help monitor for this side effect.

Serious Side Effects

_____8. Bad headaches, nausea, vomiting, blurred vision. These symptoms can be signs of increased brain pressure that can lead to blindness or even death.
_____9. Decreased vision in the dark (night blindness). Since this can start suddenly, you should be very careful when driving at night. This problem usually goes away when Soriatane treatment stops. You should be cautious when driving or operating any vehicle at night. If you develop any vision problems or eye pain stop taking Soriatane and call your prescriber.
_____10. Depression. There have been some reports of patients developing mental problems including a depressed mood, aggressive feeling, or thoughts of ending their own life (suicide). These events, including suicidal behavior, have been reported in patients taking other drugs similar to Soriatane as well as in patients taking Soriatane. Since other things may have contributed to these problems, it is not known if they are related to Soriatane. It is very important to stop taking Soriatane and call your prescriber right away if you develop such problems.
_____11. Yellowing of your skin or the whites of your eyes, nausea and vomiting, loss of appetite or dark urine. These can be signs of serious liver damage. You should get regular blood tests while on Soriatane to monitor for these effects.
_____12. Aches or pains in your bones, joints, muscles, or back; trouble moving; loss of feeling in your hands or feet. These can be abnormal changes to your bones or muscles.
_____13. Frequent urination, great thirst or hunger. Soriatane can affect blood sugar control, even if you do not already have diabetes. These are some of the signs of high blood sugar.
_____14. Shortness of breath, dizziness, nausea, chest pain, weakness, trouble speaking, or swelling of a leg. These may be signs of a heart attack, blood clots, or stroke. Soriatane can cause serious changes in blood fats (lipids). It is possible for these changes to cause blood vessel blockages that lead to heart attacks, strokes, or blood clots. You should have regular blood tests to monitor for these changes in your lipid levels.

_____15. For males: Small amounts of Soriatane are found in the semen of males taking Soriatane. Based on available information, it appears that these small amounts of Soriatane in semen pose little, if any, risk to an unborn child while a male patient is taking the drug or after it is discontinued. Discuss any concerns you have about this with your prescriber.
_____16. Take Soriatane with food.
_____17. Take Soriatane exactly as prescribed by your doctor.
_____18. If you miss a dose, do not double the next dose. Skip the missed dose and resume your normal schedule.
_____19. If you take too much Soriatane (overdose), call your local poison control center or emergency room.
_____20. I agree to have regular blood tests before, during and after treatment to monitor for adverse effects of Soriatane.
_____21. I agree to keep all of my appointments with my physicians before, during and after taking Soriatane.
_____22. I agree to not consume alcohol while taking Soriatane. Keep in mind that many "nonalcoholic" edibles and "over-the-counter" preparations actually contain some amounts of ethanol.
_____23. Avoid dietary supplements containing Vitamin A. Soriatane is related to Vitamin A. Therefore, do not take supplements containing Vitamin A, because they may add to the unwanted side effects of Soriatane. Check with your physician or pharmacist if you have any questions about vitamin supplements.
_____24. Do not share Soriatane with anyone else, even if they have the same symptoms. Your medicine may harm them or their unborn child.
_____25. Avoid non-medical ultraviolet (UV) light. Soriatane can make your skin more sensitive to UV light. Do not use sunlamps, and avoid sunlight as much as possible. If you are taking light treatment (phototherapy), your prescriber may need to change your light dosages to avoid burns.
_____26. Avoid giving blood. Do not donate blood while you are taking Soriatane and for at least 3 years after stopping Soriatane treatment. Soriatane in your blood can harm an unborn baby if your blood is given to a pregnant woman. Soriatane does not affect your ability to receive a blood transfusion.
_____27. Psoriasis gets worse for some patients when they first start Soriatane treatment. Some patients have more redness or itching. If this happens, tell your prescriber. These symptoms usually get better as treatment continues, but your prescriber may need to change the amount of your medicine.
_____28. All patients taking Soriatane should be given a Soriatane Medication Guide each time Soriatane is dispensed. Ask your pharmacist if you did not receive one at the time of dispensing.
_____29. This is a partial listing of side effects. A more complete list may be obtained from the package insert at the time of dispensing by the pharmacist.
_____30. Tell your prescriber if you have or ever had diabetes or high blood sugar, liver problems, kidney problems, high cholesterol or high triglycerides (fat in the blood), heart disease, depression, alcoholism, or an allergic reaction to a medication.

I have read the above 30 items and have been given an opportunity to ask any questions about treatment with Soriatane. I have also had treatment alternatives, including doing nothing, discussed with me.
I hereby give my consent to be placed on Soriatane.

Patient Signature: _____Date:_____

Patient Name: _____

Physician Name/Signature: _____Date:_____

Witness Name/Signature: _____Date: _____

Patient Agreement/Informed Consent for FEMALE Patients

Read each item below and initial in the space provided to show that you understand each item and agree to follow your prescriber's instructions. Do not sign this consent and do not take Soriatane if there is anything that you do not understand.

* A parent or guardian of a minor patient (under age 18) must also read and initial each item before signing the consent.

Patient's Name:_____

Initials

_____1. I understand that there is a very high risk that my unborn child could have severe birth defects if I am pregnant or become pregnant while taking Soriatane in any amount even for short periods of time. Birth defects have also happened in babies of women who become pregnant after stopping Soriatane treatment.

_____2. I understand I must not take Soriatane if I am pregnant.

_____3. I understand that I must not become pregnant while taking Soriatane and for at least 3 years after the end of my treatment with Soriatane.

_____4. I know that I must avoid drinks, food, and medicines, including over-the-counter products, that contain alcohol. This is extremely important, because alcohol changes Soriatane in the blood into a drug that takes even longer to leave the body. This means the risk of birth defects may last longer than 3 years if I swallow any form of alcohol during Soriatane therapy or for 2 months after I stop taking Soriatane.

_____5. I understand that I must avoid sexual intercourse completely, or I must use 2 separate effective forms of birth control (contraception) **at the same time.** The only exception is if I have had surgery to remove the womb (a hysterectomy) or my prescriber has told me I have gone completely through menopause.

_____6. I have been told by my prescriber that 2 effective forms of birth control (contraception) must be used at the same time for at least 1 month before starting Soriatane, for the entire time of Soriatane therapy, and for at least 3 years after Soriatane treatment has stopped.

_____7. I understand that birth control pills and injectable/implantable/insertable/topical (patch) hormonal birth control products are among the most effective forms of birth control. However, any form of birth control can fail. Therefore, I must use 2 different methods at the same time, every time I have sexual intercourse, even if 1 of the methods I choose is birth control pills, injections, or tubal ligation (tube-tying).

_____8. I understand that the following are considered effective forms of birth control:

Primary: Tubal ligation (tying my tubes), partner's vasectomy, birth control pills, injectable/implantable/insertable/topical (patch) hormonal birth control products, and an IUD (intrauterine device).

Secondary: Diaphragms, latex condoms, and cervical caps. Each must be used with a spermicide, which is a special cream or jelly that kills sperm.

I understand that at least 1 of my 2 methods of birth control must be a primary method.

_____9. I will talk with my prescriber about any medicines or dietary supplements I plan to take during my Soriatane treatment because hormonal birth control methods (for example, birth control pills) may not work if I am taking certain medicines or herbal products (for example, St. John's Wort).

_____10. I understand that if I have taken Tegison (etretinate), I must continue to follow the birth control (contraception) recommendations for Tegison.

_____11. Unless I have had a hysterectomy or my prescriber says I have gone completely through menopause, I understand that I must have 2 negative pregnancy test results before I can get a prescription for Soriatane. The first pregnancy test should be done when my prescriber decides to prescribe Soriatane. The second pregnancy test should be done during the first 5 days of my menstrual period right before starting Soriatane therapy, or as instructed by my prescriber. I will then have pregnancy tests on a regular basis as instructed by my prescriber during my Soriatane therapy.

_____12. I understand that I should not start taking Soriatane until I am ***sure*** that I am not pregnant and have negative results from 2 pregnancy tests.

_____13. I have read and understand the materials my prescriber has given to me, including the Soriatane Pregnancy Prevention Program. My prescriber gave me and asked me to watch the video about contraception (birth control). I was told about a confidential counseling line that I may call at Connetics for more information about birth control (1-888-500- DERM (3376)).

_____14. I have received information on emergency contraception (birth control).

_____15. I understand that I may receive a free contraceptive (birth control) counseling session and pregnancy testing. My prescriber can give me a Soriatane Patient Referral Form for this free consultation.

_____16. I understand that I should receive counseling from my prescriber, repeated on a regular basis, about contraception (birth control) and behaviors associated with an increased risk of pregnancy.

_____17. I understand that I must stop taking Soriatane right away and call my prescriber if I get pregnant, miss my menstrual period, stop using birth control, or have sexual intercourse without using my 2 birth control methods during and at least 3 years after stopping Soriatane treatment.

_____18. If I do become pregnant while on Soriatane or at any time within 3 years of stopping Soriatane, I understand that I should report my pregnancy to Connetics at 1-888-500- DERM (3376) or to the Food and Drug Administration (FDA) MedWatch program at 1- 800-FDA-1088. The information I share will be kept confidential (private) and will help the company and the FDA evaluate the Pregnancy Prevention Program.

_____19. I understand I should not take Soriatane prior to or during nursing (breastfeeding).

I have read and understood the above 19 items. My prescriber has answered all my questions about Soriatane. I understand that it is my responsibility not to get pregnant during Soriatane treatment or for at least 3 ***years after I stop taking Soriatane.*** I now authorize my prescriber _____ to begin my treatment with Soriatane.

Patient signature: _____ Date: _____

Parent/guardian signature (if under age 18):_____Date: _____

Please print: Patient name and address: _____

_____

_____

Telephone: _____

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 Soriatane and have answered those questions to the best of my ability.

Prescriber signature: _____Date: _____

Witness Name/Signature: _____Date:_____