

# Consumer Reports Rates Drug Cost Effectiveness

BY ALICIA AULT  
Contributing Writer

WASHINGTON — The nonprofit Consumers Union has issued the first in a series of evidence-based, patient-friendly reports listing what it calls the most cost-effective drugs, organization officials announced at a press conference.

The initial guides cover nonsteroidal anti-inflammatory agents (NSAIDs), statins, and proton pump inhibitors (PPIs).

The publisher of Consumer Reports said it hopes that patients—especially those with little or no drug benefit coverage—will use these reports to make informed choices in conjunction with their physicians.

The reports are designed to cut through the clutter of drug company advertising and scattered Internet searches. But drug makers won't be allowed to use the "Best Buy Drugs" designation in marketing or ads: Consumers Union prohibits manu-

facturers from commercializing any of its recommendations.

The guides should be familiar to anyone who has used Consumer Reports' ratings to buy a car, appliance, or bicycle. But unlike the group's analyses on other consumer goods, the Best Buy Drugs reports are free of charge.

"In each category, based on all the evidence, we've identified Best Buy Drugs—the drugs that are likely to be the best, most affordable choices for most people,"

said Joel Gurin, executive vice president of Consumers Union.

The Best Buy Drugs are not selected based on Consumers Union's own tests, however, but rather on systematic reviews conducted by the Drug Effectiveness Review Project (DERP), and on further peer review from medical experts like Mark Helfand, M.D., director of the Oregon evidence-based practice center at Oregon Health and Science University, Portland, which initiated DERP in 2003.



## SORIATANE® (acitretin) CAPSULES

Before prescribing, please see complete product information, a summary of which follows:

**CONTRAINDICATIONS AND WARNINGS:** Soriatane must not be used by females who are pregnant, or who intend to become pregnant during therapy or at any time for at least 3 years following discontinuation of therapy. Soriatane also must not be used by females who may not be using contraception while undergoing treatment and for at least 3 years following discontinuation of treatment. Acitretin is a metabolite of etretinate (Tegison), and major human fetal abnormalities have been reported with the administration of acitretin and etretinate. Potentially any fetus exposed can be affected. Clinical evidence has shown that concurrent ingestion of acitretin and ethanol has been associated with the formation of etretinate, which has a significantly longer elimination half-life than acitretin. Because the longer elimination half-life of etretinate would increase the duration of teratogenic potential for female patients, ethanol must not be ingested by female patients either during treatment with Soriatane or for 2 months after cessation of therapy. This allows for elimination of acitretin, thus removing the substrate for transesterification to etretinate. The mechanism of the metabolic process for conversion of acitretin to etretinate has not been fully defined. It is not known whether substances other than ethanol are associated with transesterification. Acitretin has been shown to be embryotoxic and/or teratogenic in rabbits, mice, and rats at oral doses of 0.3, 3 and 15 mg/kg, respectively. These doses are approximately 0.2, 0.3 and 3 times the maximum recommended therapeutic dose, respectively, based on a mg/m<sup>2</sup> comparison. Major human fetal abnormalities associated with acitretin and/or etretinate administration have been reported including meningomyelocele, meningoencephalocele, multiple synostoses, facial dysmorphism, syndactyly, absence of terminal phalanges, malformations of hip, ankle and forearm, low-set ears, high palate, decreased cranial volume, cardiovascular malformation and alterations of the skull and cervical vertebrae. Soriatane should be prescribed only by those who have special competence in the diagnosis and treatment of severe psoriasis, are experienced in the use of systemic retinoids, and understand the risk of teratogenicity. **Important Information for Women of Childbearing Potential:** Soriatane should be considered only for women with severe psoriasis unresponsive to other therapies or whose clinical condition contraindicates the use of other treatments. Females of reproductive potential must not be given a prescription for Soriatane until pregnancy is excluded. Soriatane is contraindicated in females of reproductive potential unless the patient meets ALL the following conditions:

- Must have had 2 negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial Soriatane prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue Soriatane therapy. The second pregnancy test (a confirmation test) should be done during the first 5 days of the menstrual period immediately preceding the beginning of Soriatane therapy. For patients with amenorrhea, the second test should be done at least 11 days after the last act of unprotected sexual intercourse (without using 2 effective forms of contraception [birth control] simultaneously). Timing of pregnancy testing throughout the treatment course should be monthly or individualized based on the prescriber's clinical judgment.
- Must have selected and have committed to use 2 effective forms of contraception (birth control) simultaneously, at least 1 of which must be a physical form, unless absolute abstinence is the chosen method, or the patient has undergone a hysterectomy or is clearly postmenopausal.
- Patients must use 2 effective forms of contraception (birth control) simultaneously for at least 1 month prior to initiating Soriatane therapy, during Soriatane therapy, and for at least 3 years after discontinuing Soriatane therapy. A Soriatane Patient Referral Form is available so that patients can receive an initial free contraceptive counseling session and pregnancy testing. Counseling about contraception and behaviors associated with increased risk of pregnancy must be repeated on a regular basis by the prescriber. To encourage compliance with this recommendation, a limited supply of the drug should be prescribed. Effective forms of contraception include both primary and secondary forms of contraception. Primary forms of contraception include: tubal ligation, partner's vasectomy, intrauterine devices, birth control pills, and injectable hormonal contraceptives (oral, implantable, hormonal birth control products). Secondary forms of contraception include diaphragms, latex condoms, and cervical caps; each secondary form must be used with a spermicide. Any birth control method can fail. Therefore, it is critically important that women of childbearing potential use 2 effective forms of contraception (birth control) simultaneously. It has not been established if there is a pharmacokinetic interaction between acitretin and combined oral contraceptives. However, it has been established that acitretin interferes with the contraceptive effect of microdose progesterone preparations. Microdosed "mini-pill" progesterone preparations are not recommended for use with Soriatane. It is not known whether other progestational contraceptives, such as implants and injectables, are adequate means of contraceptive therapy. Patients should be advised to consult the package insert of any medication administered concurrently with hormonal contraceptives, since some medications may decrease the effectiveness of these birth control products. 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 (see PRECAUTIONS).
- Must have signed a Patient Agreement/Informed Consent for Female Patients that contains warnings about the risk of potential birth defects if the fetus is exposed to Soriatane, about contraceptive failure, and about the fact that they must not ingest beverages or products containing ethanol while taking Soriatane and for 2 months after Soriatane treatment has been discontinued.

If pregnancy does occur during Soriatane therapy or at any time for at least 3 years following discontinuation of Soriatane therapy, the prescriber and patient should discuss the possible effects on the pregnancy. The available information is as follows: Acitretin, the active metabolite of etretinate, is teratogenic and is contraindicated during pregnancy. The risk of severe fetal malformations is well established when systemic retinoids are taken during pregnancy. Pregnancy must also be prevented after stopping acitretin therapy, while the drug is being eliminated to below a threshold blood concentration that would be associated with an increased incidence of birth defects. Because this threshold has not been established for acitretin in humans and because elimination rates vary among patients, the duration of posttherapy contraception to achieve adequate elimination cannot be calculated precisely. It is strongly recommended that contraception be continued for at least 3 years after stopping treatment with acitretin, based on the following considerations:

- In the absence of transesterification to form etretinate, greater than 98% of the acitretin would be eliminated within 2 months, assuming a mean elimination half-life of 49 hours.
- In cases where etretinate is formed, as has been demonstrated with concomitant administration of acitretin and ethanol:
  - greater than 98% of the etretinate formed would be eliminated in 2 years, assuming a mean elimination half-life of 120 days.
  - greater than 98% of the etretinate formed would be eliminated in 3 years, based on the longest demonstrated elimination half-life of 168 days.

However, etretinate was found in plasma and subcutaneous fat in one patient reported to have had sporadic alcohol intake 52 months after she stopped acitretin therapy.

• Severe birth defects have been reported where conception occurred during the time interval when the patient was being treated with acitretin and/or etretinate. In addition, severe birth defects have also been reported when conception occurred after the mother completed therapy. These cases have been reported both prospectively (before the outcome was known) and retrospectively (after the outcome was known). The events below are listed without distinction as to whether the reported birth defects are consistent with retinoid-induced embryopathy or not.

- There have been 318 prospectively reported cases involving pregnancies and the use of etretinate, acitretin or both. In 238 of these cases, the conception occurred after the last dose of etretinate (103 cases), acitretin (126) or both (9). Fetal outcome remained unknown in approximately one-half of these cases, of which 62 were terminated and 14 were spontaneous abortions. Fetal outcome is known for the other 118 cases and 15 of the outcomes were abnormal (including cases of absent hand/wrist, clubfoot, GI malformation, hypocalcemia, hypotonia, limb malformation, neonatal apnea/anemia, neonatal ichthyosis, placental dysfunction/death,

### SORIATANE® (acitretin)

undescended testicle and 5 cases of premature birth). In the 126 prospectively reported cases where conception occurred after the last dose of acitretin only 43 cases involved conception at least 1 year but less than 2 years after the last dose. There were 3 reports of abnormal outcomes out of these 43 cases (involving limb malformation, GI tract malformations and premature birth). There were only 4 cases where conception occurred at least 2 years after the last dose but there were no reports of birth defects in these cases.

- There is also a total of 35 retrospectively reported cases where conception occurred at least one year after the last dose of etretinate, acitretin or both. From these cases there are 3 reports of birth defects when the conception occurred at least 1 year but less than 2 years after the last dose of acitretin (including heart malformations, Turner's Syndrome, and unspecified congenital malformations) and 4 reports of birth defects when conception occurred 2 or more years after the last dose of acitretin (including foot malformations, cardiac malformations (2 cases) and unspecified neonatal and infancy disorder). There were 3 additional abnormal outcomes in cases where conception occurred 2 or more years after the last dose of etretinate (including chromosome disorder, forearm dysplasia, and stillbirth).
- Females who have taken Tegison (etretinate) must continue to follow the contraceptive recommendations for Tegison. Tegison is no longer marketed in the U.S.; for information, call Roche at 1-800-526-0367.
- Patients should not donate blood during and for at least 3 years following the completion of Soriatane therapy because women of childbearing potential must not receive blood from patients being treated with Soriatane.

**Important Information For Males Taking Soriatane:**

- Patients should not donate blood during and for at least 3 years following Soriatane therapy because women of childbearing potential must not receive blood from patients being treated with Soriatane.
- Samples of seminal fluid from 3 male patients treated with acitretin and 6 male patients treated with etretinate have been assayed for the presence of acitretin. The maximum concentration of acitretin observed in the seminal fluid of these men was 12.5 ng/mL. Assuming an ejaculate volume of 0 mL, the amount of drug transferred in semen was 0.125 ng, which is 1/200,000 of a single 25 mg capsule. Thus, although it appears that residual acitretin in seminal fluid poses little, if any, risk to a fetus while a male patient is taking the drug or after it is discontinued, the no-effect limit or teratogenicity is unknown and there is no registry for birth defects associated with acitretin. The available data are as follows: There have been 25 cases of reported conception when the male partner was taking acitretin. The pregnancy outcome is known in 13 of these 25 cases. Of these, 8 reports were retrospective (and 4 were prospective (meaning the pregnancy was reported prior to knowledge of the outcome)):

Timing of paternal acitretin treatment relative to conception	Delivery of healthy neonate	Spontaneous abortion	Induced abortion	Total
At time of conception	1	0	1	11
Discontinued - 1-2 weeks prior	0	0	1**	1
Discontinued - 6-8 months prior	0	1	0	1

\*Four of 5 cases were prospective  
\*\*With malformations: pattern not typical of retinoid embryopathy (bilateral cystic hygromas of neck, hypoplasia of lungs bilaterally, pulmonary atresia, VSD with overriding tricuspid arteriosus)

For All Patients: A SORIATANE MEDICATION GUIDE MUST BE GIVEN TO THE PATIENT EACH TIME SORIATANE IS DISPENSED, AS REQUIRED BY LAW.

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