

Parker & Waichman, LLP Attorneys at Law

Accutane Information Guide



Manufacturer:
Ortho-McNeil

Generic:
Isotretinoin

Date Approved:
May 1982

Status:
Black Box Warning

Approved Uses:
Severe or Cystic Acne

Off Label Uses:
Mild or moderate acne

Serious Side Effects:
Depression
Suicide
Birth Defects
Inflammatory Bowel Disease
Crohn's Disease
Ulcerative Colitis

Related Topics
Soriatane
Crohn's Disease
IBD
Ulcerative Colitis

The Case Against Accutane:

Accutane (isotretinoin) has been linked to many serious injuries. If you have used Accutane and any of the following injuries you may be entitled to compensation.

Inflammatory Bowel Disease
Premature Closure of Growth Plates
Birth Defects
Ulcerative Colitis
Crohn's Disease
Inflammatory Bowel Syndrome
Rectal Bleeding
Abdominal Pain
Central Nervous System Injuries
Bone and Muscle Loss
Cardiovascular Injuries
Liver and Kidney Damage
Pancreatitis
Lupus
Hearing and Vision Damage

The Food & Drug Administration (FDA) approved Accutane in May 1982. Accutane is prescribed to combat severe acne. In 1998, the FDA advised doctors who prescribed Accutane to watch their patients for signs of depression. Afterward Hoffman-LaRoche, the maker of Accutane notified doctors that the drug "may cause depression, psychosis, and on rare occasions suicidal ideation, suicide attempts and suicide."

However, the knowledge of the potential danger associated with Accutane did not become widely known until a Congressman's son committed suicide. Rep. Bart Stupak says his 17-year-old son's suicide on May 14, 2000 may be linked to the popular acne medicine. Bart Stupak Jr., known as "B.J.," shot himself in the head with his father's gun. Stupak was popular in school, a football player, and killed himself after a prom-night party.

In assessing how many potential suicide cases could be linked to Accutane, Rep. Stupak stated, "We are up over 100 reports, that's just what is coming in to us, so I believe there are probably over a thousand cases," Stupak said. "The average time is 88 days from when you start taking it, and the effect is very sudden. You are doing strange things at 3 a.m. and you are dead at 7 a.m."

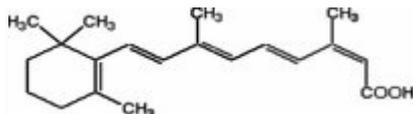
The FDA has received reports of 66 suicides and 1,373 cases of psychiatric problems among Accutane users as of early December 2000 according to a report in USA Today. Accutane's package warning first stated potential relationship between Accutane and depression in 1986. Although French officials required that Hoff-LaRoche add the risk of suicide to the package insert of the European version of Accutane in March 1997, the FDA did not require such a change in the USA until 1999.

If you or a loved one has been injured by Accutane, Parker & Waichman, LLP will evaluate your case for free. [Click here for a free case evaluation.](#)

Accutane

From Wikipedia, the free encyclopedia.

Chemical Composition



Isotretinoin chemical structure

Isotretinoin is a generic medication used for the treatment of very severe acne and most commonly known under the brands **Accutane** and **Roaccutane**. It is a retinoid, meaning it is derived from vitamin A and is found naturally in the body, produced by the liver in small quantities.

History

Prior to the development of isotretinoin, the mainstay treatment of severe acne was oral antibiotics such as the tetracyclines and erythromycin. While these drugs have proven efficacy, they worked against only one contributing factor of acne, *Propionibacterium acnes* bacteria. The antibiotics gradually became less effective over time as more resistant strains of the bacterium became prominent.

An early, effective treatment of acne was high doses of the fat soluble vitamin A. At these dose levels (sometimes 500,000 IU per day) effects such as reduced production of sebum and dry hair could be noticed. However the vitamin also had many other prominent side effects which inhibited its widespread use.

The development of the derivative of retinoic acid, isotretinoin (13-cis-retinoic acid), and its release in 1982 by Hoffmann-La Roche was a great step forward in the treatment of acne. The synthetic compound provided better therapeutic benefit than vitamin A, while also producing fewer side effects. In February 2002 Roche's patents for isotretinoin expired, there are now many other companies selling cheaper generic versions of the drug.

Today isotretinoin is usually prescribed after other acne treatments have failed to produce results. The treatment of acne usually begins with topicals, moves onto oral antibiotics (or a combination) and finally isotretinoin therapy. This is because other treatments, while less effective than isotretinoin, produce far fewer side effects.

Brand names

Isotretinoin is produced under many brand names by many manufacturers.

Some brands of isotretinoin include:

Accutane® and Roaccutane® by Roche

Accure® by Alphapharm

Oratane® by Douglas Pharmaceuticals

Isohexal® by Hexal Australia

Sotret® by Ranbaxy

Amnesteem® by Bertek

Claravis® by Barr

Ciscutan® by Pelpharma

Indications

Isotretinoin is indicated for treatment for a number of dermatological conditions, most commonly acne. It is generally not used as a first-line treatment due to the potential side effects. Antibiotics (such as the tetracyclines) are usually prescribed before isotretinoin.

Severe forms of acne (conglobata, fulminans and nodulocystic) as well as acne that scars can be successfully treated with isotretinoin.

Acne that has not responded to other treatment will usually respond to isotretinoin. Dismorphophobic patients may also be prescribed isotretinoin.

Pharmacodynamics

Isotretinoin noticeably reduces the production of sebum and shrinks the sebaceous glands. It stabilises keratinization and prevents comedones from forming. The exact mechanism of action is unknown, however it is known that it alters DNA transcription.

The dose of isotretinoin a patient receives is dependent on their weight and the severity of the condition. Generally it is prescribed from between 0.5 mg/kg/day to 2 mg/kg/day, for example a 70 kg (155 pounds) person would take from between 35 mg to 140 mg per day dependant on the severity of their condition.

It should also be noted that some studies have associated remission of the condition with

the total dose taken. It is generally advisable to take a dose of greater than 125 mg/kg over the entire treatment period to see maximum benefit.

Pharmacokinetics

Absorption

Isotretinoin, when administered orally, is best absorbed when taken after a high fat meal, as it has a high level of lipophilicity. In a crossover study, it was found that the peak plasma concentration more than doubled when taken after a high fat meal versus a fasted condition.

Distribution

Isotretinoin is primarily (99.9%) bound to plasma proteins, mostly albumin.

Metabolism

At least three metabolites have been detected in human plasma after oral administration of isotretinoin. These are 4-oxo-isotretinoin, retinoic acid and 4-oxo-retinoic acid. Isotretinoin also oxidises, irreversibly, to 4-oxo-isotretinoin.

Elimination

The metabolites of isotretinoin are excreted through both urine and feces. The mean elimination half life for isotretinoin is 21 hours, with a standard deviation from this mean of 8.2 hours.

Drug interactions

Vitamin A, in supplement form, should be strictly avoided while undertaking therapy with isotretinoin. It increases the risk of side effects associated with use.

Tetracycline antibiotics, also prescribed for acne, should also be avoided. A significant increase in the risk of pseudotumor cerebri is associated with concurrent use of these drugs.

According to some studies, vitamin E reduces the toxicity of high-dose retinoids without reducing drug efficacy. However, another study found that vitamin E does not reduce the side effects of isotretinoin.

Side effects

The most feared complication of isotretinoin is its teratogenicity, i.e., the ability to cause birth defects. Isotretinoin has many side effects, listed in the table on the right. The more severe side effects are listed here in more detail.

It is also worth noting that the following side effects can persist, even after discontinuing therapy:

- Alopecia (hair loss)
- Arthralgias
- Decreased night vision
- Degenerative disc disease
- Cartilage degeneration
- Bone disease

It should also be mentioned that isotretinoin users are not allowed to give blood for at least a month after discontinuing isotretinoin use.

Teratogenicity

Isotretinoin is a teratogen - it is highly likely that if taken during pregnancy that it will cause birth defects. In the USA, isotretinoin is in pregnancy category X. Isotretinoin must be prescribed under a policy that mandates that female patients be placed on two separate, effective forms of birth control [3]. Male patients should be informed of the risk associated with use during pregnancy, emphasising that they should not share the drug, especially with females.

In the U.S. more than 2,000 women have become pregnant while taking the drug between 1982 and 2003, with most pregnancies ending in abortion. About 160 babies with birth defects were born. Doctors normally require two separate methods of birth control for sexually active women taking isotretinoin and until one month after terminating the drug.

Depression

Several studies have emerged suggesting a possible link between isotretinoin and depression. It must however be acknowledged that its primary use is for the treatment of the most severe acne. The possibility that this severe acne is causing the depression is therefore not to be ruled out. Moreover, improvement of a patient's acne by successful treatment with isotretinoin can actually reduce symptoms of anxiety and depression. [7] Statistical evidence shows that the suicide rate among Accutane users is actually lower than average.

Emory University conducted a study of isotretinoin and depression. The study subjects were given psychological tests beforehand that showed no correlation between the severity of their acne and feelings of depression. A baseline PET scan of all the subjects was done. A second PET scan showed that individuals who had used the drug for four months showed decreased activity in the orbitofrontal cortex, a section of the brain thought to control mood and social interaction. Individuals in the control group who had not used the drug showed no

change. (Bremner *et al.* 2005)

The Journal of the American Medical Association (JAMA) Archives of Dermatology published a study in May of 2005, which appears to refute claims that Accutane can cause depression. In their conclusion the author's state, "The use of isotretinoin (Accutane) in the treatment of moderate-severe acne in adolescents did not increase symptoms of depression. On the contrary, treatment of acne either with conservative therapy or with isotretinoin was associated with a decrease in depressive symptoms."

Alleged cases of isotretinoin linked suicide

After Charles Bishop, a 15-year old student pilot, flew a light aircraft into a Tampa, Florida building on January 5, 2002, his family claimed Accutane had caused severe psychosis in the boy and filed a \$70 million lawsuit against Hoffman-La Roche. However, an autopsy found no traces of the drug in the boy's system.

Bart Stupak, a Michigan congressman, has alleged this connection ever since his son, B.J., an Accutane user, committed suicide hours after his junior prom in May 2000.

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