

SYSTEMIC MEDICATIONS
INTERNAL DRUGS FOR
MODERATE TO SEVERE PSORIASIS



**NATIONAL
PSORIASIS
FOUNDATION®**

Connect. Control. Cure.

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WHAT IS PSORIASIS?

Psoriasis is a noncontagious, lifelong skin disease that affects more than 4.5 million adults in the United States. The most common form, plaque [pronounced plak] psoriasis, appears as raised, red lesions covered with a silvery white buildup of dead skin cells, called scale.

About 10 percent to 30 percent of people with psoriasis also develop psoriatic [sore-ee-AA-tic] arthritis, which causes pain, stiffness and swelling in and around the joints. The hands, feet, wrists, ankles, knees and lower back are most often affected by this type of arthritis.



Three percent to 10 percent of the body affected by psoriasis is considered to be a moderate case. More than 10 percent is considered severe. The palm of the hand equals 1 percent of the skin. However, the severity of psoriasis is also measured by how psoriasis affects a person's quality of life. Psoriasis can have a serious impact even if it involves a small area, such as the palms of the hands or soles of the feet.

To learn more about the types of psoriasis or psoriatic arthritis, contact the National Psoriasis Foundation and request the following booklets:

- *Psoriatic Arthritis*
- *Specific Forms of Psoriasis*

Systemic medications are prescription medications that affect the entire body, and are usually reserved for patients with moderate to severe psoriasis who are not responsive to or eligible for conventional topical medications or ultraviolet (UV) light treatments.

For more information about psoriasis treatments, request the following National Psoriasis Foundation educational booklets:

- *Biologic Medications for Psoriasis & Psoriatic Arthritis*
- *Phototherapy: Light Treatment for Psoriasis*
- *Steroids*
- *Topical Treatments for Psoriasis*

BIOLOGICS

What are biologics?

Biologic medications are developed from living sources, such as cells, rather than combinations of chemicals like traditional drugs.

In January 2003, Amevive (also known by its generic name alefacept) became the first biologic medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of psoriasis. It is given by injection in a doctor's office once per week for 12 weeks.

In October 2003, Raptiva (also known by its generic name efalizumab) was approved by the FDA for the treatment of psoriasis. Patients give themselves an injection under the skin once per week.

Enbrel (also known by its generic name etanercept) became an FDA-approved biologic for the treatment of psoriasis in April 2004. Enbrel is also FDA-approved for treating psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis and ankylosing spondylitis.

Other biologics are now being developed for treating psoriasis and psoriatic arthritis.

Biologics are fairly new treatments for psoriasis and psoriatic arthritis. Their overall safety is still being evaluated; the long-term side effects are not fully known.

For more information, request the Psoriasis Foundation educational booklet *Biologic Medications for Psoriasis & Psoriatic Arthritis*.

CYCLOSPORINE

What is cyclosporine?

In 1995, Neoral (one brand name for cyclosporine) was FDA-approved to help prevent organ rejection in transplant patients. In 1997, the FDA approved Neoral as a treatment for psoriasis.

How does cyclosporine work?

Cyclosporine works by suppressing the immune system and preventing actions of certain immune cells. By preventing this immune activity, cyclosporine slows the growth of skin cells.

Who is a candidate for cyclosporine?

Adults with severe psoriasis and otherwise normal immune systems are candidates for cyclosporine.

Cyclosporine should only be used during pregnancy if the potential benefits outweigh the potential risks. For example, in the case of pustular psoriasis, which can be life threatening, cyclosporine may be the treatment of choice during pregnancy, compared to the pregnancy risks associated with treatments such as methotrexate or Soriatane.

In general, women are advised not to become pregnant while taking cyclosporine. Your doctor may recom-

mend that if you do become pregnant while taking cyclosporine, you should stop the treatment.

Others who should avoid taking cyclosporine include:

- Individuals whose immune systems are compromised (for example, anyone with lymphoma or HIV infection, or patients receiving other immune-suppressing drugs)
- Women who are breastfeeding*
- Individuals with abnormal kidney function
- Anyone with high blood pressure
- Patients with malignancies, or a history of malignancies (other than basal or squamous cell skin cancers)
- People who are undergoing radiation treatment

*To learn about treatment options for pregnant and nursing women, request the Psoriasis Foundation educational booklet *Conception, Pregnancy & Psoriasis*.

How effective is cyclosporine?

Cyclosporine can provide fairly rapid relief from symptoms. Patients may see some improvement in symptoms after two weeks of treatment, particularly if stronger doses are used. However, it may take longer, from three to four months, to reach a more complete level of control.

If rapid improvement is not essential, your doctor initially may keep the dosage low. If, after four weeks, improvement is not seen, dosage is gradually increased at one- or two-week intervals. Once the maximum recommended dosage (based on individual weight) for psoriasis treatment is reached, satisfactory improvement should be seen within six weeks. If it is not seen,

your doctor will most likely stop treatment with cyclosporine or add an additional treatment. For more severe psoriasis, including pustular or erythrodermic psoriasis, doctors often start with a high dose and gradually reduce it once patients have responded.

When cyclosporine treatment is stopped, psoriasis usually reappears between six and 16 weeks later.

Extended use of cyclosporine by transplant patients is well-established. However, long-term use as a treatment for psoriasis is more limited. Therefore, use of the drug is not currently recommended by the FDA for longer than one year. However, there are no specific guidelines for how long a patient should stay off cyclosporine before resuming treatment with the drug. Some doctors may prescribe the drug for more than one year.

Rotational therapy

Your doctor may recommend alternating cyclosporine with other forms of treatment in order to continue to manage psoriasis successfully.

Combination therapy

Donovex (also known by its generic name calcipotriene) used with low-dose cyclosporine has been shown to be safe and effective for the treatment of severe, chronic plaque psoriasis. The addition of Dovonex means a lower dosage of cyclosporine can be given, which minimizes the risk of potential side effects.

How is cyclosporine used?

Cyclosporine is taken daily by mouth and is available as either a capsule or a liquid. The liquid form must be diluted for use, preferably by mixing it with room-temperature orange or apple juice (not grapefruit juice; see “Interactions” on page 7). Patients should take cyclosporine on a consistent schedule.

Your doctor will monitor your kidney function with blood tests before and during treatment with cyclosporine.

What are the possible side effects of cyclosporine?

Taking cyclosporine can cause the following potential side effects:

- Decreased kidney function
- Headache
- High blood pressure
- High cholesterol
- Excessive hair growth
- Tingling or burning sensations in the arms or legs
- Skin sensitivity
- Increased growth of gum tissues
- Flu-like symptoms
- Upset stomach
- Tiredness
- Musculoskeletal or joint pain

Generally, these side effects go away when the dose is lowered or the drug is stopped.

A risk of long-term cyclosporine treatment is kidney damage/toxicity. In some cases, the damage to the kidneys can be irreversible.

People taking cyclosporine can have an increased risk of developing skin malignancies, particularly if they previously have been treated with PUVA (the use of the light-sensitizing drug psoralen plus ultraviolet light A).

Interactions

The doctor prescribing cyclosporine should always

be aware of any other medications, treatments or supplements you are using. Many medications interact with cyclosporine, including (but not limited to) some antibiotics, anti-inflammatories, antifungals, gastrointestinal agents, calcium channel blockers and anticonvulsants. Over-the-counter (OTC) medications such as aspirin and ibuprofen can also interact with cyclosporine. These interactions could affect the metabolism of the drug, causing you to have either too much or too little in your bloodstream.

Published reports have shown that St. John's wort, a popular herbal product used for treating depression, can reduce the blood levels of cyclosporine in transplant patients. It is not clear if the dose of cyclosporine used in psoriasis would be affected by St. John's wort. Still, psoriasis patients using cyclosporine should be cautious, because the herbal product could cause the drug to become less effective.

Grapefruit and grapefruit juice should be avoided when taking cyclosporine because they have been shown to increase levels of the drug in the blood.

METHOTREXATE

What is methotrexate?

Initially used to treat cancer, methotrexate was discovered to be effective in clearing psoriasis in the 1950s and was eventually approved for this use by the FDA in the 1970s. It is usually sold as a generic.

How does methotrexate work?

Methotrexate binds to and inhibits an enzyme involved in the rapid growth of cells. In people with psoriasis, the drug slows down the rate of skin-cell growth.

Who is a candidate for methotrexate?

Methotrexate is indicated for use in adults with severe psoriasis. Methotrexate is often prescribed for severe plaque psoriasis, erythrodermic psoriasis and acute pustular psoriasis. In addition, the drug can be used to treat psoriatic arthritis, a psoriasis-related condition similar to rheumatoid arthritis. Methotrexate can be highly effective in reducing the painful symptoms of psoriatic arthritis. For more information, request the Psoriasis Foundation educational booklet *Psoriatic Arthritis*.

The use of methotrexate is not recommended for people with the following medical conditions or histories:

- Pregnancy—pregnant women, or women and their partners who are trying to conceive a child (conception should be avoided during methotrexate treatment and for at least 12 weeks afterward)*
- Blood disorders
- Active peptic ulcers
- Severe anemia
- Cirrhosis of the liver
- Active hepatitis
- Significant liver or kidney abnormalities
- Active infectious disease
- Excessive alcohol consumption**
- Unreliability in taking medications correctly

*To learn about other treatment options for pregnant and nursing women, request the Psoriasis Foundation educational booklet *Conception, Pregnancy & Psoriasis*.

**It is recommended that any patient with moderate to severe psoriasis avoid alcohol consumption in order to be eligible for treatment with methotrexate in the future.

How effective is methotrexate?

In most psoriasis patients, improvement can begin within four to six weeks of using methotrexate. More than 80 percent of patients see some improvement within two or three months of starting treatment with methotrexate.

How is methotrexate used?

Methotrexate is taken once a week, either by mouth or by injection. It is most commonly taken orally, either in pill or liquid form. The liquid form may be mixed with fruit juice. The drug can be taken in single or divided doses, split up over a period of 24 hours. For example, a person can take a portion Saturday morning, a portion Saturday evening and the remainder Sunday morning.

A test dose of methotrexate is given first to see if the patient tolerates the drug. If the patient tolerates methotrexate, the dosage is increased to achieve clearance. Once clearance is achieved, the dose is gradually reduced to the lowest level capable of maintaining a reasonable improvement. If doing well, a person may be taken off methotrexate until symptoms return. However, some people must continue to take a maintenance dose to sustain clearance.

Patients taking methotrexate need to have regular blood tests to ensure that the drug is being safely processed by the body and is not negatively affecting the liver, blood or bone marrow. Methotrexate can cause a reduced white blood cell count, which can make a person more at risk for infection.

Normally, a doctor will not increase the dose of methotrexate if a few stubborn lesions remain. Instead, another treatment such as ultraviolet light B (UVB), laser treatment, topical steroids, Dovonex, Tazorac (also known by its generic name tazarotene) or anthralin may be added to clear the remaining lesions.

Rotational therapy

Methotrexate is sometimes rotated with other treatments such as PUVA, Soriatane (also known by its generic name acitretin) or cyclosporine in order to decrease side effects or get better results.

Combination therapy

Methotrexate can be used with PUVA or UVB to reduce the amount of UV light needed to clear the skin. In unresponsive cases of generalized pustular psoriasis, methotrexate has been used with either Soriatane or cyclosporine. It has also been used with some biologics to decrease the side effects of each medication or get better results.

What are the possible side effects of methotrexate?

Taking methotrexate can cause the following potential side effects:

- Nausea*
- Tiredness
- Difficulty sleeping
- Lightheadedness
- Mouth ulcers**
- Vomiting
- Headache
- Easy bruising and bleeding

- Fever
- Diarrhea with blood in the stool
- Chills

*Sometimes nausea can be helped by drinking milk or eating before taking the medication. Severe nausea may mean the dose is too high. Studies have shown that taking folic acid in doses of 1 to 5 milligrams (mg) per day can reduce nausea and other side effects associated with methotrexate. However, other studies have shown that folic acid may reduce methotrexate's effectiveness. Folic acid should not be taken on the same days that methotrexate is used. Check with your doctor.

**If sores appear in the mouth, the dose may be too high.

These side effects are generally manageable with careful monitoring and patient education.

The main risk of long-term methotrexate treatment is the potential for liver damage. A small percentage of patients, generally estimated to be one out of 200, will develop reversible liver scarring. This means after methotrexate is discontinued, the liver will return to normal. This is a risk after a cumulative dose of 1.5 grams (g). How long it takes to reach 1.5 g depends on the patient's dose, treatment schedule and rest periods from the drug. For example, a patient taking 15 mg per week will reach an accumulated dose of 1.5 g after approximately two years (1 g equals 1,000 mg).

When a patient reaches a cumulative dose of 1 g to 1.5 g, doctors may perform a liver biopsy to test for liver damage. In this procedure, a thin needle is in-

serted through the skin to extract a small sample of liver tissue. If significant liver damage has developed, methotrexate is usually discontinued. A large-scale European study suggested that liver damage caused by methotrexate frequently improves once the drug is discontinued. Liver biopsies will be repeated on regular intervals.

The above scenario is based on patients who do not have any other risk factors for liver disease. The risk of liver damage can increase if a patient has one or more of the following risk factors:

- Drinks alcohol
- Has abnormal kidney function
- Has diabetes
- Has had prior liver disease

Rarely, some side effects may not occur until years after the drug is used, including certain types of cancer, such as lymphoma and bone marrow toxicity.

Interactions

The doctor prescribing methotrexate should always be aware of any other medications, therapies or supplements you are using.

Methotrexate may increase sensitivity to light. This reaction can occur even when methotrexate is taken several days after exposure to ultraviolet light, causing a "sunburn recall."

Patients should not take medications for inflammation or pain (including aspirin and ibuprofen) without checking with their doctor first. These medications

may increase the effects of methotrexate, which could be harmful.

Patients must not drink alcohol; alcohol increases the chance of liver damage with methotrexate.

Sulfa drugs, especially Septra or Bactrim, also should not be taken while on methotrexate. The drug interaction of the sulfa drugs and methotrexate could be fatal.

SORIATANE

What is Soriatane?

Soriatane is an oral retinoid, which is a synthetic form of vitamin A. Synthetic retinoids were introduced as experimental drugs in the mid-1970s and were approved in the United States in the 1980s. Soriatane is currently the only oral retinoid approved by the FDA specifically for treating psoriasis. Accutane is another oral retinoid that is sometimes used as an alternative to Soriatane in treating psoriasis (see page 17 for more information about this treatment).

How does Soriatane work?

The precise mechanism of how Soriatane works to control psoriasis is unknown. In general, retinoids affect how cells regulate their behavior. Retinoids help control how cells multiply, including how fast skin cells will grow and shed from the skin's surface.

Who is a candidate for Soriatane?

Soriatane is indicated for use in adults with severe psoriasis. The Soriatane label supports the use of the drug for plaque, guttate, pustular, erythrodermic and palmoplantar psoriasis.

Because of the risk of birth defects (see the side effects section on page 16 to learn more), women of childbearing potential must have two negative

pregnancy tests before starting Soriatane treatment. They must use two effective forms of birth control while on the drug and for three years after stopping treatment.

People who take Soriatane should not donate blood during treatment and for a period of time afterward. Donated blood could expose pregnant women to Soriatane.

For more information, request the Psoriasis Foundation educational booklet *Conception, Pregnancy & Psoriasis*.

How effective is Soriatane?

Soriatane tends to work slowly for plaque psoriasis. After eight to 16 weeks of treatment, the skin lesions usually will improve, but it may take up to six months for the drug to reach its peak effect.

How is Soriatane used?

Soriatane comes in 10 mg and 25 mg capsules. The prescribed dose is taken once a day, and pills should be taken with food. The dosage is determined for each individual based on several factors, including the type of psoriasis present. For example, a person with erythrodermic psoriasis may respond to a lower dose than someone who has plaque psoriasis.

Doses may be reduced after symptoms begin to improve, depending on the patient's response. Ordinarily, retinoid treatment is stopped when lesions have cleared significantly. When lesions or other symptoms reappear, the drug may be administered again.

Rotational therapy

Soriatane may also be prescribed in rotation with other systemic medications, such as cyclosporine or methotrexate.

Combination therapy

Soriatane is most effective for treating psoriasis when it is used with phototherapy, rather than by itself. Combination therapy can speed clearing and help reduce the amount of phototherapy needed to clear symptoms, thereby reducing risks and side effects.

A 2002 clinical trial demonstrated that Dovonex ointment in combination with Soriatane was safe and effective for the treatment of severe or extensive psoriasis.

What are the possible side effects of Soriatane?

The most serious side effect of Soriatane is the risk of birth defects in developing fetuses if the mother is using the drug.

Other common side effects include:

- Hair loss
- Chapped lips
- Dry skin
- Bleeding gums
- Peeling fingertips
- Changes in blood fat levels
- Depression
- Headache
- Joint pain

These side effects, and others, seem to be dose-dependent (they go away after stopping the medication or lowering the dosage).

Interactions

The doctor prescribing Soriatane should always be

aware of any other medications, therapies or supplements you are using.

Women who use Soriatane must not drink alcohol during treatment and for two months after treatment is discontinued. Alcohol can cause Soriatane to convert to a form that may remain in the body indefinitely, increasing the risk of birth defects if the woman were to become pregnant.

OTHER SYSTEMIC MEDICATIONS

The following systemic medications are not approved by the FDA for the treatment of psoriasis. Some doctors are prescribing them “off-label” for psoriasis—a common and accepted medical practice.

Accutane

Accutane (also known by its generic name isotretinoin) is an oral retinoid that was approved as a treatment for severe cystic acne; however, some doctors have used it successfully to treat severe psoriasis. Generally, it is not as effective as Soriatane for psoriasis.

Accutane has many side effects similar to Soriatane. The most common side effects are eye and lip dryness, and nosebleeds. Bone spurs and hair loss occur to a lesser degree.

Accutane is cleared from the body much faster than Soriatane, and some doctors consider it a safer choice for young women of childbearing potential. However, it also has the potential for severe birth defects if a woman becomes pregnant while the drug is still in her system. A woman on Accutane should use reliable birth control one month before treatment, during treatment and for at least one month afterward.

Hydrea

Hydrea (also known by its generic name hydroxyurea)

is an oral cancer medication that in the 1960s was found to be effective for psoriasis. Although not as effective as methotrexate, it is less likely to cause liver damage with long-term use. It can produce significant improvement in stable plaque psoriasis, but it also has potentially dangerous side effects, including bone marrow toxicity. Long-term use has been associated with skin cancer.

Mycophenolate mofetil

Mycophenolate mofetil has been used for the prevention of organ transplant rejection, as well as in the treatment of several inflammatory or autoimmune skin diseases. It can be used in combination with cyclosporine, and some doctors use it when tapering patients off of cyclosporine. Because it is an immunosuppressive agent, people with compromised immune systems should not take it.

Sulfasalazine

Sulfasalazine is an oral medication reported to be effective for some people with psoriasis and psoriatic arthritis. It is significantly less effective than methotrexate. However, sulfasalazine tends to have less dangerous side effects. Therefore, trying this medication may be worthwhile for some. Many people cannot tolerate sulfasalazine because of allergy to sulfa, or side effects, including nausea, vomiting and loss of appetite.

6-Thioguanine

6-Thioguanine is an oral medication approved for treating certain types of leukemia. It has been reported to be effective for psoriasis in some cases, including treatment of pustular psoriasis. However, 6-Thioguanine must be used under close medical supervision due to the potential side effects associated with suppression of the bone marrow.

STAY INFORMED AND INVOLVED. TAKE ACTION.

The National Psoriasis Foundation is committed to improving the lives of people with psoriasis and psoriatic arthritis. Join the Psoriasis Foundation to make a difference in the lives of millions of people with these diseases. Donate today!

Call **800.723.9166**

Visit **www.psoriasis.org**

E-mail **getinfo@psoriasis.org**

The following educational materials are available from the National Psoriasis Foundation:

- Alternative Approaches
- Biologic Medications for Psoriasis & Psoriatic Arthritis
- Conception, Pregnancy & Psoriasis
- Genital Psoriasis
- Phototherapy: Light Treatment for Psoriasis
- Psoriasis: How It Makes You Feel
- Psoriasis Research: Progress & Promise
- Psoriasis on Specific Skin Sites
- Psoriatic Arthritis
- Scalp Psoriasis
- Specific Forms of Psoriasis
- Steroids
- Sun & Water Therapy
- Systemic Medications: Internal Drugs for Moderate to Severe Psoriasis
- Topical Treatments for Psoriasis
- You & Your Doctor: Things to Consider
- Your Diet & Psoriasis

More updated information may be available at
www.psoriasis.org

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MISSION STATEMENT

Our mission is to improve the quality of life of people who have psoriasis and psoriatic arthritis. Through education and advocacy, we promote awareness and understanding, ensure access to treatment, and support research that will lead to effective management and, ultimately, a cure.

The National Psoriasis Foundation, a charitable 501(c)(3) organization, depends on your tax-deductible donations to support more than 5 million people affected by psoriasis and/or psoriatic arthritis. The Psoriasis Foundation is governed by a volunteer Board of Trustees and is advised on medical issues by a volunteer Medical Board. For more information, or to obtain a copy of the Foundation's Annual Report, call 800.723.9166.

National Psoriasis Foundation educational materials are reviewed by members of our Medical Board and are not intended to replace the counsel of a physician. The Psoriasis Foundation does not endorse any medications, products or treatments for psoriasis or psoriatic arthritis and advises you to consult a physician before initiating any treatment.

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