



Brief Summary—Consult package insert for full prescribing information.

DESCRIPTION

Aldara™ is the brand name for imiquimod which is an immune response modifier. Each gram of the 5% cream contains 50 mg of imiquimod in an off-white oil-in-water vanishing cream base consisting of isostearic acid, cetyl alcohol, stearyl alcohol, white petrolatum, polysorbate 60, sorbitan monooleate, glycerin, xanthan gum, purified water, benzyl alcohol, methylparaben, and propylparaben.

INDICATIONS AND USAGE

Aldara 5% cream is indicated for the treatment of external genital and perianal warts (condyloma acuminata) in individuals 12 years old and above.

CONTRAINDICATIONS

None known

WARNINGS

Aldara cream has not been evaluated for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma virus (HPV) disease and is not recommended for these conditions.

PRECAUTIONS

General

Local skin reactions such as erythema, erosion, excoriation/flaking, and edema are common. Should severe local skin reaction occur, the cream should be removed by washing the treatment area with mild soap and water. Treatment with Aldara cream can be resumed after the skin reaction has subsided. There is no clinical experience with Aldara cream therapy immediately following the treatment of genital/perianal warts with other cutaneously applied drugs; therefore, Aldara cream administration is not recommended until genital/perianal tissue is healed from any previous drug or surgical treatment. Aldara has the potential to exacerbate inflammatory conditions of the skin.

Information for Patients

Patients using Aldara 5% cream should receive the following information and instructions: The effect of Aldara 5% cream on the transmission of genital/perianal warts is unknown. Aldara 5% cream may weaken condoms and vaginal diaphragms. Therefore, concurrent use is not recommended.

1. This medication is to be used as directed by a physician. It is for external use only. Eye contact should be avoided.
2. The treatment area should not be bandaged or otherwise covered or wrapped as to be occlusive.
3. Sexual (genital, anal, oral) contact should be avoided while the cream is on the skin.
4. It is recommended that 6-10 hours following Aldara 5% cream application the treatment area be washed with mild soap and water.
5. It is common for patients to experience local skin reactions such as erythema, erosion, excoriation/flaking, and edema at the site of application or surrounding areas. Most skin reactions are mild to moderate. Severe skin reactions can occur and should be reported promptly to the prescribing physician.
6. Application of Aldara cream in the vagina is considered internal and should be avoided. Female patients should take special care in applying the cream at the opening of the vagina because local skin reactions on the delicate moist surfaces can result in pain or swelling, and may cause difficulty in passing urine.
7. Some reports have been received of localized hyperpigmentation and hyperpigmentation following Aldara use. Follow-up information suggests that these skin color changes may be permanent in some patients.
8. Uncircumcised males treating warts under the foreskin should retract the foreskin and clean the area daily.
9. Patients should be aware that new warts may develop during therapy, as Aldara is not a cure.

Carcinogenicity, Mutagenesis, and Impairment of Fertility

Rodent carcinogenicity data are not available. Imiquimod was without effect in a series of eight different mutagenicity assays including Ames, mouse lymphoma, CHO chromosome aberration, human lymphocyte chromosome aberration, SHE cell transformation, rat and hamster bone marrow cytogenetics, and mouse dominant lethal test. Daily oral administration of imiquimod to rats, at doses up to 8 times the recommended human dose on a mg/m² basis throughout mating, gestation, parturition and lactation, demonstrated no impairment of reproduction.

Pregnancy

Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. Imiquimod was not found to be teratogenic in rat or rabbit teratology studies. In rats at a high maternally toxic dose (28 times human dose on a mg/m² basis), reduced pup weights and delayed ossification were observed. In developmental studies with offspring of pregnant rats treated with imiquimod (8 times human dose), no adverse effects were demonstrated.

Nursing Mothers

It is not known whether topically applied imiquimod is excreted in breast milk.

Pediatric Use

Safety and efficacy in patients below the age of 12 years have not been established.

ADVERSE REACTIONS

In controlled clinical trials, the most frequently reported adverse reactions were those of local skin and application site reactions; some patients also reported systemic reactions. These reactions were usually mild to moderate in intensity; however, severe reactions were reported with 3X/week application. These reactions were more frequent and more intense with daily application than with 3X/week application. Overall, in the 3X/week application clinical studies, 1.2% (4/327) of the patients discontinued due to local skin/application site reactions. The incidence and severity of local skin reactions during controlled clinical trials are shown in the following table.

**3X/WEEK APPLICATION
WART SITE REACTION AS ASSESSED BY INVESTIGATOR**

	MILD/MODERATE				SEVERE			
	FEMALES		MALES		FEMALES		MALES	
	5% Imiquimod N=114	Vehicle N=99	5% Imiquimod N=157	Vehicle N=157	5% Imiquimod N=114	Vehicle N=99	5% Imiquimod N=157	Vehicle N=157
Erythema	61%	21%	54%	22%	4%	0%	4%	0%
Erosion	30%	8%	29%	6%	1%	0%	1%	0%
Excoriation/Flaking	18%	8%	25%	8%	0%	0%	1%	0%
Edema	17%	5%	12%	1%	1%	0%	0%	0%
Induration	1%	0%	2%	0%	3%	0%	0%	0%
Ulceration	5%	1%	4%	1%	3%	0%	0%	0%
Scabbing	4%	0%	13%	3%	0%	0%	0%	0%
Vesicles	3%	0%	2%	0%	0%	0%	0%	0%

Remote site skin reactions were also reported in female and male patients treated 3X/week with imiquimod 5% cream. The severe remote site skin reactions reported for females were erythema (3%), ulceration (2%), and edema (1%); and for males, erosion (2%), and erythema, edema, induration, and excoriation/flaking (each 1%).

Adverse events judged to be probably or possibly related to Aldara reported by more than 5% of patients are listed below; also included are soreness, influenza-like symptoms and myalgia.

**3X/WEEK APPLICATION
FEMALES MALES**

	5% Imiquimod (n=117)	Vehicle (n=103)	5% Imiquimod (n=156)	Vehicle (n=158)
APPLICATION SITE DISORDERS:				
APPLICATION SITE REACTIONS				
Wart Site:				
Itching	32%	20%	22%	10%
Burning	26%	12%	9%	3%
Pain	8%	2%	2%	1%
Soreness	3%	0%	0%	1%
FUNGAL INFECTION*	11%	3%	2%	1%
SYSTEMIC REACTIONS:				
Headache	4%	3%	5%	2%
Influenza-like symptoms	3%	2%	1%	0%
Myalgia	1%	0%	1%	1%

*Incidence reported without regard to causality with Aldara.

Adverse events judged to be possibly or probably related to Aldara and reported by more than 1% of patients include: **Application Site Disorders:** Wart Site Reactions (burning, hyperpigmentation, irritation, itching, pain, rash, sensitivity, soreness, stinging, tenderness); **Remote Site Reactions** (bleeding, burning, itching, pain, tenderness, tinea cruris); **Body as a Whole:** fatigue, fever, influenza-like symptoms; **Central and Peripheral Nervous System Disorders:** headache; **Gastro-Intestinal System Disorders:** diarrhea; **Musculo-Skeletal System Disorders:** myalgia.

OVERDOSAGE

Overdosage of Aldara 5% cream in humans is unlikely due to minimal percutaneous absorption. Animal studies reveal a rabbit dermal lethal imiquimod dose of greater than 1600 mg/m². Persistent topical overdosing of Aldara 5% cream could result in severe local skin reactions. The most clinically serious adverse event reported following multiple oral imiquimod doses of >20 mg was hypotension which resolved following oral or intravenous fluid administration.

DOSE AND ADMINISTRATION

Aldara cream is to be applied 3 times per week, prior to normal sleeping hours, and left on the skin for 6-10 hours. Following the treatment period cream should be removed by washing the treated area with mild soap and water. Examples of 3 times per week application schedules are: Monday, Wednesday, Friday; or Tuesday, Thursday, Saturday application prior to sleeping hours. Aldara treatment should continue until there is total clearance of the genital/perianal warts or for a maximum of 16 weeks. Local skin reactions (erythema) at the treatment site are common. A rest period of several days may be taken if required by the patient's discomfort or severity of the local skin reaction. Treatment may resume once the reaction subsides. Non-occlusive dressings such as cotton gauze or cotton underwear may be used in the management of skin reactions. The technique for proper dose administration should be demonstrated by the prescriber to maximize the benefit of Aldara therapy. Handwashing before and after cream application is recommended. Aldara 5% cream is packaged in single-use packets which contain sufficient cream to cover a wart area of up to 20 cm²; use of excessive amounts of cream should be avoided. Patients should be instructed to apply Aldara cream to external genital/perianal warts. A thin layer is applied to the wart area and rubbed in until the cream is no longer visible. The application site is not to be occluded.

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Disability Insurance: what you need to know before you buy

By Lawrence B. Keller, CLU, ChFC, RHU

You may have heard that the disability insurance policies available today are dramatically different from those available a few years ago. Although this may be true — especially for physicians who perform invasive procedures — quality coverage can still be found. It is important to understand how policies are offered and to know what provisions should be included in an individual disability policy.

Disability insurance can be purchased on an individual or group basis. Group insurance is usually provided by an employer or purchased individually from a sponsoring medical association, such as through the American Academy of Dermatology Group Insurance Plans, offered through JLT Services Corporation.

Although initially low in cost, group policies do have limitations. They can be canceled (by the association or insurance company), rates increase as you get older, and premiums are subject to adjustments based on the claims experience of the group. In addition, group and association contracts may contain restrictive definitions of disability as well as less-generous contract provisions.

Most insurance companies will issue disability insurance coverage equal to approximately 60 percent of earned income; however, interns, residents, fellows and physicians just entering practice are provided with "special limits." These special limits permit them to purchase benefits in excess of what their current earnings would normally allow.

COSTS

Premium rates are based on several factors including age, gender, monthly benefit amount, riders added to the policy and the occupational classification the insurance company assigns to your medical specialty. The younger you are when the purchase is made, the lower the cost of the insurance. Therefore, you should purchase a policy as early in your career as possible to lock in lower premium rates.

Although women are considered better risks for life insurance coverage, this is not the case with disability insurance. Rates for females are substantially higher and their policies can cost 50 to 75 percent more than men. The occupational classification assigned by the insurance company, to your medical specialty, will significantly impact the premium rates as well as the policy provisions offered to you. Generally, if you perform invasive procedures, you will be placed in the "surgical" category; where the definition of disability may be more restrictive and the premiums charged will be higher as compared to those of a non-invasive, non-surgical physician. Each insurance company has their own occupational classification guide and insurance companies may treat the same medical specialty differently.

Although it is an invasive specialty, dermatology is unique in that some companies do not place dermatologists in the "surgical" category. As a result, the definition of disability available is more liberal and the premium rates are lower than if had you been classified as a surgeon.

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WHAT TO LOOK FOR

The renewability provision is one of the key features of an individual disability income insurance policy. This provision defines your rights when it comes to keeping your disability policy in force. If you purchase a policy that is *non-cancellable* and *guaranteed renewable*, you can remain in control of your financial security. The insurance company cannot cancel, increase your premiums, change any provisions or add restrictions to the policy — even if the issuing company no longer offers similar policies in the future.

DEFINITION OF TOTAL DISABILITY

Arguably, the definition of disability is the most important aspect of a disability policy. As a physician, you must pay careful attention to the definition of disability found in your policy as it will ultimately determine how any claim you make for benefits will be judged. There are three definitions of "disability" commonly found in the insurance industry, and each has significant differences.

Although difficult to find, **own-occupation** (also known as true or pure own-occupation) is usually the definition of choice for dermatologists as it is the most liberal definition of total disability available. This type of policy pays benefits if you are disabled and "not able to perform the material and substantial duties of your occupation." Therefore, you would collect full disability benefits if you could no longer practice dermatology and/or perform dermatologic surgery, even if you decided to work in another occupation or medical specialty, earning the same or more income than you did as a dermatologist.

More common is **modified own-occupation**. This type of disability policy has become the most prevalent in the industry today and typically pays benefits if you are "unable to perform the substantial and material duties of your occupation *and you are not working*." Although benefits are still contingent upon your ability to practice dermatology and/or perform dermatologic surgery, this definition will not allow you to continue receiving full disability benefits if you are working in another occupation or medical specialty.

The **any occupation** definition — the third and most restrictive of the three described here — is commonly found in group or association policies. Under this definition, you are eligible to receive benefits only if you are found to be "unable to work in any occupation which you are reasonably suited to by your education, training or experience." Unfortunately, it is the insurance company that makes this determination and physicians, being as educated and well-trained as they are, will find it extremely difficult to collect benefits on this type of policy. You should take every precaution to avoid purchasing a policy that contains this definition.

Many policies offered to physicians today might incorporate an own-occupation with a modified own-occupation" definition. Here, the policy would contain a true "Own-Occupation" definition for a limited time period (typically one, two or five years), and then convert to the more restrictive modified own-occupation definition described above. Until recently, in certain states such as California and Florida, and for certain medical specialties, this often was the best definition of disability made available.

OPTIONAL RIDERS

Unless your policy contains a residual disability rider, you may have to be totally disabled to collect any benefits. While an own-occupation policy protects your ability to practice dermatology and/or perform dermatologic surgery, it may not sufficiently protect your income level. There are many disabilities that might allow you to continue working in your occupation, on a limited basis, while suffering a loss of income. Adding a residual disability rider to your policy would allow you to continue receiving benefits, proportionate to your loss of income, if you returned to dermatology on a part-time basis.

Furthermore, with policies such as Modified "Own-Occupation" or "Any Occupation, this rider might allow you to continue receiving benefits if you decided to work in another occupation, or if the insurance company determined that you could work in another "reasonable" occupation with reduced earnings.

A Cost of Living Adjustment (COLA) Rider is designed to help your benefits

keep pace with inflation after your disability has lasted for 12 months. This adjustment can be a flat percentage or tied to the Consumer Price Index. Ideally, you want a COLA that is adjusted annually on a compound interest basis with no "cap" on the monthly benefit. Although important, if cutting the cost of coverage is an issue, this might be the first optional rider to consider excluding from your policy.

A **future purchase option rider** is a must for young physicians. It provides you with the ability to increase your disability coverage, regardless of your future health, as your income rises. It is important to know when you can increase your coverage, as well as by what increments, on any given option date. Some companies may allow you to use your entire option in one year as long as your then current income warrants the increase; Others, however, may limit the amount that you can purchase.

Policies vary greatly in terms of the definition of disability made available, the contract provisions offered and the premiums charged. It is more important than ever that you take the time to compare each of the policies you are considering, and understand how and why they differ. The best approach is to employ the services of a professional insurance agent who specializes in working with physicians. He or she will not only be familiar with your occupation, but with which companies' policies are best suited to your particular specialty. Then you and the agent can decide which insurance company's policy best meets your individual insurance needs. **RR**

Lawrence B. Keller, CLU, ChFC, RHU is the founder of Physician Financial Services, an independent New York City-based firm, specializing in insurance, investments, and financial services for physicians. He can be reached for questions or comments toll-free at (866) 442-6262 x166, locally at (212) 867-9080 x166, or by e-mail to lkeller@sfnonline.com.

JLT Services Corporation, AAD Group Insurance Plans, may be reached at (888) 747-6866, or visit www.aad-insurance.com.