**Practice Trends** 



# MANAGING YOUR DERMATOLOGY PRACTICE

# Is Your Overhead Too Low?

get a lot of questions and complaints from physiabout cians overhead. How should I define it? How do I calculate

it? And, of course, how do I lower it? Many physicians are surprised when I tell them that lowering their overhead isn't necessarily a good thing. In fact, it may be too low already.

Numerous studies have shown that practices with higher overhead generally produce higher net incomes for their physicians. The money has to be judiciously spent, of course, but keeping overhead costs too low can be counterproductive.

Too much cutting of operating expenses may be costing you revenue. Insufficient office space or too few staff may be crimping the office's efficiency and reducing the number of patients that can be seen.

Overhead is generally defined as the expense of maintaining your practice, not including depreciation, and is usually calculated first as an absolute number, then as total expenses as a percentage of total gross income. The percentage figure can be misleading, however.

If you're trying to decide whether your

overhead is too high or too low, you'll need an itemized breakdown. That will require some "billable hours" from your accountant, but those hours will pay for themselves many times over because the itemization will allow you to see where you could be spending less and where you could be spending more.

It's important to understand that overhead is not always the enemy. It is an easy target because everyone can focus on it-

#### ALDARA®

[al dar' a] Cream, 5% (imiquimod)

**Brief Summary of Prescribing Information** See Package Insert for Full Prescribing Information

To report SUSPECTED ADVERSE REACTIONS, contact Graceway Pharmaceuticals, LLC at 1-800-328-0255 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

#### 1 INDICATIONS AND USAGE

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1.1 Actinic Keratosis Aldara Cream is indicated for the topical treatment of clinically typical, nonhyperkreatotic, nonhyperkrephic actinic keratoses on the face or scalp in immunocompetent adults.

1.2 Superficial Basal Cell Carcinoma Aldara Cream is indicated for the topical treatment of biopsy-confirmed, primary superficial basal cell carcinoma (SBCD) in immunocompetent adults, with a maximum tumor diameter of 2.0 cm, located on the trunk (excluding anogenital skin), neck, or extremities (excluding hands and feet), only when surgical methods are medically less appropriate and patient follow-up can be reasonably assured. The histological diagnosis of superficial basal cell carcinoma should be established prior to treatment, since safety and efficacy of Aldara Cream have not been established for other types of basal cell carcinomas, including nodular and morpheaform (fibrosing or sclerosing) types. 1.3 External Genital Warts Aldara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older. 1.4 Limitations of Use Aldara Cream has been evaluated in children ages 2 to 12 years with molliuscum contagiosum and these studies falled to demonstrate efficacy. Jese Use in Specific Populations (8.4)]. 1.5 Unevaluated Populations The safety and efficacy of Aldara Cream in inmunosuppressed patients have not been established. Aldara Cream should be used with caution in patients with pre-existing autoimmune conditions. The efficacy and safety of Aldara Cream have not been established. patients with pre-existing autoimmune conditions. The efficacy and safety of Aldara Cream have not been established for patients with Basal Cell Nevus Syndrome or Xeroderma Pigmentosum.

#### 4 CONTRAINDICATIONS

#### **5 WARNINGS AND PRECAUTIONS**

5 WARNINGS AND PRECAUTIONS
5.1 Local Inflammatory Reactions intense local inflammatory reactions including skin weeping or erosion can occur after few applications of Aldara Cream and may require an interruption of dosing. [see Dosage and Administration (2) and Adverse Reactions (6)]. Aldara Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease. Administration of Aldara Cream is not recommended until the skin is completely healed from any previous drug or surgical treatment. 5.2 Systemic Reactions Flu-like signs and symptoms may accompany, or even precede, local inflammatory reactions and may include malaise, fever, nausea, myalgias and digros. An interruption of dosing should be considered. [see Adverse Reactions (6)] 5.3 Ultraviolet Light Exposure Exposure to sunlight (including sunlamps) should be avoided or minimized during use of Aldara Cream because of concern for heightened sunburn susceptibility. Patients should be warned to use protective clothing (e.g., a hat) when using Aldara Cream. Patients with sunburn should be advised not to use Aldara Cream until fully recovered. Patients who may have considerable sun exposure, e.g., due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using Aldara Cream. thins patients with inherent sensitivity to sunlight should exercise caution when using Aldara Cream. Aldara Cream shortened the time to skin tumor formation in an animal photoco-carcinogenicity study [see Nonclinical Toxicology (13.1)]. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure. 5.4 Unevaluated Uses: Actinic Keratosis Safety and efficacy have not been established for Aldara Cream in the treatment of actinic keratosis with repeated use, i.e., more than one treatment course in the same area. The safety of Aldara Cream applied to areas of skin greater than 25 cm² (e.g., 5 cm x5 cm) for the treatment of actinic keratosis has not been established fose Olinical Pharmacology (12.3)] 5.5 Unevaluated Uses: Superficial Basal Cell Carcinoma The safety and efficacy of Aldara Cream have not been established for other types of basal cell carcinomas (BCC), including nodular and morpheaform (fibrosing or sclerosing) types. Aldara Cream is not recommended for treatment of BCC subtypes other than the superficial variant (i.e., sBCC). Patients with SBCC treated with Aldara Cream should have regular follow-up of the treatment site. [see Clinical Studies (14.2)]. The safety and efficacy of treating sBCC lesions on the face, head and anogenital area have not been established. 5.6 Unevaluated Uses: External Genital Warts Aldara Cream has not been evaluated for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease. treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease

#### 6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. 6.1 Clinical Trials Experience: Actinic Keratosis The data described below reflect exposure to Aldara Cream or vehicle in 436 subjects enrolled in two double-blind vehicle-controlled studies. Subjects applied Aldara Cream or vehicle to a 25 cm² contiguous treatment area on the face or scalp 2 times per week for 16 weeks.

Table 2: Selected Adverse Reactions Occurring in >1% of Aldara-Treated Subjects and at a Greate Frequency than with Vehicle in the Combined Studies (Actinic Keratosis)

Preferred Term	Aldara Cream (n=215)	Vehicle (n=221)
Application Site Reaction	71 (33%)	32 (14%)
Upper Resp Tract Infection	33 (15%)	27 (12%)
Sinusitis	16 (7%)	14 (6%)
Headache	11 (5%)	7 (3%)
Carcinoma Squamous	8 (4%)	5 (2%)
Diarrhea	6 (3%)	2 (1%)
Eczema	4 (2%)	3 (1%)
Back Pain	3 (1%)	2 (1%)
Fatigue	3 (1%)	2 (1%)
Fibrillation Atrial	3 (1%)	2 (1%)
Infection Viral	3 (1%)	2 (1%)
Dizziness	3 (1%)	1 (<1%)
Vomiting	3 (1%)	1 (<1%)
Urinary Tract Infection	3 (1%)	1 (<1%)
Fever	3 (1%)	0 (0%)
Rigors	3 (1%)	0 (0%)
Alopecia	3 (1%)	0 (0%)

Table 3: Application Site Reactions Reported by >1% of Aldara-Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Studies (Actinic Keratosis)

Included Term	Aldara Cream n=215	venicie n=221
Itching	44 (20%)	17 (8%)
Burning	13 (6%)	4 (2%)
Bleeding	7 (3%)	1 (<1%)
Stinging	6 (3%)	2 (1%)
Pain	6 (3%)	2 (1%)
Induration	5 (2%)	3 (1%)
Tenderness	4 (2%)	3 (1%)
Irritation	4 (2%)	0 (0%)

Local skin reactions were collected independently of the adverse reaction "application site reaction" in an effort to provide a better picture of the specific types of local reactions that might be seen. The most frequently reported local skin reactions were erythema, flaking/scaling/dryness, and scabbing/crusting. The prevalence and severity of local skin reactions that occurred during controlled studies are shown in the following table.

### Table 4: Local Skin Reactions in the Treatment Area as Assessed by the Investigator (Actinic Keratosis)

	(n=215)		(n=220)		
	All Grades*	Severe	All Grades*	Severe	
Erythema	209 (97%)	38 (18%)	206 (93%)	5 (2%)	
Flaking/Scaling/Dryness	199 (93%)	16 (7%)	199 (91%)	7 (3%)	
Scabbing/Crusting	169 (79%)	18 (8%)	92 (42%)	4 (2%)	
Edema	106 (49%)	0 (0%)	22 (10%)	0 (0%)	
Erosion/Ulceration	103 (48%)	5 (2%)	20 (9%)	0 (0%)	
Weeping/Exudate	45 (22%)	0 (0%)	3 (1%)	0 (0%)	
Vesicles	19 (9%)	0 (0%)	2 (1%)	0 (0%)	

\*Mild, Moderate, or Severe
The adverse reactions that most frequently resulted in clinical intervention (e.g., rest periods, withdrawal from study) were local skin and application site reactions. Overall, in the clinical studies, 2% (5/215) of subjects discontinued for local skin/application site reactions. Of the 215 subjects treated, 35 subjects (16%) on Nelhole cream had at least one rest period. Of these Aldara Cream and 3 of 220 subjects (1%) on vehicle cream had at least one rest period. Of these Aldara Cream subjects, 32 (91%) resumed therapy after a rest period. In the AK studies, 22 of 678 (3.2%) of Aldara-treated subjects developed treatment site infections that required a rest period off Aldara Cream and were treated with antibiotics (19 with oral and 3 with topical). Of the 206 Aldara subjects with both baseline and 8-week post-treatment scarring assessments, 6 (2.9%) had a greater degree of scarring scores at 8-weeks post-treatment than at baseline. 6.2 Clinical Trials Experience: Superficial Basal Cell Carcinoma The data described below reflect exposure to Aldara Cream or vehicle in 364 subjects enrolled in two double-blind, vehicle-controlled studies. Subjects applied Aldara Cream or vehicle 5 times per week for 6 weeks. The incidence of adverse reactions reported by >1% of subjects during the studies is summarized below.

#### Table 5: Selected Adverse Reactions Reported by >1% of Aldara-Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Studies (Superficial Basal Cell Carcinoma)

Preferred Term	(n=185) N %	(n=179) N %
Application Site Reaction	52 (28%)	5 (3%)
Headache	14 (8%)	4 (2%)
Back Pain	7 (4%)	1 (<1%)
Upper Resp Tract Infection	6 (3%)	2 (1%)
Rhinitis	5 (3%)	1 (<1%)
Lymphadenopathy	5 (3%)	1 (<1%)
Fatigue	4 (2%)	2 (1%)
Sinusitis	4 (2%)	1 (<1%)
Dyspepsia	3 (2%)	2 (1%)
Coughing	3 (2%)	1 (<1%)
Fever	3 (2%)	0 (0%)
Dizziness	2 (1%)	1 (<1%)
Anxiety	2 (1%)	1 (<1%)
Pharyngitis	2 (1%)	1 (<1%)
Chest Pain	2 (1%)	0 (0%)
Nausea	2 (1%)	0 (0%)

The most frequently reported adverse reactions were local skin and application site reactions including erythema, edema, induration, erosion, flaking/scaling, scabbing/crusting, itching and burning at the application site. The incidence of application site reactions reported by >1% of the subjects during the 6-week treatment period is summarized in the following table.

## Table 6: Application Site Reactions Reported by >1% of Aldara-Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Studies (Superficial Basal Cell Carcinoma)

Included Term	Aldara Cream n=185	venicie n=179	
Itching	30 (16%)	1 (1%)	
Burning	11 (6%)	2 (1%)	
Pain	6 (3%)	0 (0%)	
Bleeding	4 (2%)	0 (0%)	
Erythema	3 (2%)	0 (0%)	
Papule(s)	3 (2%)	0 (0%)	
Tenderness	2 (1%)	0 (0%)	
Infection	2 (1%)	0 (0%)	

Local skin reactions were collected independently of the adverse reaction "application site reaction" in an effort to provide a better picture of the specific types of local reactions that might be seen. The prevalence and severity of local skin reactions that occurred during controlled studies are shown in the following table.

#### Table 7: Local Skin Reactions in the Treatment Area as Assessed by the Investigator

(Superficial Basal Cell Carcinoma)					
	Aldara Cream n=184				
	All Grades*	Severe	All Grades*	Severe	
Erythema	184 (100%)	57 (31%)	173 (97%)	4 (2%)	
Flaking/Scaling	167 (91%)	7 (4%)	135 (76%)	0 (0%)	
Induration	154 (84%)	11 (6%)	94 (53%)	0 (0%)	
Scabbing/Crusting	152 (83%)	35 (19%)	61 (34%)	0 (0%)	
Edema	143 (78%)	13 (7%)	64 (36%)	0 (0%)	
Erosion	122 (66%)	23 (13%)	25 (14%)	0 (0%)	
Ulceration	73 (40%)	11 (6%)	6 (3%)	0 (0%)	
Vesicles	57 (31%)	3 (2%)	4 (2%)	0 (0%)	
*Mild. Moderate, or Severe					

and look for ways to decrease it. Compulsive attention to it, however, is often a sign that more important aspects of the practice are being neglected.

Consider revenue, for example. More often than not, it is better to increase gross receipts than to decrease overhead. As a famous businessman once told me, "Your ability to cut costs is limited, but your ability to increase revenue is unlimited."

Negotiate better contracts with thirdparty payers. Improve collections, possibly with the credit card system I've discussed in several recent columns. Learn to code better and train your staff to do so as well. Use your time more efficiently. Don't worry so much about overhead. Would you rather keep 60% of \$800,000 or 40% of \$2 million?

I recently spoke with a prominent cosmetic dermatologist in New York City whose spa was bringing in a steady \$1 million per year in revenue, but with 80% overhead. He was talking about closing it down because the overhead was too high! He didn't understand that his spa was making him money, regardless of the overhead percentage. By closing the spa, he would have traded a tidy profit of 20 cents on the dollar for zero cents on the dollar.

That's why you have to be careful when using percentage as a yardstick of your overhead. Overhead percentage doesn't reflect overhead; it reflects the ratio of overhead to revenue. Without looking at the numbers themselves, both revenue and overhead, you can get a distorted view.

Let's compare two hypothetical dermatology practices: One is primarily medical and the other is surgical. The medical practice has an overhead percentage of 60% and the surgical practice 40%, but in real dollars, their overheads are exactly the same. How can that be? Is one more efficient than the other? No, the difference is in total revenue; the surgical practice generates substantially higher gross receipts than does the medical practice. When the revenue goes up, the

overhead percentage drops, even though the overhead in real dollars is the same. Once again, would you rather keep 60% of \$800,000 or 40% of \$2 million?

Don't get me wrong. Overhead is not something you should ignore, but neither should you obsess over it on a regular basis. You would be far better off seeing patients with that time. The incremental cost of seeing an additional patient is almost zero, and the revenue is almost pure profit, since you've already paid your overhead.

Concentrate on finding new ways to increase revenue or expand your practice, and your overhead will take care of itself.

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# The average number of doses not received per subject due to rest periods was? doses with a range of 2 to 22 doses; 79% of subjects (15/19) resumed therapy after a rest period. Overall, in the clinical studies, 2% (4/185) of subjects discontinued for local skin/application site reactions. In the sBCC studies, 17 of 1266 (1.3%) Aldara-treated subjects developed treatment site infections that required a rest period and treatment with antibiotics. 6.3 Clinical Trials Experience: External Genital Warts in controlled clinical trials for genital warts, the most frequently reported adverse reactions were local skin and application site reactions. Some subjects also reported systemic reactions. Overall, 1.2% (4/327) of the subjects 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. Table 8: Local Skin Reactions in the Treatment Area as Assessed by the Investigator

Table 8: Local Skin Reactions in the Treatment Area as Assessed by the Investigator (External Genital Warts)

	Aldara Cream			Vehicle				
	Femal n=11		Male: n=15		Female n=99		Males n=15	
	All Grades*	Severe	All Grades*	Severe	All Grades*	Severe	All Grades*	Severe
Erythema	74 (65%)	4 (4%)	90 (58%)	6 (4%)	21 (21%)	0 (0%)	34 (22%)	0 (0%)
Erosion	35 (31%)	1 (1%)	47 (30%)	2 (1%)	8 (8%)	0 (0%)	10 (6%)	0 (0%)
Excoriation/ Flaking	21 (18%)	0 (0%)	40 (26%)	1 (1%)	8 (8%)	0 (0%)	12 (8%)	0 (0%)
Edema	20 (18%)	1 (1%)	19 (12%)	0 (0%)	5 (5%)	0 (0%)	1 (1%)	0 (0%)
Scabbing	4 (4%)	0 (0%)	20 (13%)	0 (0%)	0 (0%)	0 (0%)	4 (3%)	0 (0%)
Induration	6 (5%)	0 (0%)	11 (7%)	0 (0%)	2 (2%)	0 (0%)	3 (2%)	0 (0%)
Ulceration	9 (8%)	3 (3%)	7 (4%)	0 (0%)	1 (1%)	0 (0%)	1 (1%)	0 (0%)
Vesicles	3 (3%)	0 (0%)	3 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Remote site skin reactions were also reported. 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 excoration/flaking (each 1%). Selected adverse reactions judged to be probably or possibly related to Aldara Cream are listed below.

	Females		Males	
	Aldara Cream n=117	Vehicle n=103	Aldara Cream n=156	Vehicle n=158
Application Site Disorders: Application Site Reactions				
Wart Site:				
Itching	38 (32%)	21 (20%)	34 (22%)	16 (10%)
Burning	30 (26%)	12 (12%)	14 (9%)	8 (5%)
Pain	9 (8%)	2 (2%)	3 (2%)	1 (1%)
Soreness	3 (3%)	0 (0%)	0 (0%)	1 (1%)
Fungal Infection*	13 (11%)	3 (3%)	3 (2%)	1 (1%)
Systemic Reactions:				
Headache	5 (4%)	3 (3%)	8 (5%)	3 (2%)
Influenza-like symptoms	4 (3%)	2 (2%)	2 (1%)	0 (0%)
Myalgia	1 (1%)	0 (0%)	2 (1%)	1 (1%)

Adverse reactions judged to be possibly or probably related to Aldara Cream and reported by more than 1% of subjects included: Application Site Disorders: burning, hypopigmentation, irritation, itching, pain, rash, sensitivity, soreness, stinging, tenderness Remote Site Reactions: bleeding, burning, itching, pain, rash, sensitivity, soreness, stinging, tenderness Remote Site Reactions: bleeding, burning, itching, pain, redereness, tinge acruis 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. 6.4 Clinical Trials Experience: Dermal Safety Studies Provocative repeat insult patch test studies involving induction and challenge phases produced no evidence that Aldara Cream causes photoallergenicity or contact sensitization in healthy skin; however, cumulative irritancy testing revealed the potential for Aldara Cream cause irritation, and annication eith reactions under sensetate in the control of the production of the production of the control of the production of photoallergenicity or contact sensitization in healthy skin; however, cumulative irritancy testing revealed the potential for Aldara Cream to cause irritation, and application site reactions were reported in the clinical studies [see Adverse Reactions (6]]. 6.5 Postmarketling Experience The following adverse reactions have been identified during post-approval use of Aldara Cream. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Body as a Whole: angioedema. Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infraction, syncope. Endocrine: thyroiditis. Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma Hepatic: abnormal liver function Neuropsychiatric: agitation, cerebrovascular accident, convulsions (Including febric convulsions), depression, insommia, multiple selerosis aggravation, paresis, suicide. Respiratory: dyspnea. Urinary System Disorders: proteinuria. Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation. Vascular: Henoch-Schonlein purpura syndrome 8 IUSE IN SPECIFIC POPILIATIONS

#### **8 USE IN SPECIFIC POPULATIONS**

B USE IN SPECIFIC POPULATIONS

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Pregnancy Category C: Note: The Maximum Recommended Human Dose (MRHD) was set at 2 packets per treatment of Aldara Cream (25 mg imiquimod) for the animal multiple of human exposure ratios presented in this label. If higher doses than 2 packets of Aldara Cream are used clinically, then the animal multiple of human exposure valid be reduced for that dose. A non-proportional increase in systemic exposure with the reduced for that dose. A non-proportional increase in systemic exposure with increased dose of Aldara Cream was noted in the clinical pharmacokinetic study conducted in actinic keratosis subjects (see Clinical Pharmacology (12.3)). The AUC after topical application of 6 packets of Aldara Cream was 8 fold greater than the AUC after topical application of 2 packets of Aldara Cream was set of 6 packets per treatment of Aldara Cream was topically administered oan individual, then the animal multiple of human exposure valued be either 1/3 of the value provided in the label (based on body surface area comparisons) or 1/8 of the value provided in the label (based on body surface area comparisons) or 1/8 of the value provided in the label (based on body surface area comparisons) or 1/8 of the value provided in the label (based on AUC comparisons). The surface of the carcinogenicity studies described in this label. The animal multiples of human exposure calculations were based on weekly dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure calculations were based on value of the carcinogenicity studies described in this label. The animal multiples of human exposure calculations were based on well of the provided of the provided in the label (based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, rorturding topuges and

noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (41 MRHD based on AUC comparisons). There are no adequate and well-controlled studies in pregnant women. Aldara Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. 8.3 Nursing Mothers It is not known whether imiquimod is excreted in human milk following use of Aldara Cream. Because many drugs are excreted human milk, caution should be exercised when Aldara Cream is administered to nursing women. 8.4 Pediatric potential benefit justifies the potential risk to the fetus. 8.3 Nursing Mothers It is not known whether imiquimod is excreted in human milk following use of Adara Cream. Because many drugs are excreted in human milk following use of Adara Cream. Because many drugs are excreted in human milk, caution should be exercised when Aldara Cream is administered to nursing women. 8.4 Pediatric Use AK and sBCC are not conditions generally seem within the pediatric population. The safety and efficacy of Aldara Cream was evaluated in two randomized vehicle-controlled, double-billow trials involving 702 pediatric subjects with molluscum contagiosum (MC) (470 exposed to Aldara; median age 5 years, range 2-12 years). Subjects with molluscum contagiosum (MC) (470 exposed to Aldara; median age 5 years, range 2-12 years). Subjects applied Aldara Cream or vehicle 3 times weekly for up to 1 fo weeks. Complete clearance (no MC lesions) was assessed at Week 18. In Study 1, the complete clearance rates assessed at Week 18. In Study 1, the complete clearance rates assessed at Week 18. In Study 1, the complete clearance rates were 24% (60/253) in the Aldara Cream group compared with 26% (26/166) in the vehicle group. In Study 2, the clearance rates were 24% (60/253) in the Aldara Cream group compared with 26% (26/166) in the vehicle group. These studies failed to demonstrate efficacy. Similar to the studies conducted in adults, the most frequently reported adverse reaction from 2 studies in children with molluscum contagiosum was application site reaction. Adverse events which occurred more frequently in Aldara-treated subjects compared with vehicle-treated subjects generally resembled those seen in studies in indications approved for adults and also included of titis media (5% Aldara vs. 3% vehicle). Erythema was the most frequently reported local skin reaction. Severe local skin reactions reported by Aldara-treated subjects in the pediatric studies included erythema (28%), edema (8%), scabbing/crusting (5%), flaking/scaling (5%), ero

<u>Topical</u> overdosing of Aldara Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions. The most clinically serious adverse event reported following multiple oral imiquimod doses of >200 mg (equivalent to imiquimod content of >16 packets) was hypotension, which resolved following oral or intravenous fluid administration.

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility In an oral (gavage) rat carcinogenicity study, imiquimod was administered to Wistar rats on a 2X/week (up to 6 mg/kg/day) or daily (3 mg/kg/day) dosing schedule for 24 months. No treatment related tumors were noted in the oral rat carcinogenicity study up to the highest dosse steated in this study of 6 mg/kg administered 2X/week in male rats (75X MRHD based on weekly AUC comparisons), 4 mg/kg administered 2X/week in male rats (75X MRHD based on weekly AUC comparisons), 1 a dermal mouse carcinogenicity study, imiquimod cream (up to 5 mg/kg/application imiquimod or 0.3% imiquimod cream) was applied to the backs of mice 3X/week for 24 months. A statistically significant increase in the incidence of liver adenomas and carcinomas was noted in high dose male mice compared to control male mice (251X MRHD based on weekly AUC comparisons). An increased number of skin papillomas was observed in vehicle cream control group animals at the treated site only. The quantitative composition of the vehicle cream used in the dermal mouse carcinogenicity study is the same as the vehicle cream used for Aldara Cream, minus the active moiety (imiquimod). In a 52-week dermal photococarcinogenicity study, the median time to onset of skin tumor formation was decreased in hairless mice following chronic topical dosing (3X/week; 40 weeks of treatment followed by 12 weeks of observation) with concurrent exposure to UV radiation (5 days per week) with the Aldara Cream vehicle alone. No additional effect on tumor development beyond the vehicle effect was noted with the addition of the active ingredient, imiquimod, to the vehicle cream. Imiquimod revealed no evidence of mutagenic or clastogenic potential based on the results of five in vitro genotoxicity tests (Arme assay, muse myphoman £15789 assay, Chinese hamster ovary cell chromosome aberration assay, human lymphocyte chromosome aberration assay and SHE cell transformation assay) and three in vivo genotoxicity tests (arm and hamste 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility In an oral (gayage) rat carcinogenicity study



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## **MedPAC** Looks At Hospitalists' **Recent Growth**

WASHINGTON The explosive growth of hospitalists has caught the notice of the Medicare Payment Advisory Commission, which advises Congress on cost, quality, and access issues affecting the federal health program.

The number of hospitalists has nearly doubled in the last 5 years and will rise to 24,000 in 2008, according to information presented by MedPAC staff at a recent meeting. Citing figures from the Society for Hospital Medicine, the staff said that 40% of Medicare beneficiaries will receive care from a hospitalist by 2010, which is double the current number.

The MedPAC staff and some of the commissioners expressed concern that the explosion of hospitalist care could increase Medicare's overall spending. According to the staff, hospitalists are usually compensated through a combination of fixed salary and volume-based bonus incentives.

Those volume-based incentives may be driving hospitalists to admit and consult more often, said Zach Gaumer, a MedPAC staff member—and currently, he continued, Medicare's payment system rewards volume, not quality and efficiency.

Hospitalists have shown that they can "create measurable efficiency gains," he said, citing a study that showed that patients treated by hospitalists had a shorter length of stay and lower costs than those who were looked after by a general internist or family physician (N. Engl. J. Med. 2007;357:2589-600). There seemed to be no impact, however, on mortality or readmissions, said Mr. Gaumer.

The consistent presence of a hospitalist, however, may improve patient safety and lead to quicker adoption of process-improvement initiatives, he added.

On balance, the collaboration between hospitals and physicians can be a plus for providers and patients, said MedPAC staff member Ann Mutti.

The commission should aim for Medicare incentives that encourage appropriate care and the right mix of care, she said.

-Alicia Ault