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The Dermatology Dispensing Debate

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ABSTRACT

The in-office dispensing of topical skin care products by dermatologists is a source of frequent debate. Guidelines for proper dispensing have been penned by various medical organizations, yet the controversy continues. With the increasing number of physician-dispensed lines available for sale, combined with mounting medical financial issues, the ongoing debate surrounding in-office dispensing will continue.

Key Words: Physician dispensing, guidelines, ethics

One of the hottest current debates in dermatology surrounds the premise that dispensing provides a valuable service to patients,¹⁻³ while opponents argue that dispensing is only a source of physician profit.^{4,5} Most states do not allow the dispensing of prescription pharmaceuticals, which means only over-the-counter (OTC) skin care products can be directly sold to patients. This includes moisturizers, sunscreens, serums, toners, cleansers, vitamins, colored cosmetics, OTC acne formulations, hair care products, and nail adornments, to name a few. In short, anything sold in a mass market retailer, such as Wal-Mart[®] or Target, can be sold by a physician as long as that physician holds a business license and pays the appropriate sales tax. No one would argue that it is unethical for these products to be sold to consumers, but the situation may be different when it involves a doctor-patient relationship. Perhaps this issue deserves further consideration.

Professionalism

The first point of controversy surrounds the issue of professionalism. Physicians are classified as professionals, meaning that they give advice and make decisions from a selfless perspective. The patient seeks this advice because he or she feels that the physician will put aside personal financial gain and treat the patient in the best manner possible. The sale of office-dispensed products tests this premise. The dispensing physician may argue that the best product to improve the patient's skin can only be found in a product sold from their office. This means that the opportunity to purchase such a product can provide the patient with enhanced care and allows the physician to offer a valuable service. In addition, some proponents suggest that on-site purchases can save time and allow the patient to get a recommendation and product simultaneously. However, other physicians contend that the practice may promote unprofessional or unethical conduct when a retail component is incorporated into a clinic setting. Certainly, there are two perspectives to this argument.

The key to finding the truth in this controversy is to analyze the value of products sold in a physician's office. Is there any topical OTC product that is so unique in a physician-dispensed line that it could not be obtained in

the mass market? Is there any ingredient available in a physician-dispensed line that must be used over all other similarly functioning ingredients available in mass market retailers? Is the physician providing something important or a biased recommendation? This is the key ethical question that all dispensing physicians must critically ask themselves.

The Price of In-Office Dispensed Products

The second point of controversy involves the price of in-office dispensed products. Most manufacturers of these lines recommend that physicians double the wholesale price to obtain the retail price. This may appear to be only a 100% mark up, but in actuality, it is much more. The manufacturer has already taken a 200%-500% profit margin to arrive at the wholesale price, which means that the physician in selling a product to the patient at 300%-600% above its cost. Certainly, a profit must be made on the sale of any OTC formulation, but the key ethical question is how much profit can be justified.

The Efficacy of In-Office Dispensed Lines

The third point of controversy is the efficacy of in-office dispensed lines. Most dispensed products are designed to function in the personal hygiene or anti-aging realm, not the pharmaceutical realm. This means that product expectations are reduced while product safety is increased. Dispensed lines are not intended to replace prescription therapies, but rather to enhance their efficacy. This may be the case with dispensed acne treatment products containing benzoyl peroxide that are combined with topical prescription retinoids and antibiotics to deliver control of noninflammatory acne lesions. Perhaps dispensed anti-aging creams might increase the tolerability of tretinoin, but what else can they offer? Does the topical botanical cocktail really deliver something beneficial to the skin that can be medically documented by the physician? It is this evidence-based approach to office-dispensed products that is lacking in some instances, depending on the research efforts of the product line manufacturer. Compatibility is called into question when uniting the science of pharmaceuticals with their certainty of efficacy and the puffery of claims associated with some anti-aging creams.

The Meaning of the Physician-Businessperson

The prior discussion leads to our fourth issue, which is the meaning of the physician-businessperson. Is it possible to be a physician-businessperson or is this phrase an oxymoron? In the US, a modern business model for some entrepreneurial physicians is labeled the medspa. Physicians operating medspas come from no particular background and may be dermatologists, plastic surgeons, family practitioners, internists, gynecologists, etc. They supervise the treatments provided by a staff of nurses and aestheticians including

body massages, laser hair removal, cellulite wraps, manicures, botulinum toxin injections, intense pulsed light facial peels, and hyaluronic acid filler injections, to name a few. The business concept seems to combine the minimally risky aesthetic medical procedures with the relaxation and adornment practices learned in cosmetology school. These establishments frequently sell physician dispensed product lines as an additional source of income. These products are recommended by the aestheticians and nurses that provide the services and not by the supervising physician, who does not see every client. If the recommendation to purchase from an in-office dispensed line does not come directly from the physician, does the product purchase carry the same value? Is it a medical service or a business venture similar to a cosmetic counter at a department store? Is the physician functioning in a medical realm or a business realm?

Patient Evaluation of the Products

The final point of controversy is the ability of the patient to objectively evaluate product purchases. This may be difficult when the patient feels compelled to listen to the sales pitch of an aggressive aesthetician or is directed to walk by the sales counter when exiting the medical office. The patient may conceive that products must be purchased in order to continue a favorable patient-physician relationship, or to receive medical care in the office. A patient in a medical office is a captive audience and this situation must not be abused. The patient should have the option to discuss product sales or opt out of the conversation when checking in to a medical office. Perhaps this discussion should take place at the front desk. Patients could be asked about product sales and their wishes obeyed.

Guidelines

Many professional organizations, such as the American Medical Association and the American Academy of Dermatology, have weighed in with opinions regarding the practice of office dispensing.^{6,7} While the wording and details vary from organization to organization, the basic spirit of the recommendations are to preserve medical ethics. Indeed, this is key. However, there is no agreement among physicians as to what constitutes ethical dispensing. Thus far, this discussion has perhaps raised more questions than it has answered. Only through this type of soul searching can the true value of in-office dispensing be determined.

Conclusions

Moving forward, it would seem that many issues could be resolved by developing a physician board that would approve products for in-office dispensing, much like the US FDA provides approval for pharmaceuticals. This board could evaluate the efficacy of skin care lines manufactured for in-office dispensing that is based on

research provided by the manufacturer. Performance guidelines could be established requiring rigid scientific studies to meet predetermined endpoints. Only dispensed lines that meet these requirements would be certified for in-office sales. This type of certification would raise the bar on product performance and perhaps offer something truly unique in skin care. Perhaps a proposal such as this could quell the controversy regarding physician dispensing.

References

1. Farris PK. Office dispensing: a responsible approach. *Semin Cutan Med Surg* 19(3):195-200 (2000 Sep).
2. Higham R. Integration of moisturizers and cleansers into a busy dermatology practice. *Cutis* 76(6 suppl):32-3 (2005 Dec).
3. Nestor MS. Dermatology practice management enhancement: implications for dermatology in the age of managed care. *Semin Cutan Med Surg* 19(3):163-9 (2000 Sep).
4. Miller RC. Dermatologists should guard their patients' purse, not pick their pockets! *Arch Dermatol* 135(3):255-6 (1999 Mar)
5. Epstein E. Are we consultants or peddlers? *Arch Dermatol* 134(4):508-9 (1998 Apr).
6. AMA Council on Ethical and Judicial Affairs. Sale of health-related goods from physicians' offices. CEJA Opinion 8.063 issued December 1999 and adopted June 1999. <http://www.ama-assn.org/ama/pub/category/8486.html>. Last accessed October 25, 2007.
7. AAD Position Statement on Dispensing. Approved October 1998 and amended September 1999. <http://www.aad.org/NR/rdonlyres/FCAAC923-3F36-4B36-8C35-945472973888/0/Dispensing.pdf>. Last accessed October 25, 2007.

The American Academy of Dermatology's Position Statement on Dispensing

(Approved by the Board of Directors October 12, 1998; Amended by the Board of Directors September 26, 1999)

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<http://www.aad.org/NR/rdonlyres/FCAAC923-3F36-4B36-8C35-945472973888/0/Dispensing.pdf>

Dermatologists should not dispense or supply drugs, remedies or appliances unless it is manifestly in the best interest of their patients.

Dermatologists who dispense in office should do so in a manner with the best interest of their patient as their highest priority, as it is in all other aspects of dermatologic practice.

It is ethical to dispense, by sale, prescription or non-prescription drugs, to patients in a dermatologist's office except in the following circumstances:

1. When the dermatologist places his/her own financial interests above the welfare of his/her patients.
2. When creating an atmosphere which is coercive to patients such that they feel compelled to purchase drugs from the dermatologist.
3. When dispensing drugs under a dermatologist's private label without clearly listing the ingredients, including generic names of the drugs.
4. When dispensing to patients drugs which are easily available at proprietary pharmacies without advising patients of this availability.
5. When representing drugs as being a special formula not elsewhere available, when that is not the case.
6. When selling health-related products whose claims of benefit lack validity.
7. When refusing to give refills of drugs except that they be purchased from the dermatologist.
8. When charging patients at an excessive mark-up rate.

Treatment of Hand and Foot Psoriasis with Emphasis on Efalizumab

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ABSTRACT

Hand and foot psoriasis is a chronic and debilitating disease that manifests as plaque-type or pustular-type lesions. Although the palms and soles represent only 2% of the total body surface area, psoriasis of these regions may lead to physical dysfunctions that can greatly impair dexterity, mobility, and the quality of life of affected individuals. Deregulation of T-lymphocyte-mediated immune response is important in the pathophysiology of psoriasis. Efalizumab (Raptiva[®], Genentech) is an anti-CD11a monoclonal antibody that disrupts the interaction between T cells and antigen-presenting cells, thereby inhibiting various T-cell-mediated immune processes that include activation and trafficking. Recent evidence indicates that efalizumab may be beneficial for patients with hand and foot psoriasis.

Key Words: Hand and foot, psoriasis, efalizumab, monoclonal antibody

Pathophysiology and Prevalence

Psoriasis is a chronic, inflammatory, autoimmune skin disease that affects approximately 2% of the US population. The cutaneous lesions characteristic of psoriasis can cause physical, psychological, and social dysfunctions in affected individuals.¹ The pathophysiology of psoriasis consists of an abnormal immune response. T cells in the dermis and epidermis are overactivated, which triggers the release of proinflammatory cytokines and hyperproliferation of keratinocytes. This, in turn, manifests as the skin lesions that are the hallmark of psoriasis.

Hand and Foot Psoriasis

For hand and foot psoriasis, lesions may occur on:

- the palms of the hands
- the soles of the feet
- the dorsal surface of the hands and feet.

In addition to exhibiting plaque-type lesions, this variant of psoriasis can also include fissuring, crusting, erythema, and recurrent painful pustules. Hand and foot psoriasis occurs in approximately one-third of the psoriatic population, and interestingly, many patients with this disease do not have psoriasis on other parts of their body. The biological basis for the differences in affected body area is not known.^{2,3}

Hand and foot psoriasis may make routine tasks, such as writing, hand shaking, and walking very difficult for affected individuals. Not only can this profoundly affect their quality of life, it can also greatly affect their family members and caregivers. To better understand these impacts, investigators conducted a survey of patients with and without hand and foot involvement to compare disease severity.² The results indicated that patients with hand and foot psoriasis reported significantly greater functional disability and physical discomfort, such as burning and soreness, as compared with those who did not have hand and foot involvement.

Interestingly, the survey revealed that the added disabilities were related to physical activities in general and not to social issues, which dispels the assumption that psoriasis on the hands and feet can lead to greater psychosocial dysfunction than psoriasis on other parts of the body. Furthermore, the survey found that for patients who experienced associated pain and discomfort from hand and foot psoriasis, complete clearing of the lesions was not as important to them as pain reduction.

Limitations of Conventional Treatment

Hand and foot psoriasis is often refractory to treatment, and the lack of effective therapeutic options creates an unmet medical need. (See Table 1 for a summary of treatment modalities.) Topical therapies elicit insufficient response rates, in part because it is more difficult for drugs to penetrate the thicker skin of the palms and soles, as compared with skin absorption on other regions of the body. The biological basis for the difficulty in treating with conventional systemic agents remains unclear. At present, a combination of topical psoralen photochemotherapy and systemic retinoids is frequently used. Other treatment options include cyclosporine and methotrexate; each has proven to be beneficial for some patients. However, several of these systemic treatments must be administered at high doses in order to be effective for the hands and feet. This can lead to significant side-effects, such as a higher risk of skin cancer, infections, teratogenicity, and hyperlipidemia.⁴⁻⁶

Efalizumab

Efalizumab is a recombinant, humanized anti-CD11a monoclonal IgG1 antibody that has been approved for the treatment of moderate-to-severe chronic plaque psoriasis in adult patients.⁷ The biological basis for the therapeutic benefits of efalizumab is its inhibition of T-cell-mediated immune responses. Efalizumab targets

Mode	Therapy	Efficacy	Adverse Events (AEs)*
Systemic Agents	Acitretin vs. etretinate ⁸	93% vs. 90% reduction in number of pustules for patients treated with acitretin (n=30) vs. etretinate (n=30) for 12 weeks.	Hypervitaminosis A, hypertriglyceridemia, high teratogenicity, photosensitivity, xerosis, epistaxis
	Alefacept ^{9,10}	4 patient cases; 2 patients achieved substantial improvement and increased quality of life ⁹ , and 2 patients achieved clearance. ¹⁰	Decreased CD4 cell count
	Cyclosporine ¹¹	48% vs. 19% of patients treated with cyclosporine (n=31) vs. placebo (n=27) achieved 50% reduction in pustule number after 1 month; the mean number of pustules was reduced by 76% after 12 months of cyclosporine treatment.	Hypertension, hypertrichosis
	Efalizumab ¹²	46.2% vs. 18% patients treated with efalizumab (n=52) vs. placebo (n=28) achieved PGA rating of clear, almost clear or mild after 12 weeks.	Flare-up or worsening of psoriasis
	Etanercept ¹³	Case report of a patient who achieved almost total clearance after 19 weeks of etanercept therapy.	No AEs reported
	Itraconazole ¹⁴	Report of 7 patients treated with itraconazole; pustules disappeared within 2 weeks of initiation of therapy; however, erythematous-squamous lesions improved but never fully healed.	No AEs reported
	Oral liorzole ¹⁵	After 12 weeks of treatment, patients treated with liorzole had significantly lower palmoplantar PASI (n=7; median 3, range 1.8±14.1) than patients treated with placebo (n=8; median 12.1, range 5±18; p=0.02). Liorzole-treated patients also demonstrated significantly fewer fresh pustules and lower overall disease severity.	Pruritus, cheilitis, xerosis
Topical Agents	Occlusive vs. nonocclusive calcipotriol ¹⁶	Patients treated with either occlusive (n=19) or nonocclusive (n=20) calcipotriol demonstrated 75% improvement from baseline after 6 weeks of treatment.	No AEs reported
	Occlusive triamcinolone vs. nonocclusive clobetasol propionate ¹⁷	Lesions were completely cleared in 13/19 patients vs. 3/19 patients after 4 weeks when treated with occlusive triamcinolone vs. nonocclusive clobetasol propionate, respectively.	No AEs reported
	Topical methotrexate ¹⁸	10/12 patients with hand involvement and 9/12 patients with foot involvement achieved mild or moderate improvement; none of the patients achieved clearance.	No AEs reported
	Tar ¹⁹	76.5% of patients treated with coal tar (n=17) vs. 45.5% of patients treated with petrolatum (n=11) achieved 50% improvement at 8 weeks.	No AEs reported
Phototherapy	Psoralen-UVA ²⁰	5/7 patients with hand and foot psoriasis treated with PUVA responded favorably; 4 patients experienced complete remission and 1 experienced partial remission.	Increased risk of burns and skin cancer

Table 1: Summary of reports discussing treatment modalities investigated for hand and food psoriasis.

*Adverse events reported are specific to the cited case reports/ studies.

the T-cell adhesion molecule, leukocyte function-associated antigen 1 (LFA-1), which is present on the surface of T cells and is made up of a heterodimer of CD11a and CD18 proteins. Interaction between LFA-1 and intracellular adhesion molecule 1 (ICAM-1), a cell surface protein of the antigen-presenting cell (APC), serves as the predominant adhesion interface between T cells and their APCs. LFA-1/ICAM-1 interaction is critical for T-cell activation and trafficking. By binding to the CD11a subunit of LFA-1 with high affinity and specificity, efalizumab prevents CD11a interaction with ICAM-1, thereby inhibiting the initiation of an immune response and the release of inflammatory cytokines involved in keratinocyte proliferation and the development of psoriatic lesions.²¹

Efalizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis

The safety and efficacy of efalizumab for the treatment of moderate-to-severe plaque psoriasis have been well documented in multiple, phase III, randomized, placebo-controlled, multicenter studies.²²⁻²⁵ In these studies, 27%-33% of efalizumab-treated patients achieved 75% improvement on the Psoriasis Area and Severity Index (PASI-75) after 12 weeks of treatment. Furthermore, after 24 weeks of continuous efalizumab treatment, 44% of treated patients achieved PASI-75.^{24,26} Leonardi, et al. found that response can be maintained with long-term treatment, i.e., 45% of patients achieved PASI-75 after 144 weeks of continuous efalizumab treatment.²⁷

Efalizumab for the Treatment of Hand and Foot Psoriasis

A recently published case report series suggested benefits for efalizumab in the treatment of patients with hand and foot psoriasis.⁴ The report presents cases of 17 patients: four men and 13 women with plaque-type (n=11) or pustular-type (n=5) hand and foot psoriasis, and one patient with both plaque- and pustular-type. The age range of the patients was 29-33 years and the range of their disease duration was 3-30 years. Hand and foot psoriasis in these patients was refractory to various treatments, including topicals, methotrexate, cyclosporine, prednisone, acitretin, psoralen UVA phototherapy, and the tumor necrosis factor inhibitor etanercept. Each of these patients received subcutaneous injections of efalizumab (1mg/kg/wk), and the treatment outcome was measured by PASI, the Physician's Global Assessment (PGA), or the affected body surface area. With efalizumab treatment, the patients achieved 50%-100% clearance of their hand and foot psoriasis as early as 2 weeks following the start of treatment. For two of the patients, it took approximately 1 year to achieve 85% and 100% clearance of their disease. One patient had additional psoriasis in the fingernails and toenails with pitting and onycholysis, which also cleared

with efalizumab treatment. Efalizumab was generally well tolerated by all of the patients in this case series, with one occurrence each of hemolytic anemia and mild myalgia; three patients developed mild flu-like symptoms, which were determined to be reversible drug-related adverse events.

A 12-week, phase IV, randomized, double-blind, placebo-controlled study was recently completed to assess the efficacy and safety of efalizumab in 75 enrolled patients with chronic moderate-to-severe hand and foot psoriasis. The study population included patients with or without pustules, and with or without psoriasis at locations other than the hands and feet, who had a PGA rating of moderate (3) or severe (4) for hand and/or foot psoriasis and no previous exposure to the study drug. Patients were administered efalizumab 1mg/kg/wk (n=52) or placebo (n=28). In a preliminary report of the data collected, 46.2% of efalizumab-treated patients achieved a PGA rating of clear (0), almost clear (1) or mild (2) after 12 weeks of treatment versus 17.9% of placebo-treated patients.^{12,28} The incidence of adverse events in patients treated with efalizumab was similar to those treated with placebo, which was consistent with the safety profile observed in previous phase III studies.

Conclusion

Physicians and caregivers may sometimes underestimate the impact of hand and foot psoriasis on affected individuals; simple routine and important functions can become physically and psychosocially challenging for these patients. Efforts to find effective long-term therapeutic options with favorable safety profiles remain an elusive achievement. As a prerequisite to fulfilling this unmet medical need, basic research must be conducted to gain a thorough understanding of the pathophysiology of hand and foot psoriasis and to further determine whether there are distinct disease pathways that lead to the plaque versus pustular forms of this disease. To date, the options available for treatment have been limited by inadequate response to therapy and/or toxicity related to increased dosage and long-term use. As noted above, recently published case studies and preliminary results from a phase IV study have shown potential benefits of efalizumab in the treatment of hand and foot psoriasis. It would be of great interest to evaluate the effects of efalizumab in the long-term treatment of hand and foot psoriasis.

References

1. Fortune DG, Main CJ, O'Sullivan TM, et al. Quality of life in patients with psoriasis: the contribution of clinical variables and psoriasis-specific stress. *Br J Dermatol* 137(5):755-60 (1997 Nov).

2. Pettey AA, Balkrishnan R, Rapp SR, et al. Patients with palmoplantar psoriasis have more physical disability and discomfort than patients with other forms of psoriasis: implications for clinical practice. *J Am Acad Dermatol* 49(2):271-5 (2003 Aug).
3. Enfors W, Molin L. Pustulosis palmaris et plantaris. A follow-up study of a ten-year material. *Acta Derm Venereol* 51(4):289-94 (1971).
4. Fretzin S, Crowley J, Jones L, et al. Successful treatment of hand and foot psoriasis with efalizumab therapy. *J Drugs Dermatol* 5(9):838-46 (2006 Oct).
5. Marsland AM, Griffiths CE. Treatments for chronic palmoplantar pustular psoriasis. *Skin Therapy Lett* 6(12):3-5 (2001 Nov).
6. Marsland AM, Chalmers RJ, Hollis S, et al. Interventions for chronic palmoplantar pustulosis. *Cochrane Database Syst Rev* (1):CD001433 (2006).
7. Raptiva® [efalizumab] (package insert). South San Francisco, Calif: Genentech, Inc. (2005 Jun).
8. Lassus A, Geiger JM. Acitretin and etretinate in the treatment of palmoplantar pustulosis: a double-blind comparative trial. *Br J Dermatol* 119(6):755-9 (1988 Dec).
9. Myers W, Christiansen L, Gottlieb AB. Treatment of palmoplantar psoriasis with intramuscular alefacept. *J Am Acad Dermatol* 53(2 Suppl 1):S127-9 (2005 Aug).
10. Prossick TA, Belsito DV. Alefacept in the treatment of recalcitrant palmoplantar and erythrodermic psoriasis. *Cutis* 78(3):178-80 (2006 Sep).
11. Erkkö P, Granlund H, Remitz A, et al. Double-blind placebo-controlled study of long-term low-dose cyclosporin in the treatment of palmoplantar pustulosis. *Br J Dermatol* 139(6):997-1004 (1998 Dec).
12. Leonardi CL, Sobell JM, Sofen H, et al. Phase IV study to evaluate the safety and efficacy of efalizumab for treatment of hand and foot psoriasis. *J Am Acad Dermatol* 56(2):AB48 (2007 Feb).
13. Weinberg JM. Successful treatment of recalcitrant palmoplantar psoriasis with etanercept. *Cutis* 72(5):396-8 (2003 Nov).
14. Mihara M, Hagari Y, Morimura T, et al. Itraconazole as a new treatment for pustulosis palmaris et plantaris. *Arch Dermatol* 134(5):639-40 (1998 May).
15. Bhushan M, Burden AD, McElhone K, et al. Oral liarozole in the treatment of palmoplantar pustular psoriasis: a randomized, double-blind, placebo-controlled study. *Br J Dermatol* 145(4):546-53 (2001 Oct).
16. Duweb GA, Abuzariba O, Rahim M, et al. Occlusive versus nonocclusive calcipotriol ointment treatment for palmoplantar psoriasis. *Int J Tissue React* 23(2):59-62 (2001).
17. Kragballe K, Larsen FG. A hydrocolloid occlusive dressing plus triamcinolone acetonide cream is superior to clobetasol cream in palmo-plantar pustulosis. *Acta Derm Venereol* 71(6):540-2 (1991).
18. Kumar B, Sandhu K, Kaur I. Topical 0.25% methotrexate gel in a hydrogel base for palmoplantar psoriasis. *J Dermatol* 31(10):798-801 (2004 Oct).
19. Kumar B, Kumar R, Kaur I. Coal tar therapy in palmoplantar psoriasis: old wine in an old bottle? *Int J Dermatol* 36(4):309-12 (1997 Apr).
20. De Rie MA, Van Eendenburg JP, Versnick AC, et al. A new psoralen-containing gel for topical PUVA therapy: development and treatment results in patients with palmoplantar and plaque-type psoriasis, and hyperkeratotic eczema. *Br J Dermatol* 132(6):964-9 (1995 Jun).
21. Werther WA, Gonzalez TN, O'Connor SJ, et al. Humanization of an anti-lymphocyte function-associated antigen (LFA)-1 monoclonal antibody and re-engineering of the humanized antibody for binding to rhesus LFA-1. *J Immunol* 157(11):4986-95 (1996 Dec).
22. Lebwohl M, Tying SK, Hamilton TK, et al. A novel targeted T-cell modulator, efalizumab, for plaque psoriasis. *N Engl J Med* 349(21):2004-13 (2003 Nov).
23. Gordon KB, Papp KA, Hamilton TK, et al. Efalizumab for patients with moderate to severe plaque psoriasis: a randomized controlled trial. *JAMA* 290(23):3073-80 (2003 Dec).
24. Menter A, Gordon K, Carey W, et al. Efficacy and safety observed during 24 weeks of efalizumab therapy in patients with moderate to severe plaque psoriasis. *Arch Dermatol* 141(1):31-8 (2005 Jan).
25. Leonardi CL, Papp KA, Gordon KB, et al. Extended efalizumab therapy improves chronic plaque psoriasis: results from a randomized phase III trial. *J Am Acad Dermatol* 52(3 Pt 1):425-33 (2005 Mar).
26. Gottlieb AB, Hamilton T, Caro I, et al. Long-term continuous efalizumab therapy in patients with moderate to severe chronic plaque psoriasis: updated results from an ongoing trial. *J Am Acad Dermatol* 54(4 Suppl 1):S154-63 (2006 Apr).
27. Leonardi C, Menter A, Hamilton T, et al. Efalizumab: results of a 3 year continuous dosing study for the long-term control of psoriasis. *Br J Dermatol*, submitted June 2007.
28. Genentech. Genentech announces positive results from a phase IV study of Raptiva in patients with moderate-to-severe hand and foot psoriasis [press release]. February 2, 2007. <http://www.gene.com/gene/news/press-releases/display.do?method=detail&id=10447>, last accessed August 13, 2007.

Update on Drugs

Class	Name/Company	Approval Dates and Comments
<i>Antifungal Agent</i>	Terbinafine hydrochloride <i>Lamisil</i> [®] Novartis Pharmaceuticals	The US FDA approved this antifungal agent in September 2007 for the treatment of tinea capitis in young children ≥ 4 years of age. The new granular formulation, which can be sprinkled on children's food, is intended to improve patient compliance and treatment outcomes. The recommended dosage is based on the child's weight and administered once daily for 6 weeks.
<i>Antiviral Agent</i>	Famciclovir TEVA Pharmaceutical Industries	The US FDA approved the first generic formulation of famciclovir (comparable brand, Famvir [®] , Novartis) in August 2007 for the treatment of herpes zoster (shingles).
<i>Antibacterial Agent</i>	Ceftobiprole <i>BAL5788</i> Basilea Pharmaceutica/ Janssen-Ortho	Health Canada accepted a Review New Drug Submission for this antibacterial agent in September 2007 for the treatment of complicated skin and skin structure infections, including diabetic foot infections. Ceftobiprole is a novel broad-spectrum cephalosporin antibiotic effective against drug-resistant bacteria.

Drug News

<i>Antipsoriatic Agent</i>	<p>During the recent World Congress of Dermatology meeting, lead investigator, Craig Leonardi, presented data from an international multicenter, randomized, double-blind placebo-controlled Phase III study, which showed that two-thirds of the subjects treated with the injectable medication, ustekinumab (CNTO 1275, Centocor/ Johnson & Johnson), experienced marked improvement in their psoriasis when compared with placebo. Ustekinumab is a novel fully-humanized monoclonal antibody that targets interleukin-12 and interleukin-23. These proteins are believed to play an integral role in immune-mediated inflammatory diseases, such as psoriasis. Over 1,200 patients with moderate-to-severe psoriasis were randomized to one of three treatment arms: one of two different doses of the study drug, or placebo. At week-12, as measured by the PASI, 76% of patients who were administered the higher dose, and 67% of those who received the lower dose, achieved at least 75% improvement in their symptoms, compared with only 4% in those who received placebo. Furthermore, approximately 50% of the subjects who were treated with the higher dose of the study medication experienced clearing of almost all psoriatic lesions, and exhibited substantial improvement in other associated symptoms, as compared with only 1% of the placebo group.</p> <p><i>Leonardi C, et al. CNTO 1275 (anti-IL-12/23p40) Treatment of psoriasis: phase 3 trial results. At the 21st meeting of the World Congress of Dermatology (October 1-5, 2007) Buenos Aires, Argentina; Book 1, Abstract 1543.</i></p>
<i>US FDA Regulations</i>	<p>In September 2007, the US FDA has gained additional powers following the passage of a bill by the US Senate. The new legislation will enable the US FDA to require new warnings on approved prescription drugs if warranted; mandate the completion of post-approval studies; or limit its distribution in cases where concerns arise regarding a product's safety. Fines for up to \$10 million can be imposed for noncompliance. These changes were proposed in response to the recent controversial delayed handling by the US FDA of potentially severe or life-threatening side-effects that were linked to certain prescription medications. The new regulations are intended to improve postmarketing surveillance programs and place emphasis on long-term patient safety. Pharmaceutical companies will be required to announce results from clinical studies of marketed products in a public database. More information on the US FDA's Drug Safety Initiative can be found at:</p> <p>http://www.fda.gov/cder/drugSafety.htm.</p>

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