

## New Corticosteroids

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### ABSTRACT

*Corticosteroids have dominated the class of anti-inflammatory agents for the past 50 years. In the last ten years, seven new corticosteroids have been developed for topical use. Characteristics common to these several chemically different corticosteroids are their class III, or high potency (USP) designation and their improved safety profile. Allergic contact dermatitis is an unexpected adverse effect that is caused by some of them, in particular budesonide and, to a somewhat lesser degree, the labile "prodrug" corticosteroids, such as prednicarbate and prednisolone aceponate.*

**KEY WORDS:** corticosteroids, anti-inflammatory agents

### Introduction

No drugs have dominated this class of anti-inflammatory agents as successfully as the corticosteroids. Since their introduction to dermatology a half-century ago, these molecules have been developed both as topical and systemic agents. However, the side effects associated with their use, including percutaneous absorption and cutaneous atrophy, have become increasingly unacceptable. The pharmaceutical industry has responded by introducing a new generation of topical corticosteroids which are "softer", and early indications are that they are safer<sup>1</sup>.

Not long after Sulzberger and Witten demonstrated the effectiveness of hydrocortisone in the 1950s, the new more effective fluorinated hydrocortisone analogues became available in the 1960s. In the 1970s and '80s, superpotent steroids were introduced. These inclusions meant that there was a great range of potency of these drugs. In 1984, Cornell and Stoughton proposed a potency rating of topically applied corticosteroids. This classification was based primarily on the vasoconstrictor assay or skin-blanching effect of corticosteroid preparations<sup>1</sup>. More recently, the USP has created a classification of potency ranking for these drugs: low, medium, high and very high based upon the consensus of the USP Dermatology Advisory Panel.

### A New Generation of Corticosteroids

Over the past several years, a new series of corticosteroids have been introduced. Of this series, we have included seven agents for review. European and North American based clinical trials have demonstrated that the newer corticosteroids with their improved risk-benefit ratio are as efficacious as products currently in use. Although not all claims have been substantiated, it appears that these drugs have fewer side effects. They act primarily on the upper level of the skin where they interact with the inflammatory mediators, while simultaneously sparing the deeper layers. Not only are the reduced side effects desirable, but there is evidence to show that patients are more compliant<sup>2</sup>.

While longer clinical follow-up is necessary, current research shows:

- that the newer corticosteroids are potent, belonging to the high potency class of products, with one exception, namely fluocortinbutylester, which can be regarded as less potent because it is transformed in the skin into a nonactive fluocortolone 21-acid.
- that systemic side effects are reduced because of rapid biotransformation, even when used in the wet wrap method to

treat atopic dermatitis. However, in very young children and in erythrodermic patients, one should beware of potential hypothalamus and pituitary axis (HPA) suppression, even with the new corticosteroids.

- that local safety with short-term use appears satisfactory<sup>1</sup>. Indeed, the new generation of corticosteroids does not cause as much cutaneous atrophy or systemic absorption as the older corticosteroids do. This is because of their molecular configuration, which displays a rapidly declining concentration gradient in the skin. They act primarily in the top layers where the most important mediators of the inflammatory reaction are. The action in deeper layers is much diminished. With restricted duration of treatment (up to 6 weeks) clinical safety has been claimed. However, skin atrophy and some telangiectasia have been noted.

### **Classifications**

The new corticosteroids can be classified in several ways. Chemically, they can be divided as follows:

- Asymmetric acetonides: budesonide
- C<sub>21</sub>-carboxylesters: alclometasone, flucortinbutylester, and methylprednisolone aceponate.
- C<sub>17</sub>-prednicarbonates: 17-prednicarbate
- Carbothiates: fluticasone propionate
- Mometasone furoate

Another way to classify these drugs is by chemical stability:

- Some of these drugs can be regarded as pro-drugs, that undergo metabolism and acryl-exchanges, immediately after application to form the active molecule. They include: prednicarbate, methylprednisolone aceponate, alclometasone, and flucortin butylesters.

### **The Issue of Side Effects**

The object of the changes made in the corticosteroid molecule between the 1950s and the mid-1980s, was to obtain better skin penetration, slower enzyme degradation, and greater affinity for the cytosol receptors<sup>1</sup>. However, the changes that increased potency, also led to more side effects.

While systemic side effects are of concern, cutaneous side effects are more common and include problems such as striae formation, atrophy, purpura, peri-oral dermatitis, steroid rosacea, hypertrichosis, and steroid acne<sup>1</sup>.

Side effects are generally related to the duration and potency of the application, the manner of application (i.e., occlusion), the presence of penetration-enhancing substances, and the state of the skin barrier. The anatomic site of application and the patient's age can also adversely influence the side effect profile<sup>1</sup>.

### **Application**

Several of the new corticosteroids may only need to be applied once daily, in contrast to the older corticosteroids, for which a twice-daily application was recommended.

### **Contact Allergy**

The increase in the number of reports of contact allergic reactions, following the introduction of some of these newer corticosteroids, was unexpected.

In order to explain the increased allergenicity of the newer corticosteroids, data from the literature and clinical studies were reviewed and an attempt was made to define some of the more important groups of cross-reacting molecules<sup>4</sup>.

Group A – hydrocortisone type: no substitution on the D-ring, except a short chain ester on C<sub>17</sub> or C<sub>21</sub> or a thioester on C<sub>21</sub>.

Group B – triamcinolone type: C<sub>16</sub>, C<sub>17</sub>-cis-ketal or -diol structure.

Group C – betamethasone type: C<sub>16</sub>-methylsubstitution, no side chain on C<sub>17</sub>; possible side chain on C<sub>21</sub>.

Group D – hydrocortisone-17-butyrate type: long chain ester at C<sub>17</sub> and/or C<sub>21</sub> with or without C<sub>16</sub>-methylsubstitution.

Tixocortol pivalate (1% petrolatum) was identified as a good screening agent for Group A. Budesonide (1% ethanol) was found to be a marker for the Group B, but also for certain esters, such as hydrocortisone-17-butyrate in Group D. Budesonide is virtually a 1:1 mixture of two diastereomers (R- and S-isomer). The R-isomer is the marker for the B Group, the S-isomer for the D Group. There is no marker for the Group C, but it seems that its members cause almost no contact sensitivity and do not cross-react with other groups.

In recent studies<sup>5,6</sup> it has been shown that Group D should be divided into two subgroups. Corticosteroids with a methylsubstitution on C<sub>16</sub> and halogenation on the B ring can be classified as Group D<sub>1</sub>. To this group belong not only the older molecules like betamethasone dipropionate, betamethasone-17-valerate, and clobetasol propionate, but also the newer stable corticosteroids: fluticasone propionate and mometasone fuoroate. They rarely cause positive patch test results, and can safely be used even in patients who are allergic to other corticosteroids.

The corticosteroids with a long ester on C<sub>17</sub>, possibly a side chain on C<sub>21</sub>, no methyl substitution on C<sub>16</sub>, and no halogenation on the B ring can be classified in Group D<sub>2</sub>. To this group belong hydrocortisone-17-butyrate and hydrocortisone-17-valerate, as well as the "labile" new corticosteroids like prednicarbate and methylprednisolone aceponate. They can cause allergic reactions. Budesonide (S-isomer) is the marker for this Group D<sub>2</sub>, but they can cross-react with Group A. Flucortin butylester belongs to Group C.

# Electrolysis For The Treatment Of Hypertrichosis And Hirsutism

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## ABSTRACT

*There are three electrolysis modalities. In galvanic electrolysis, a direct electric current is passed down a needle inserted into the hair follicle, destroying the follicle. In thermolysis a high frequency alternating current is passed down the needle and produces destructive heat. The blend is the third modality which combines galvanic electrolysis and thermolysis. Electrolysis satisfactorily removes hair from women and men with hypertrichosis, but women with hirsutism require concomitant hormonal management. Scarring does not occur with properly performed electrolysis.*

*Shaving one to five days before electrolysis greatly increases efficacy because it ensures that only growing anagen hairs are epilated. The judicious use of ice packs and the recent availability of EMLA (lidocaine/prilocaine cream) have been beneficial in reducing the sensations of electrolysis.*

**KEY WORDS:** Galvanic electrolysis, thermolysis, hypertrichosis, hirsutism

## Introduction

Electrolysis has been used to produce permanent hair loss since 1875, when Dr. Charles Michel first used it in St. Louis, Missouri to remove the ingrown hairs of trichiasis<sup>1</sup>. The term electrolysis is a generic term referring to the permanent removal of hair by the insertion of a needle into the hair follicle. The needle acts as a conductor to carry the appropriate current to the base of the hair follicle, and particularly to the dermal papilla.

In galvanic electrolysis a direct electric (galvanic) current is passed down the needle into the hair follicle. The current acts on tissue saline to produce sodium hydroxide, which destroys the lower hair follicle and dermal papilla. Galvanic electrolysis is the most certain method of permanent hair removal, but is slow and can require a minute or more for each hair.

In thermolysis (also called short-wave, diathermy, high radio frequency) the high frequency current passed down the needle produces heat, which destroys the base of the follicle. Thermolysis is much faster than galvanic electrolysis and requires only a few seconds. This procedure involves the generation of much higher energy for only a fraction of a second. The flash method is best used with insulated needles, which protect the upper hair follicle and restricts high energy delivery to the lower end of the follicle. The widely referenced method employed by Kligman and Peters should be referred to<sup>2</sup>.

The blend method shortens treatment time. It combines galvanic electrolysis, for the localized destruction of the hair papilla, and high frequency thermolysis to shorten treatment time. In this combination, the heat produced from thermolysis increases the temperature of the sodium hydroxide produced by galvanic electrolysis. This, in turn, increases efficiency in destroying the hair follicle. The several electrolysis options outlined result in permanent hair removal, but the choice of modality depends upon the experience and preference of the operator.

Electrolysis procedures and equipment are standardized and in most jurisdictions monitored by regulators. Electrolysis is safe and scarring does not occur when properly performed by trained electrologists. Much of the scarring previously attributed to electrolysis actually resulted from inappropriate plucking and/or picking. However, if the electrolysis operator is unskilled or if the current used is too high, scarring may occur.

Hyperpigmentation may occur, especially so in patients with Skin Types III and IV, but is usually of a transient nature. Disease transmission may be of concern, but with proper regulatory standards in place, such an occurrence is minimized<sup>2,3,4,5,6</sup>.

## When to Use Electrolysis

Electrolysis can be most advantageously employed for localized areas of hair removal. The regions that are most frequently of cosmetic concern for women are the face, eyebrows, breasts,

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lower abdomen and inner thighs (bikini area), and the axillae. Men sometimes wish to have hair removed from between the eyebrows, around the ears, as well as in areas where ingrown hairs are a problem (the beard area) and on the upper back and shoulders.

Electrolysis is effective but often impractical for large hirsute areas such as the trunk or limbs. Hair removal in such cases can be achieved, but frequent visits are required for up to three hours a week for one or two years and few can afford the time or expense.

A woman undergoing menopausal changes may develop hairs on the chin. In most instances this may require three to six visits, lasting 15 to 30 minutes each. Further followup visits would be required over a period of months to deal with hair regrowth. One or two visits per year afterwards may be required. An individual with dense moustache hair would require more sessions over 12-24 months. Permanent hair removal of a few unwanted hairs around the nipples would require 1 to 5 hours of electrolysis at appropriate intervals.

Rates for electrolysis vary considerably, but typical studio rates are \$40.00 to \$60.00 per hour.

treated. This is important because in some body areas more than 70% of the hairs may be in telogen phase, and telogen hairs do not respond satisfactorily to electrolysis<sup>4,6</sup>.

Minimal postinflammatory erythema and occasional whealing are normal after electrolysis, but these disappear within an hour in most people. Discomfort is usually minimal and *EMLA* (lidocaine/prilocaine cream) and ice packs may be used<sup>7</sup>.

The use of electronic tweezers is not a valid option. This procedure does not produce permanent hair removal because hair is not an electric conductor.

### Conclusion

Of the three modalities, galvanic electrolysis is slow and used the least. Thermolysis and the blend are probably used equally as often. Both are effective and the choice depends on operator preference and experience. There is not clear, documented difference.

The effectiveness of electrolysis is well documented<sup>4,6</sup>, and it is most effective in dealing with hair removal from localized areas. Electrolysis is not as effective in hair removal from large hirsute areas.

HAIR TYPE	VISITS	COST (Estimated)
Chin hairs—few	3 – 6 visits 15 – 30 minutes/visit	\$40 – 60/hour CDN
Moustache hair—dense	Weekly sessions for 6 months, then every second week for 6 months, then once or twice/month for one year	\$40 – 60/hour CDN
Nipple hairs	1 – 5 hours at appropriate intervals	\$40 – 60/hour CDN

### Hypertrichosis and Hirsutism

In hypertrichosis there is little or no new hair growth and the results of electrolysis are rapidly evident. However, in dealing with hirsutism, new hair growth is continually occurring. For best results a team approach might be considered. Electrolysis could be combined with hormonal administration under the direction of an endocrinologist.

Instructing patients about good grooming and stressing that shaving is not harmful will help to maximize improvement and appearance<sup>5,8</sup>.

### Electrolysis Results

The results of electrolysis are well documented. As well, post-treatment biopsy and histopathology studies have shown its effectiveness<sup>4,6</sup>. Electrolysis may be performed on patients with varying skin types, all hair types and colours, or on most anatomic sites on the body. It does not adversely effect nevi or tattoos. Hair removal can also be carried out in the periorbital area.

Shaving one to five days prior to electrolysis greatly increases its efficacy because it ensures that only growing anagen hairs are

### References

- 1 Michel CE. Trichiasis and districhiasis with an improved method for their radical treatment. *St. Louis Clinical Record* 2:145-8 (1875).
- 2 Kligman AM, Peters L. Histologic changes of human hair follicles after electrolysis: a comparison of two methods. *Cutis* 34(2):169-76 (1984 Aug).
- 3 Wagner RF Jr, Tomich JM, Grande DJ. Electrolysis and thermolysis for permanent hair removal. *J Am Acad Dermatol* 12(3):441-9 (1985 Mar).
- 4 Hobbs ER, Ratz JL, James B. Electrosurgical epilation. *Dermatol Clin* 5(2):437-44 (1987 Apr).
- 5 Richards RN, Meharg GE. Electrolysis: Observations from 13 years and 140,000 hours of experience. *J Am Acad Dermatol* 33(4):662-6 (1995 Oct).
- 6 Richards RN, Meharg GE. *Cosmetic And Medical Electrolysis And Temporary Hair Removal*. 2nd Edition. Toronto: Medric Ltd (1997).
- 7 Wagner RF, Flores CA, Argo LF. A double blind placebo controlled study of a 5% lidocaine/prilocaine cream (EMLA) for topical anesthesia during thermolysis. *J Dermatol Surg Oncol* 20(2):148-50 (1994 Feb).
- 8 Richards RN, McKenzie MA, Meharg GE. Electroepilation (electrolysis) in hirsutism. 35,000 hours' experience on the face and neck. *J Am Acad Dermatol* 15(4 Pt. 1): 693-7 (1986 Oct).
- 9 Richards RN, Uy M, Meharg GE. Temporary hair removal in patients with hirsutism: a clinical study. *Cutis* 45(3):199-202 (1990 Mar).

**The following chart lists a number of these new generation steroids.**

Product	Safety	Class	Side Effects	Allergy group
<b>Budesonide</b> <i>Entocort</i> Astra	Stable, asymmetric acetone. Undergoes rapid biotransformation in the liver with fewer systemic effects.	III (high)	There may be a problem with contact sensitivity.	Group B
<b>Mometasone Furoate</b> <i>Elocom</i> Schering-Plough	This stable drug is a chlorinated topical steroid. It has low penetration with high biliary excretion, and low resorption in the circulation with rapid biotransformation in the liver. Consequently, there is minimal systemic activity. The result: local side effects are rare.	III (high)	Contact hypersensitivity is very rare.	Group D <sub>1</sub>
<b>17-Carbonates:</b> <b>Prednicarbate</b> <i>Dermatop Emollient Cream</i> Hoechst-Roussel  <i>Prednitop</i> Hoechst	Labile pro-drug, transformed in the skin into prednisolone.	III (high)	Contact hypersensitivity is not rare. Can cross-react with group A.	Group D <sub>2</sub>
<b>C-21-Carboxylates:</b> <b>1. Fluocortin butylester</b> <i>Varlane</i> Schering Corp.-Essex  <b>2. Alclometasone Dipropionate</b> <i>Modraderm</i> Schering-Plough <i>Aclovate</i> Glaxo Wellcome  <b>3. Methylprednisolone aceponate</b> <i>Advantan</i> Schering Corp.-Essex	In the skin, biotransformed into the nonactive fluocortolone-21-acid.  No longer available in Europe  Labile pro-drug. Transformed in the skin into methylprednisolone, in the liver into nonactive derivatives.	II (medium)  III (high)  III (high)	Contact hypersensitivity is probably rare.  Contact hypersensitivity is not rare.  Contact hypersensitivity is not rare.	Group C  Group D <sub>2</sub>  Group D <sub>2</sub>
<b>Carthioates:</b> <b>Fluticasone propionate</b> <i>Cutivate</i> Glaxo Wellcome	Fluticasone is a fluorinated topical corticosteroid, which is rapidly metabolized in the liver. This results in a locally potent steroid with a low HPA inhibitory potency.	III (high)	Contact hypersensitivity is very rare.	Group D <sub>1</sub>

Because these agents act via hepatic and extra hepatic biotransformation, they offer a greater systemic safety. However, in very young children, and in erythrodermic patients, one should consider HPA suppression, even with the new corticosteroids.

With restricted duration of treatment (up to 6 weeks), clinical safety has been claimed.

Some of the newer corticosteroids, particularly budesonide and, to a lesser extent, prednicarbate and alclometasone dipropionate, are more prone to cause contact allergic reactions.

**Conclusion**

Over the past several years, a new series of corticosteroids have been introduced. They act primarily on the upper level of the skin where they interact with the most important inflammatory mediators, while simultaneously sparing the deeper layers. Trials currently underway worldwide are demonstrating that the newer

corticosteroids with their improved risk-benefit ratio are as efficacious as products currently in use with better safety. There are also unsubstantiated claims that these drugs have fewer side effects. Fewer side effects are not only desirable from a clinical point of view, but have also been shown to increase patient compliance with therapy<sup>2</sup>.

**References**

- Degreef H, Doms-Goossens A. The new corticosteroids: are they effective and safe? *Dermatol Clin*, 11(1):155-60 (1993 Jan).
- Hadzija BW, Ambrose WW. Comparison of cosmetic and physicochemical properties of six topical corticosteroid creams. *Cutis*, 57(2 Suppl):13-8 (1996 Feb).
- Oranje AP. American Academy of Dermatology, New Orleans (1999 Mar).
- Coopman S, Degreef H, Doms-Goossens A. Identifications of cross reaction patterns in allergic contact dermatitis from topical corticosteroids. *Br J Dermatol* 121(1):27-34 (1989).
- Matura M. *Contact Allergy to Locally Applied Corticosteroids* [dissertation]. KU Leuven, Belgium (1998 Sep).
- Goossens A, Matura M. *Corticosteroids in Occupational Skin Diseases*, 3rd edition by Adams R. WB Saunders Company, Philadelphia, USA (1999).

## Update on Drugs

Class	Name/Company	Approval Dates and Comments
<b>Corticosteroids</b>	<b>Alendronate</b> <i>Fosamax</i> Merck	The US FDA approved this drug in June, 1999, for treatment of glucocorticoid-induced osteoporosis in patients receiving glucocorticoids in a daily dosage equivalent to $\geq 7.5$ mg prednisone and who have low bone mineral density.
<b>Anticancer Agents</b>	<b>Alitretinoin</b> <i>Panretin Gel 0.1%</i> Ligand Pharmaceutical	The US FDA approved this small molecule, nonpeptide hormone in January, 1999, for topical therapy for cutaneous lesions in patients with AIDS-related Kaposi's Sarcoma. In June, 1999, HPB Ottawa issued a Notice of Compliance for this gel for the same indications.
<b>Anthelmintic Agents</b>	<b>Malathion</b> <i>Ovide 0.5% Lotion</i> Medicis Pharmaceutical	The US FDA approved this lotion in May, 1999, for treatment of head lice and their ova.
<b>HIV and AIDS</b>	<b>Abacavir Sulfate</b> <i>Ziagen</i> Glaxo Wellcome Inc	HPB Ottawa approved this nucleoside analogue reverse transcriptase inhibitor in June, 1999, for the treatment of HIV and AIDS.
<b>Anticancer Agents</b>	<b>Interferon alpha-2a</b> <i>Roferon-A</i> Hoffmann-La Roche	The European Commission (CPMP) approved this drug in June, 1999, for the adjuvant treatment of malignant melanoma patients at risk of relapse following resection.
<b>Topical Anesthetics</b>	<b>Lidocaine Patch 5%</b> <i>Lidoderm</i> Endo Pharmaceuticals	The US FDA approved this topical anesthetic in May, 1999, for treatment of pain associated with postherpetic neuralgia. The patch is an adhesive material with 5% lidocaine applied to a nonwoven polyester felt backing. The lidocaine is released into the epidermal and dermal layers of the skin.
<b>Antidiabetic Agents</b>	<b>Pexiganan acetate</b> <i>Locilex cream 1%</i> Magainin Pharmaceuticals	The US FDA has deemed this new drug as NOT approvable in July, 1999. It was intended to treat diabetic foot ulcers.
<b>Photodynamic Therapy</b>	<b>Aminolevulinic acid</b> <i>Levulan Photodynamic Therapy</i> DUSA Pharmaceuticals	The US FDA issued an approvable letter in June, 1999, for the treatment of multiple actinic keratoses of the face and scalp.
<b>Drug News</b>		
<b>Antifungal Agents</b>	<b>Ketoconazole</b> <i>Teva</i>	The US FDA approved this generic version of 200 mg ketoconazole tablets in June, 1999. They are AB rated and bioequivalent to Janssen's Nizoral <sup>®</sup> tablets.
<b>Antiviral Agents</b>	In May, 1999, The Canadian Dermatology Committee (CDC) recommended that all children entering preschool or elementary school should be immunized against chicken pox. Previously, the CDC and the American Academy of Pediatrics advocated that this immunization should take place between the ages of 12-18 months.	
<b>Antirejection Therapy</b>	The US FDA approved a generic formulation of cyclosporine ( <i>SangCya</i> —Sangstat) in May, 1999. The generic formulation appears to be bioequivalent and therapeutically equivalent to <i>Neoral</i> , and both have been more consistent in bioavailability than <i>Sandimmune</i> .	

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Articles are indexed by drug names, trade-names (italicized), and disease terms.

**Drug name**      **Issue #: Page #**

Isotretinoin      5: 3,4 (bold entries refer to major references)

17-Beta-Estradiol	5:6	Butylcyanoacrylate	<b>5:3-4</b>	Doxorubicin	1:6;3:4
22-Oxacalcitrol	4:4	<i>Caelyx</i>	1:6;3:4	Dysmenorrhoea	4:2
Abacavir	3:4,6	Calcipotriol	3:5	<i>Dysport</i>	5:2
ABX-EGF	4:3	<i>Candida albicans</i>	2:4	Dystonia	5:1
ABX-IL8	4:3	<i>Cell Cept</i>	4:4	Eczema, infected	1:3-4
ACE inhibitors	3:2	Cerebral palsy	5:1-2	Efavirenz	1:6;3:4
Acne in females	1:4	Cerebrospinal fluid leak closure	5:3	Electrolysis	<b>6:3-4</b>
Acne vulgaris	1:3-4;4:1-2,5;5:6	Cervical dystonia	5:1-2	<i>EMLA cream</i>	3:5;5:4,6;6:3-4
Actinic keratoses	1:4	Cetirizine	1:6;2:6;3:5	<i>EMLA patch</i>	2:6
Actinomycotic mycetoma	1:3	Chemical peel	1:3	Erythema nodosum leprosum	1:2,4;3:4
<i>Activelle</i>	3:5	Chicken pox	6:6	Estradiol/norethindrone	3:5
Acyclovir	1:3;3:4	Chronic fatigue syndrome	5:1	Estrogen + cyproterone	1:4
Adapalene solution 0.1%	3:3	Cicatricial pemphigoid	1:3	Estrogen + progestin	1:4
<i>Adatosil</i>	5:4	Cimetidine	1:3	Estrogen/progestogen	4:1
AE-941	4:3	<i>Claritin</i>	2:6	Facial plastic surgery	5:3
AGN-4310	4:3	Clindamycin, topical	1:3	Facial wrinkles	1:4; <b>5:1-2</b>
AIDS	3:6	Clofazimine	1:3	Famciclovir	1:6;3:4
Alatrofloxacin (IV)	3:3	Combisor	4:4	<i>Famvir</i>	1:6;3:4
Alclometasone dipropionate	<b>6:1-2,5</b>	<i>Combivir</i>	3:4	Fibromyalgia	5:1
Alcohol	3:2	Corneal perforations	5:3	Finasteride 1mg tab	3:5,6
<i>Aldara</i>	2:6;3:4;3:6	Corticosteroids	1:3;3:1;6:1-2,5	Firm scars/acne scars	2:1
Aldesleukin	3:6;4:6	Cranio-facial surgery	2:1	Fluconazole	2:4-5
Alitretinoin gel 0.1%	2:6	Crohn's disease	3:2	Fluocortin butylester	<b>6:1-2,5</b>
Anal fissures	1:4	Crow's feet	5:1	Fluticasone propionate	5:6; <b>6:1-2,5</b>
Androgenetic alopecia	4:2	CTLA4-Ig Antibodies	4:3	Folliculitis caused by <i>S. aureus</i>	1:3-4
Anthralin and coal tar	3:2	<i>Cutivate cream</i>	5:6	Fordeyce disease	1:4
Antifungal therapy	2:3	Cyanoacrylates	5:3-4	<i>Fosamax</i>	6:6
Antihistamines	2:6	Cyclosporin	2:6	<i>Foscan</i>	5:6
Antimalarials	3:2	Cyclosporine	1:3;3:5	Galvanic Electrolysis	<b>6:3-4</b>
Antiretroviral agents	1:6	Cyproterone acetate/ ethinyl estradiol	3:3;4:1	Gingko biloba	5:6
APC-2059	4:3	Dacarbazine	4:6	Ginseng	5:6
Apthous ulcers	1:4	Dapsone	1:3	Glabellar frown lines	2:1;5:1
<i>Apligraf</i>	1:6,3;5	Darier's disease	1:4	<i>GluStitch</i>	5:4
<i>Artecoll</i>	<b>2:1-2,3,5</b>	Dark shadowed eyelids	2:1	Gold salts	3:2
Arthrocondidia	2:4	<i>Denavir</i>	2:6	Graft vs host disease	1:4
Aspirin	5:4	Denileukin diftitox	1:6;3:4	Graftskin	1:6;3:5
Atopic dermatitis	1:3;5:6	Dental prostheses	2:1	Granuloma annulare	1:3
Atrophic skin disease	2:2	Depressed corners of the mouth	2:1	Griseofulvin	2:4
Atrophic vaginitis	5:6	Depressions after rhinoplasty	2:1	Hair transplantation	<b>5:3-4</b>
<i>Avita</i>	3:3	<i>Dermabond</i>	2:6;5:4	Hansen's disease	1:3
Azelaic acid	1:3	Dermatitis herpetiformis	1:3	Headache	5:1
<i>Bactroban Cream</i>	3:3;5:6	Dermatomyositis, systemic	1:4	Hemi-facial spasm	5:1
Becaplermin gel 0.01%	3:4;4:6;5:6	Dermatophytes	2:4	Hemorrhoids	1:4
<i>Benealfa</i>	4:4	Dermatophytoma	2:3	Herpes genitalis	1:3,6;3:4
Beta blockers	<b>3:1-2</b>	Dermatoses of the scalp	4:6	Herpes labialis	2:6
Beta-hemolytic streptococci	1:4	Dermatitis, subcorneal pustular	1:3	Herpes simplex	1:3;3:4
Betamethasone valerate foam	4:6	Diabetic ulcer	3:4;4:6;5:6	Herpes zoster	1:3;3:4
Blastomycosis	5:6	<i>Diane 35</i>	3:3; <b>4:1-2,5</b>	Hidradenitis suppurativa	1:4
Blepharospasm	5:1-2	<i>Dianette</i>	<b>4:1-2,5</b>	Hip implants	2:1
BMS 188667	4:3	<i>Diastabol</i>	3:3-4	Hirsutism	1:4;4:1;6:3
Bone cement	2:1	<i>Differin</i>	3:3	<i>HistoAcryl</i>	5:4
<i>BOTOX</i>	5:2	<i>Diflucan</i>	2:5	Histoplasmosis	5:6
Botulinum toxin type-A	<b>5:1-2</b>	<i>Dovonex</i>	3:5	HIV	2:4;3:1,4
Budesonide	<b>6:1-2,5</b>			HIV-1	1:6

Horizontal forehead lines	5:1	Mucocutaneous candidiasis	2:4	<i>S. pyogenes</i>	1:3,4
Horizontal frontal furrows	2:1	Mupirocin	1:4;3:3;5:6	SAHA syndrome	4:2
Horizontal neck lines	5:1	Mycobacterial infection	1:4	<i>SangCya</i>	2:6;3:5;6:6
Hu 1124	4:3	Mycophenolate Mofetil	4:4	Sarcoid	1:3,4
Hydroquinone 4%/glycolic acid/ antioxidant complex	3:5	Mycosis fungoides	1:4	Seborrhea	4:1
Hyperhidrosis	<b>5:1-2</b>	N-2-butylcyanoacrylate	<b>5:3-4</b>	Silicone	5:4
Hyperpigmentation, facial	1:4;6:3-4	Nail disorders	4:6	Single crow's feet	2:1
Hypertrichosis	<b>6:3-4</b>	Nasolabial folds	2:1	Skin augmentation	3:5
Ichthyosis vulgaris	1:4	<i>NeuroBloc</i>	5:2	Skin infections	1:4
ICM 3	4:3	Nevirapine	1:6;3:4	Skin roughness, facial	1:4
Ichthyosis congenita	1:4	Nitroglycerin	1:4	Skin substitute	3:5
Imiquimod	2:6;3:4,6	Norgestimate/ethinyl estradiol	3:3	Soft tissue augmentation	<b>2:1,5;4</b>
Impetigo	1:4;5:6	NSAID's	3:2;5:4	Split thickness skin grafting	5:3
<i>Indermil</i>	5:4	Octylcyanoacrylate	2:6; <b>5:3-4</b>	<i>Sporanox</i>	2:5;5:6
Inflammatory papules	2:6	<i>Ontak</i>	1:6,3:4	Squamous cell carcinoma	5:6
Interferon	3:2	Onycholysis	4:6	St. John's wort	5:6
Intra-ocular lenses	2:1	Onychomycosis	2:3	Strabismus	5:1-2
IR-502, T-cell receptor (TCR)	4:3	<i>Ortho Tri-cyclen</i>	3:3;4:5	SU 5271	4:4
Isotretinoin	1:4;4:2,5	<i>Ovide 0.5% Lotion</i>	6:6	Sulfasalazine	1:4
Itraconazole	<b>2:3-5;5:6</b>	Oxiconazole nitrate	3:3	<i>Sustiva</i>	1:6;3:4
Kaposi's sarcoma	1:4,6;2:6;3:4	Paclitaxel	4:4,6	T. versicolor	3:3
Keloids	2:2	<i>Panretin</i>	2:6;6:6	Tacalcitol	4:4
Keratosis follicularis	1:4	Paronychia	4:6	<i>Taxop</i>	4:6
Ketoconazole	2:4;6:6	Pemphigoid	1:3	T-cell lymphoma	1:6;3:4;4:6
Köbner phenomenon	3:2	Penciclovir	2:6	Temozolomide	4:6
<i>Lamisil</i>	2:5;4:6	Peptide therapeutic psoriasis vaccine	4:3	Temporal mandibular joint pain	5:1
Lamivudine 150mg	3:4	Perioral lines	2:1	Terbinafine	<b>2:3-5;4:6</b>
Laser resurfacing	1:3	Pexiganan acetate	6:6	Tetracycline	4:2
Leprosy, dapson resistant	1:3	Philtrum augmentation	2:1	Thalidomide	1:2,4;3:3-4
Leprosy, lepromatous	1:3,4	<i>Photofrin Benzoporphyrin</i>	4:4	Thermolysis	<b>6:3-4</b>
<i>Levulan Photodynamic Therapy</i>	6:6	Pityriasis rubra pilaris	1:4	Tinea pedis	4:6
LFA3-TIP	4:3	Platysmal bands	5:1	Tissue adhesives	<b>5:3-4</b>
Lidocaine	2:1,6;4:6	PMMA microspheres	2:1-2	Tretinoin gel 0.25%	3:3
<i>Lidoderm patch</i>	4:6;6:6	<i>Pneumocystis carinii</i>	1:4	Tretinoin	1:4
Lip augmentation	2:1	Pneumonia	1:4	Trimethoprim	1:4
Liposuction	5:6	Polychondritis, relapsing	1:3	Trovafoxacin (oral)	3:3
<i>LiquiBand</i>	5:4	Polymethylmethacrylate	3:5	Tuberculosis	1:6
Lithium	3:1	Polymyositis	1:4	Unevenness and dimples after facelifting	2:1
<i>Locilex cream 1%</i>	6:6	Polysystic ovary disease (PCO)	4:2	Unlabelled drug use	<b>1:1-5</b>
Loratidine	2:6	Porfimer sodium	4:4	Upper limb spasticity	5:2
Low-tension lacerations	5:3	Post-herpetic neuralgia	4:6	Urticaria	1:3,6;3:5
Lupus erythematosus, cutaneous	1:4	Post-inflammatory facial hyperpigmentation	1:4	UV induced skin discoloration	3:5
Lupus erythematosus, systemic	1:3	Prednicarbate	<b>6:1-2,5</b>	Uvadex	4:6
<i>Lustra</i>	3:5	<i>Priftin</i>	1:6	<i>Vagifem</i>	5:6
<i>Luxiq 0.12%</i>	4:6	<i>Proleukin</i>	3:6;4:6	Varicella vaccine	1:3;3:6
Lyme disease vaccine	2:6;3:4,6	<i>Propecia</i>	3:5,6	Vasculitis	1:4
Male pattern hair loss	1:1,3;5,6	Protease inhibitors	1:6	Venous leg ulcers	1:6
Malignant melanoma	4:6	Psoriasis	1:1,4;2:6; <b>3:1-2,5;4:3</b>	Verruca plana	1:4
Maxacalcitol	4:4	Punctal occlusion	5:3	<i>Viquin Forte</i>	3:5
Melasma	1:3,4	Pyoderma gangranosum	1:3	<i>Viramune</i>	1:6;3:4
Metastatic melanoma	3:6;4:6	Refractory aspergillosis	5:6	Vitamin A acid	1:4
Methotrexate	1:1,4	Refractory pain associated with spasticity	5:1	Vitiligo	1:3
Methoxsalen	4:6	<i>Regranex</i>	3:4;4:6;5:6	Vulvar & Vaginal atrophy	3:5
Methylprednisolone aceponate	<b>6:1-2,5</b>	Retinoic acid	1:4	VX-497	4:4
Metronidazole 0.75%	2:6;3:5	Rhinitis, chronic	1:6	Warts	1:3;2:6;3:4
Miglitol	3:3-4	Rifapentine	1:6	Wire-brush surgery	1:3
Minocycline	4:2	<i>Roferon-A</i>	6:6	Wound closure	2:6; <b>5:3-4</b>
Minoxidil	1:1;3:6	Rosacea	1:4;2:6;3:5	<i>Ziagen</i>	3:4,6;6:6
Mizolastine	3:3,5	Roxithromycin	5:6	Zidovudine 300mg	3:4
Mometasone furoate 0.1% & salicylic acid 5%	4:4; <b>6:1-2,5</b>	<i>Rulid</i>	5:6	<i>Zovirax</i>	3:4
Monoclonal antibody products	4:3	<i>S. aureus</i>	1:3,4	<i>Zyplast</i>	2:2
				<i>Zyrtec</i>	1:6;2:6