Topical agents such as clindamycin, erythromycin and benzoyl peroxide have been mainstays in the treatment of acne vulgaris for the past two decades. Previous studies have demonstrated that the combination of erythromycin and benzoyl peroxide was more effective than either agent used alone.1,2 This article reviews the pivotal studies for Clindoxyl® Gel, a combination of 1% clindamycin phosphate and 5% benzoyl peroxide that is supplied in a ready-to-use tube, so compounding is not necessary.

**Indications and Clinical Use**

Clindoxyl® Gel was approved by TPP Canada in November 2001, and is indicated in the topical treatment of moderate acne vulgaris characterized by comedones and papulopustules.

This product is contraindicated in patients with a history of hypersensitivity to products containing clindamycin, lincomycin, benzoyl peroxide or any other component of the preparation. Relative contraindications also include: a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis.

**Review of Clinical Studies**

Three pivotal, randomized, controlled, double-blind trials were performed with Clindoxyl® Gel involving a total of 673 patients.3 Results from two of these studies have previously been reported.4 Inclusion criteria in all 3 studies included facial acne vulgaris with a minimum of 12 comedones, 12 papules and/or pustules, and a maximum of:

<table>
<thead>
<tr>
<th>Agent</th>
<th>Non-inflammatory Lesions</th>
<th>Inflammatory Lesions</th>
<th>% patients with good-excellent improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindoxyl®</td>
<td>14.8 (32%)*</td>
<td>12.5 (53%)</td>
<td>51</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>5.0 (10%)</td>
<td>9.1 (37%)</td>
<td>40</td>
</tr>
<tr>
<td>Benzoyl Peroxide</td>
<td>12.8 (25%)</td>
<td>10 (37%)</td>
<td>38</td>
</tr>
<tr>
<td>Vehicle</td>
<td>1.2 (1%)</td>
<td>4 (14%)</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 1: Reduction in lesion count and Global Improvement Scores at end of study (week 11).

*denotes mean lesional count reduction from baseline (% reduction from baseline).
3 nodulocysts. Patients were randomized to receive Clindoxyl®, clindamycin, benzoyl peroxide, or vehicle gel and instructed to apply the study medication to the entire face once daily in the evening for 11 weeks. Efficacy evaluations comprised lesion counts and investigator global assessments.

In all studies, no significant differences in demographic features or lesional counts were noted between treatment groups at baseline.

A summary of results from pooling the data from the 3 studies is shown in Table 1. Clindoxyl® demonstrated a significantly greater reduction of non-inflammatory lesions than clindamycin and vehicle groups (with P values ranging from 0.000-0.037) at 11 weeks. Furthermore, Clindoxyl® was significantly more effective than the vehicle at reducing inflammatory lesions at week 11. Pooling data from the 3 studies demonstrated that Clindoxyl® treated patients had a significantly greater mean and percent reduction in total lesion counts, and greater mean global improvement scores at week 11 when compared to the other treatment groups.

**Adverse Events**

In the three pivotal studies, 343 adverse events were reported on 255 patients. No significant difference in frequency of adverse events between the treatment groups was noted (Table 2). Of the 113 adverse events reported with Clindoxyl®, nine were related to the study medication (7 cases of mild-to-moderate pruritus, erythema, and dryness; 1 case of worsening of acne; 1 case of mild paresthesia). Overall tolerance was rated excellent in 94% of the patients who were treated with Clindoxyl® Gel.

**Summary**

Clindoxyl® Gel, a combination of 1% clindamycin phosphate and 5% benzoyl peroxide, is efficacious and well tolerated in the treatment of moderate acne vulgaris. Furthermore, this combination product is more efficacious than either agent individually.

**References**


<table>
<thead>
<tr>
<th>Agent</th>
<th>Number of Patients</th>
<th>Number of Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindoxyl®</td>
<td>78 (42%)</td>
<td>113</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>67 (36%)</td>
<td>84</td>
</tr>
<tr>
<td>Benzoyl Peroxide</td>
<td>74 (39%)</td>
<td>97</td>
</tr>
<tr>
<td>Vehicle</td>
<td>36 (33%)</td>
<td>49</td>
</tr>
</tbody>
</table>

Table 2: Frequency of Adverse Events
Systemic Antibiotic Therapy for Acne: A Review
R. Kunynetz, MD, FRCPC
Division of Dermatology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

ABSTRACT
Acne is a multifactorial disease of the pilosebaceous unit in the skin. Four contributing pathogenic factors need to be elucidated and include excess sebum production, follicular hyperkeratinization, colonization of the pilosebaceous unit by Propionibacterium acnes, which is a gram positive anaerobic diphtheroid, and the release of inflammatory mediators into the follicle and dermis. One or more of these factors are targeted by each of the systemic therapies for this disease and its variant, including systemic antibiotic therapies, which will be reviewed here.

Key Words: acne, antimicrobial agents, tetracyclines, macrolides, clindamycin, trimethoprim-sulfamethoxazole

A limited number of antimicrobial agents have proven to be effective in acne therapy, both topically and systemically. Antimicrobials not only affect colonization of the follicle by Propionibacterium acnes, (as seen by reduced Wood’s lamp fluorescence of porphyrins in P. acnes), but also affect the inflammatory mediators in the follicle and dermis by decreasing neutrophil chemotaxis, and by modifying both complement pathways. Through inhibition of lipase production via protein synthesis inhibition, antimicrobials also result in a reduction of skin surface sebum fatty acid composition.

Tetracyclines
The tetracycline family of antibiotics is broad spectrum with activity against many gram-positive and gram-negative bacteria, as well as mycoplasma, Chlamydia, Rickettsiae, Spirochetes and some parasites. Activity is becoming more limited by the emergence of resistant strains of gram-negatives, group A Streptococcus, and P. acnes. They inhibit protein-synthesis by binding to the 30S ribosomal subunit.

Pharmacokinetics
Absorption on an empty stomach is mandatory except with minocycline or doxycycline, which do not vary in the presence or absence of food. Absorption is decreased by concurrent ingestion of dairy products, aluminum hydroxide gels, calcium, magnesium, iron or zinc salts, and bismuth subsalicylate.

Tetracycline has a half-life of 8.5 hours while longer acting synthetic minocycline (11-13 hours) and doxycycline (14-22 hours) require dosing every 12-24 hours instead of q6h with tetracycline. Both synthetic drugs are lipid-soluble, which accounts for their superior tissue penetration. Doxycycline can be used in renal-failure patients without dosage adjustment, as it is primarily excreted in the gastrointestinal tract. All three drugs should be used with caution in hepatic failure due to potential hepatotoxicity.

Drug Interactions
Anticonvulsants (barbiturates, phenytoin, and carbemazepine) reduce the half-life and serum concentration of doxycycline, but not tetracycline. The latter can increase lithium levels. Tetracyclines potentiate oral anticoagulants by decreasing vitamin K bacterial production or impairing prothrombin effects. Though earlier reports suggested a possible decreased oral contraceptive effect due to tetracycline, a recent study concluded that concomitant use of oral antibiotics and oral contraceptives is not associated with a substantially increased risk of pregnancy.

Potential Adverse Effects
The most common adverse reactions are gastrointestinal in origin such as epigastric burning, nausea, vomiting and bloating. Taking the drug with food can reduce such reactions, though absorption may be decreased (except with minocycline or doxycycline). Esophagitis and esophageal ulcers have been reported when ingestion took place just before bedtime with little or no water, and may be associated with hiccups or even mediastinitis.

Liver inflammation is rare, however minocycline has been reported to be associated with fulminant hepatic failure necessitating liver transplantation.

Adverse blood reactions are rare including hemolytic and non-hemolytic anemia, thrombocytopenia, eosinophilia, neutropenia, and minocycline-associated leukemoid reaction.

Phototoxic reactions are usually dose related and present with erythema and edema or porphyria-like skin blistering and fragility. These are more related to tetracycline or doxycycline than minocycline. Photo-onycholysis may accompany the cutaneous changes or present alone. Photoxic reactions usually reverse themselves when the offending drug is discontinued. Fixed-drug eruptions are rare and usually affect the penis. Other common areas of fixed drug eruptions are face and hands (not genitals in females). Anaphylactic reactions have been reported with tetracycline or minocycline use. Cross-reactivity is frequent between...
tetracycline and doxycycline, because their chemical structures are similar. Tetracycline’s and minocycline’s structures differ to a greater extent and so less cross-reactivity is seen. Exanthema from doxycycline, and exfoliative dermatitis from minocycline, have been reported. In addition, erythema multiforme and Stevens-Johnson syndrome, purpuric eruptions such as Sweet’s syndrome, and diffuse pustulosis with lymphadenopathy have also been described.1

Tetracyclines are contraindicated in pregnancy and in children under the age of 9, because they can cause brown discoloration in deciduous teeth. Depression of bone growth has also been reported in children. Minocycline has also been associated with permanent tooth discoloration in adults. Patients were given minocycline from age 15 or 16 for as little as 1 month to as long as 5 years before the onset of pigmentation in the teeth. Tetracycline forms insoluble complexes by chelating with iron.1

Pseudotumor cerebri syndrome has been associated with tetracyclines. It may present with headache (75%), transient visual disturbances (41%), diplopia (41%), pulsatile tinnitus (17%), and nausea and vomiting (25%) usually within 8 weeks of initiation of therapy.7

Gynecomastia has been associated with minocycline, and spondylodiscitis from Enterobacter has been associated with tetracycline.2,8

Doxycycline has been suspected in cases of anosmia (loss of smell) and dysosmia (abnormal smell perception).1

Minocycline has long been associated with specific adverse effects: vertigo, and blue pigmentation of skin, teeth, nails, and visera. Vertigo is experienced more in females (70% vs. 28% of males) and can be minimized by gradual dose increases and by taking the medication in the evening.1 Hyperpigmentation or blue-black discoloration can be seen after only 3-6 months of therapy and tends to locate in scar tissue or sun-exposed sites, usually fading on cessation of therapy. Q-switched ruby laser has been reported effective for treating this condition.5 The cause is thought to be iron deposits, oxidized minocycline deposits, iron-minocycline complex and melanin.1 Buccal mucosa, conjunctiva, lips, and affected bone are visible through oral alveolar and palatal mucosa.1 Legs are the most common site and mimic bruises, however other sites include the thyroid, substantia nigra, and conjunctival cysts. Atherosclerotic plaques and pigmented osseous cutis have also been reported. Black discoloration of breast milk has been described.1

More recently minocycline-associated side effects of a potentially more-serious nature have been described, i.e., the exacerbation of systemic lupus.1 Cases are seen typically in young females after several years of therapy, and resolve quickly on drug cessation.1 The syndrome includes joint pain swelling and stiffness, malaise, and positive anti-nuclear antibody. Pleuritic chest pain and fever may or may not be present, however, characteristic skin, renal and neurologic systems are not affected. Patients developing arthralgias (especially in females) while on minocycline therapy require anti-nuclear antibody and liver enzyme quantification.

A hypersensitivity syndrome similar to that seen with anticonvulsants has presented after an average of 24 days of therapy. Its symptoms include fever, lymphadenopathy, eosinophilia, lymphocytosis, hepatitis, and many forms of rashes ranging from toxic epidermal necrolysis, pustulosis, and exfoliative dermatitis to non-specific exanthesms.5 Splenomegaly, pulmonary edema, and renal involvement are present, though joints are spared. Minocycline therapy must be immediately replaced by systemic steroids. Liver failure with further transplantation has been reported.6

A serum sickness-like reaction may present after taking minocycline for an average of 15 days.6 Urticaria or exanthem with fever, joint pains, and lymphadenopathy are characteristic.5 Pneumonitis presenting with shortness of breath and acute hepatic failure has also been cited.6

**Bacterial Resistance**

Tetracycline-resistant P. acnes has been shown to be resistant to doxycycline, but not to minocycline at 100 mg/day.1

**Macrolides**

Erythromycin is a prototype of the macrolide family of antibiotics, which include the newer azithromycin (Zithromax®), clarithromycin (Biaxin®), dirithromycin (Dynabac®), and roxithromycin (Rulid®). Of the four, only azithromycin has been significantly studied in acne therapy.9,10 Their mechanism of action is the same for all: bacterial cell wall penetration with reversible binding to the 50S ribosomal unit with RNA-dependent protein synthesis inhibition.2

**Antimicrobial Activity**

The activity of azithromycin against gram-positive organisms such as staphylococci and streptococci is one-half to a quarter of that of erythromycin. Erythromycin-resistant strains of staphylococcus and streptococcus show cross-resistance to the new agents. Anaerobic activity is similar to erythromycin, but gram-negative activity is greater. Azithromycin has activity against pathogens found in human and animal bites, atypical mycobacteria, and Borrelia burdorferi.2 Its minimum inhibitory concentration against P. acnes is similar to other macrolides.10

**Pharmacokinetics**

The newer macrolides’ main advantage is consistent oral bioavailability:

- Clarithromycin - 50%, independent of food
- Azithromycin - 37%, 1 hr a.c. or 2 hr p.c.
• Both have higher tissue concentrations than erythromycin.

In contrast to primary renal excretion with clarithromycin, azithromycin’s is hepatic. Its metabolites are not bioactive, unlike clarithromycin’s. Dosage adjustment is not needed with azithromycin in renal impairment. Its serum half-life is 11-14 hours, followed by an increased half-life of 68 hours.2

**Drug Interactions**

Erythromycin through drug-drug interaction inhibits the cytochrome P-450 enzyme system, thus decreasing the metabolic clearance of carbamazepine, theophylline, phenytoin, digoxin, warfarin, terfenadine and methylprednisolone. Clarithromycin, unlike azithromycin, can also inhibit this enzyme system.2

Pharmacokinetics of the HIV drug zidovudine (Retrovir®) are not altered by azithromycin, but clarithromycin reduced absorption by 20% and is best given 2 hours before or after zidovudine.2

**Adverse Effects**

Azithromycin and clarithromycin are well tolerated and cause gastrointestinal upset in about 3% of patients, appreciably less than erythromycin at 20-35%.9 Erythromycin-induced hepatotoxicity is seen more with the estolate form due to cholestasis. Rarely have reports of pancreatitis, exacerbation of myasthenia gravis, and pruritic eruptions from erythromycin been cited. Ototoxicity seems to be associated with higher than normal doses than that used for acne, presenting with high-frequency sensorineural hearing loss and vertigo.1 Clarithromycin and azithromycin have similar adverse effects such as headache (1-2%), elevated liver enzymes (<1%), and changes in white blood cell count (1%).9

**Clindamycin**

Clindamycin, a derivative of lincomycin, binds to the 50S portion of the ribosome and inhibits protein synthesis.

**Antimicrobial Activity**

Clindamycin is active against most anaerobes, gram-positive *cocc* i and some protozoa. Enterococci are generally resistant. Most aerobic gram-negative organisms are resistant. Its anaerobic activity includes *P. acne*.2

**Pharmacokinetics**

Clindamycin is well absorbed from the gastrointestinal tract and distributed in good concentrations to most tissues except cerebral spinal fluid and bile.2 It is metabolized in the liver with dosage adjustments needed for hepatic insufficiency.

---

### Table 1: Systemic antibiotics and acne.

*set cost to patient ranging from generic to brand name sources in Canadian dollars. Does not include dispensing fee, which varies greatly.

<table>
<thead>
<tr>
<th>Antibiotic in general</th>
<th>Characteristics</th>
<th>Cost/Month *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics in general</td>
<td>Vaginal candidiasis; resistant strains; gram-negative folliculitis; pseudomembranous colitis (especially clindamycin and broad spectrum antibiotics).</td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td><em>P. acnes</em> sensitive; inexpensive; dietary restriction in timing of dose; tooth discoloration (under age 9); avoid during pregnancy; photosensitivity</td>
<td>$2.57 (120 tabs)</td>
</tr>
<tr>
<td>Minocycline</td>
<td><em>P. acnes</em> very sensitive; lipophilic; expensive minimal resistance and photosensitivity; rarely pigmentation scars; oral mucosa; dizziness (dose related); hypersensitivity reaction with hepatitis; avoid during pregnancy and in children under 9 years of age.</td>
<td>$34.10 - $39.97 (30 tabs)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>Lipophilic: <em>P. acnes</em> very sensitive; resistance rare; higher photosensitivity, so patient should test sun tolerance; expensive; avoid during pregnancy and in children under 9 years of age.</td>
<td>$19.34 - $53.73 (30 tabs)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td><em>P. acnes</em> sensitive but increasing resistance; gastrointestinal upset may limit dose; hepatotoxicity more with estolate form; inexpensive; ok for use in pregnancy and in children under 9 years of age; not first line therapy.</td>
<td>$5.98 - $58.06 (60 - 120 tabs)</td>
</tr>
<tr>
<td>Trimethoprim-Sulfamethoxazole</td>
<td>Lipophilic: <em>P. acnes</em> very sensitive; crystalluria (push fluids); bone marrow suppression; hypersensitivity reactions (erythema multiforme, toxic epidermal necrolysis).</td>
<td>$4.03 (30 tabs)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td><em>P. acnes</em> very sensitive; somewhat lipophilic; pseudomembranous colitis makes it third-line drug.</td>
<td>$35.86 (60 tabs)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Sensitivity spectrum similar to other macrolides; drug-drug interaction via cytochrome-P-450 enzyme; no dosage change in renal insufficiency; best taken 1 hour a.c. or 2 p.c.; low gastrointestinal intolerance; less frequent dosing — three times/week instead of t.i.d. for other antibiotics</td>
<td>$65.12 (12 tabs)</td>
</tr>
</tbody>
</table>
Drug Interactions
Neuromuscular blockers such as tubocurarine may have enhanced effects.2

Adverse Effects
*Clostridium difficile* toxin-mediated colitis has been reported in incidences from 0.1-10%.2 This is similar to the rate seen with ampicillin or cephalosporins.7 Gastrointestinal effects include nausea, vomiting, anorexia, and elevated hepatic enzymes. The most frequent side effect is a generalized morbilliform rash, though others reported include urticaria, maculo-papular rash, pruritus, fever, hypotension, polyarthritis, anaphylaxis and erythema multiforme/Stevens-Johnson syndrome.2

Trimethoprim-Sulfamethoxazole (TMP-SMX)
This drug combination selectively attacks bacterial nucleic acid synthesis of tetrahydrofolic acid, which is essential for endogenous protein metabolism in bacteria.2

Antimicrobial Activity
TMP-SMX is active against many gram-positive aerobic cocci (e.g., S. aureus, S. pyogenes, and S. viridans) but S. pneumonia is increasingly resistant to the drug.2 *P. aeruginosa* is invariably resistant, but other *Pseudomonas* species are often sensitive. Anaerobes are usually not susceptible to it.

Pharmacokinetics
Both trimethoprim and sulfamethoxazole are well absorbed in oral form and have half-lives of 11 and 9 hours, respectively. They are excreted renally and are found widely in body fluids and tissues.2

Drug Interactions
TMP-SMX inhibits warfarin metabolism, prolonging prothrombin time. Interference in folic acid metabolism of patients on methotrexate dictates caution in their concomitant use.

Adverse Effects
The more common side effects are minor gastrointestinal upset and hypersensitivity reactions. Stevens-Johnson syndrome and toxic epidermal necrolysis are the most serious, though less ominous pustular eruptions, Sweet’s syndrome, and maculopapular eruptions in patients with AIDS have been reported.2 Reported hematologic changes include aplastic anemia, neutropenia, agranulocytosis, and thrombocytopenia. Headache, fatigue and tremor reflect possible nervous system effects. Potential renal changes include crystalluria, nephrolithiasis and interstitial nephritis. Cholestatic hepatitis is rare.

In pregnancy, if sulfamethoxazole is given near term, it can cause kernicterus in the infant.4 Trimethoprim is a folate antagonist and should be used with caution during pregnancy.

Antibiotic Resistance In Acne Therapy
Bacterial resistance to antibiotic therapy has quickly evolved to encompass not only therapy of true infections, but also propionibacteria, pathogenic in acne. *Propionibacteria* have been found to be resistant to one or more antibiotics in the UK, France, Germany, Japan, New Zealand and the US.3 Prevalence studies from the Dermatology Out-patients’ Clinic at Leeds sampled 2,853 patients between 1991 and 1996, and showed a steady increase of antibiotic-resistant *propionibacteria* from 34.5% in 1991, to 60% in 1996. Erythromycin resistance was the most common and resistance to minocycline was uncommon. Triple-resistance to tetracycline, erythromycin and clindamycin was seen in 16%. Not only is this a concern for the patient, but as well, antibiotic acne therapy promotes resistant coagulase-negative *staphylococcus* and *propionibacteria* on the skin of close contacts to treated patients.3 A profile of acne patients likely to carry such *propionibacteria* is shown in Table 2:

| Likely                                      | • treated with long-term sequential antibiotics  |
|                                            | • poor responders                                |
|                                            | • relapers                                      |
|                                            | • poor compliers                                |
|                                            | • repeated dermatology outpatient visits over long periods |
| Less Likely                                | • patients treated in primary care only          |
| Unlikely                                   | • previously untreated patients                  |
|                                            | • responders                                    |
|                                            | • patients treated without antibiotics           |

Table 2: Likelihood of patients to carry *propionibacteria*.3

The fact that carriage of erythromycin-resistant *propionibacteria* is associated with therapeutic failure of oral erythromycin therapy has been well established. In topical therapy, the addition of either zinc or benzoyl peroxide to erythromycin renders good therapeutic results in patients with erythromycin-resistant *P. acnes* and decreases the number of such organisms on the skin.3 A majority of follicles in non-responding patients have subtherapeutic antibiotic levels.12 This variation is determined by sebum excretion rates, the degree of hyperkeratinization and ducital volumes. Since other therapies such as benzoyl peroxide and azelaic acid do not promote resistance, yet are effective against resistant and sensitive *propionibacteria*, alteration of the follicular microenvironment is hypothesized to be responsible for the
reduction in resistant P. acnes colonization.\textsuperscript{3} This would explain the decrease in resistant P. acnes in 20 patients treated with isotretinoin by Leyden.\textsuperscript{11}

The induction of resistant strains is more likely with longer treatment durations and sequential or concomitant use of structurally unrelated antimicrobials, which select for multiple-drug resistant flora. The onset of the resistant strains occurs between 12 and 24 weeks of therapy.\textsuperscript{3} Emergence of such strains may be related to poor patient compliance allowing for skin and serum drug levels to drop below the MIC of the drug for the given isolates.

There are multiple reasons for antibiotic poor response:\textsuperscript{3}

- Inadequate dose
- Inadequate duration
- Inadequate instruction on how to take/use medication
- Poor compliance
- High sebum excretion rate
- Folliculitis due to overgrowth of gram-negatives, staphylococci or malassezia
- P. acnes resistance

P. acnes resistance to erythromycin has been associated with three specific point mutations in 23S mRNA, which are associated with three phenotypic types of resistant propionibacteria differing in the degree of resistance and cross-resistance to other macrolides and clindamycin.\textsuperscript{3} The mutations appear to be stable and the resistant strains may persist on the skin for long periods despite discontinuation of the drug.

Given the high rate of P. acnes resistance induction, oral erythromycin should be reserved for acne during pregnancy or young children. Erythromycin should not be first line acne therapy.

An acne therapy consensus panel published their “checklist” for minimizing the selection and spread of resistant strains of P. acnes in acne therapy.\textsuperscript{3} These are:

- Prescribe antibiotics only when absolutely needed.
- Prescribe for as short a duration as possible.
- If further therapy is required, re-use the same antibiotic if it is still effective.
- Use benzoyl peroxide for at least 5-7 days or longer between courses to eliminate resistant strains from the skin.
- Avoid the use of concomitant but chemically dissimilar topical and oral antibiotics in the patient.
- Educate patients about medication use and stress compliance.
- Re-educate patients not to expect an endless supply of alternative therapies.
- Retinoids do not promote resistance.

The trend appears to favor the use of oral isotretinoin sooner rather than later in not only severe, but in less severe acne.

**Conclusion**

Despite being the most longstanding systemic therapy for acne, when compared to retinoids and hormonal therapy, antimicrobials will continue to be an effective treatment only if they are used selectively and responsibly. This would involve more in-depth controlled studies into dosage, duration and the role of concomitant therapies. Otherwise, we are in danger of losing this effective and economical treatment in the control of this potentially permanently scarring disease.

**References**

## Update on Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Name/Company</th>
<th>Approval Dates and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipsoriasis Agent</strong></td>
<td><strong>Alefacept</strong></td>
<td>The US FDA’s Dermatologic and Ophthalmic Drug Advisory Committee recommended approval of this selective immunomodulator in May 2002, for the treatment of moderate-to-severe chronic plaque psoriasis.</td>
</tr>
<tr>
<td><strong>Wound Care</strong></td>
<td><strong>Sodium Hyaluronate</strong></td>
<td>The US FDA granted marketing approval in April 2002. Clinical trial results for this product demonstrated an 88% effectiveness rate in healing refractory leg and foot ulcers.</td>
</tr>
<tr>
<td><strong>Depigmenting Agents</strong></td>
<td><strong>Hydroquinone, Tretinoin,</strong></td>
<td>The US FDA granted marketing approval in April 2002, as a short-term treatment for moderate-to-severe melasma of the face in the presence of measures for sun avoidance, including the use of sunscreens.</td>
</tr>
<tr>
<td></td>
<td><strong>Flucinolone Acetonide</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>Tri-Luma® Cream</strong></td>
<td></td>
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<td></td>
<td><strong>Galderma Laboratories</strong></td>
<td></td>
</tr>
<tr>
<td><strong>OTC Products</strong></td>
<td><strong>Loratidine</strong></td>
<td>The US FDA’s Nonprescription Drugs Advisory Committee endorsed approval of this drug in April 2002, as an OTC treatment for chronic idiopathic urticaria, or chronic hives of unknown cause. The committee also recommended that the indications might be broadened to include general hives once sufficient data are submitted.</td>
</tr>
<tr>
<td></td>
<td><strong>Claritin®</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>Schering-Plough</strong></td>
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</tbody>
</table>

### Drug News

**Drug Warning**

Baxter Bioscience issued a warning letter in May 2002, to health care providers regarding the possible association between immune globulin intravenous (human) (IGIV) administration and thrombotic events. They suggest strict attention to the precautionary statements included in the package insert for Gammagard S/D, that recommend exercising caution in the prescribing of IGIV for patients with a history of cardiovascular disease of thrombotic episodes.

**New Drugs and Side-Effects**

A study published in a recent issue of the *Journal of the American Medical Association* estimates that 20% of recently approved prescription drugs have serious side-effects that may only be discovered after a drug has been on the market for years. Researchers suggest that health care providers prescribe older medication whenever possible and that the US FDA set higher standards for approval of new drugs when effective alternatives are available.

*JAMA 287:2215-20 (2002)*

**Atopic Dermatitis Agents**

According to data presented by D. Pariser, et al, at the Society for Investigative Dermatology Congress in Los Angeles, in May 2002, atopic eczema affecting babies, as well as sensitive skin areas such as the face has been successfully treated with the new non-steroid pimecrolimus cream (Elidel®). In patients aged 3 months to 18 years, Elidel® reduced the severity of eczema by an average of 64% over 6 weeks. The prescription medication was first launched in the US in February 2002, for the treatment of mild-to-moderate atopic eczema in patients aged 2 years and older. In March 2002, it gained its first European approval, in Denmark, for the short term treatment of atopic eczema and intermittent long term treatment to prevent progression to flares in patients aged 3 months and above.

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