

Stress as an Influencing Factor in Psoriasis

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ABSTRACT

Emotional stress may influence the development and exacerbation of psoriasis. The proportion of psoriasis patients who believe stress affects their skin condition (i.e., “stress responders”) is considerably high, ranging from 37% to 78%. Stress may worsen psoriasis severity and may even lengthen the time to disease clearance. Although a pathogenic association appears likely, additional well-controlled studies are necessary to confirm such a causal relationship. Dysregulation of the hypothalamus-pituitary-adrenal and sympathetic adrenomedullary systems has been proposed as one possible underlying cause of stress-induced flares of psoriasis. While stress may be an exacerbating factor, psoriasis itself may contribute to significant adverse psychological sequelae. Breaking this stress cycle may be an important part of any therapeutic approach. Thus, stress reduction through psychotherapy and pharmacotherapy may be useful in treating psoriatic patients who are stress responders.

Key words: anxiety, depression, chronic inflammatory disease, psoriasis, stress

Psoriasis is a chronic, inflammatory skin disease with an approximate 2-3% prevalence in the general population.¹ The etiology of psoriasis is not fully understood, but it appears to be multifactorial, involving both genetic and environmental influences. Among these factors, emotional stress (hereafter simply referred to as “stress”) is considered to play an important role in the onset and exacerbation of psoriasis.²

Stress has been indicated as a trigger in many dermatologic conditions, including atopic dermatitis, acne vulgaris, and chronic urticaria. With each of these conditions, one encounters both patients who experience a close chronologic association between stress and exacerbation of their skin disease, and patients for whom their emotional states seem to be unrelated to the natural course of their cutaneous disorder. These two groups are considered “stress responders” and “non-stress responders,” respectively.³

Just as in many dermatologic conditions, psoriasis appears to worsen with stress in a significant segment of patients. Studies report that the proportion of psoriasis patients who are stress-responders ranges from 37% to 78%.⁴

Significance of Stress

Studies define stress along three general categories: 1) major stressful life events (e.g., change of employment, major personal illness, financial problems), 2) psychological or personality

difficulties, and 3) lack of social support.⁵ Regardless of how stress is defined, studies consistently support a relationship between stress and psoriasis.⁵⁻¹² Furthermore, a majority of patients consider stress to be the main cause for exacerbation of their psoriasis, ranking it above infections, trauma, medications, diet, or weather.⁶

For example, Seville⁷ examined 132 psoriasis patients whose psoriasis had completely cleared with anthralin therapy and were followed over 3 years. Fifty-one patients (39%) recalled specific incidents of stress within 1 month prior to psoriasis exacerbation. The study further observed that the incubation time from specific incidents of stress to psoriasis exacerbation was between 2 days to 1 month.⁷ In a subsequent study, Al’Abadie et al.⁸ assessed 113 psoriasis patients and determined the incubation time from stressful event to onset of psoriasis was significantly longer than that from stressful event to exacerbation of psoriasis.⁸

In a study of 127 psoriasis patients, Gupta et al.⁵ found differences between patients who reported that stress flared their psoriasis (stress responders) and patients who reported no association (non-stress responders). Stress-responders described significantly more flare-ups during the 6 months prior to admission, experienced more psoriasis-related daily stress, and relied more upon the approval of others. They also had more severe psoriasis in “emotionally charged” body areas, such as the scalp, face, neck, forearms, hands, and genital region. However,

total percentage of body surface affected by psoriasis was not significantly different.

Similarly, Zachariae et al.⁹ showed that stress responders differed significantly from non-stress responders. Stress responders tended to self-report greater disease severity than non-stress responders, even though clinical measures of disease severity (e.g., Psoriasis Area Severity Index) did not vary between groups. Stress responders were, however, found to have more plaques of psoriasis on visible areas than non-visible regions.⁹

Unlike these above studies, Verhoeven et al.¹⁰ found a significant association between stress and disease severity. This prospective study of 62 psoriasis patients determined high levels of daily stressors to be related to an increase in disease severity 4 weeks later.¹⁰

Finally, stress may not only worsen psoriasis severity, but it may also adversely affect treatment outcomes. Fortune et al.¹³ found that psychological stress impaired the rate of clearance of psoriasis in patients undergoing psoralen + ultraviolet A (PUVA) treatment. Patients with high-levels of worry cleared with PUVA therapy almost two times slower than those with low-levels of worry.¹³

Physiologic Effects of Stress

Normal physiologic response to stress involves activation of the hypothalamus-pituitary-adrenal (HPA) axis and sympathetic adrenomedullary (SAM) axis, both of which interact with immune functions. Generally, in normal individuals, stress elevates stress hormones (i.e., increases cortisol levels). However, according to available studies, exposure to stress in psoriatic patients has been associated with diminished HPA responses and upregulated SAM responses.¹⁴⁻¹⁷ More specifically, when psoriasis sufferers are under such emotional pressures lower plasma cortisol levels¹⁴ and higher epinephrine and norepinephrine levels¹⁵ can be induced, when compared with controls.

Similarly, Evers et al.¹⁶ found psoriasis patients had significantly lower cortisol levels at moments when daily stressors are at peak levels. The study also reported that psoriasis patients with overall high levels of daily stressors exhibited lower mean cortisol levels, as compared to psoriatics with overall low levels of daily stressors.¹⁶ Furthermore, Richards et al.¹⁷ observed physiologic differences in response to stress between psoriasis patients who are stress responders and those who are non-stress responders. Specifically, stress-responders had lower salivary and serum cortisol levels than non-stress responders following a social performance stressor.¹⁷

These blunted HPA axis and elevated SAM system responses to stress may be crucial in better understanding the inflammatory characteristics of psoriasis, particularly in stress-responders. For instance, decreased secretion of cortisol and increased levels of epinephrine and norepinephrine may stimulate the release of mast cells, affect skin barrier function, and upregulate proinflammatory cytokines, which could thereby maintain or exacerbate psoriasis severity.¹⁶ Some authors have commented that this decreased cortisol response may be similar to how psoriasis flares with steroid withdrawal, as evidenced by the well known phenomena of steroid-induced psoriasis rebound.¹⁷

Stress and Psoriasis: A Vicious Cycle

Psoriasis itself can serve as a stressor for patients. Psoriasis can be a disfiguring skin disease with much attached social stigmata. Accordingly, patients often suffer significant interpersonal and psychological distress. Patients commonly experience difficulties in social interactions, especially in meeting new individuals and forming romantic relationships. In general, most patients demonstrate adverse psychological consequences, including poor self-esteem, anxiety, depression, and for some, even develop suicidal ideation.¹⁸

As psoriasis can cause considerable stress for patients and increased levels of stress are likely to exacerbate psoriasis, the disease process, thus, becomes a self-perpetuating, vicious cycle.¹⁹ Therefore, treatment considerations for psoriasis should integrate methods of stress reduction, including psychotherapy and pharmacotherapy, especially for known stress responders.

Stress Evaluation and Management

The best approach to evaluating if an individual is a stress responder is to simply ask the patient, "Do you believe stress frequently worsens the severity of your psoriasis?" If the patient answers "yes" to this question, a clinician may want to consider further evaluating the impact of stress on the patient's life. Useful questions may include: Have you experienced any recent stressful life events? Do you feel depressed or anxious? Do you have friends or family members that provide you with adequate social support? Do you feel you can manage the level of stress in your life? Ultimately, these questions should help guide a treating physician in determining if their patient is a stress responder. However, a clinician should be cognizant that the terms "stress responder" versus "non-stress responder" only refer to whether or not the patient's psoriasis worsens with emotional stress. These terms do not indicate whether or not the patient has an underlying diagnosable psychiatric disorder, which is a separate issue requiring an alternate clinical approach.

As such, it is important to determine if the patient meets the diagnostic criteria for major depression, generalized anxiety, or other psychiatric disorders, as described by the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition) published by the American Psychiatric Association.²⁰ Obviously, all patients with diagnosable psychiatric disorders should be advised to seek appropriate mental health care. As for patients who are stress responders, but are otherwise psychologically well-functioning individuals, they should be made aware of the potential benefits of stress reduction in improving their skin condition. Some relatively easy and feasible stress reduction techniques are yoga, deep breathing exercises, and meditation, just to name a few. More intensive approaches to stress reduction, like psychotherapy or pharmacotherapy, may also be reasonable recommendations. Whether a patient is simply experiencing situational stress or suffering from a diagnosable psychiatric disorder, it may be advisable for that individual to consult a mental health professional as long as emotional factors (such as stress) play an important role in the natural history of their psoriasis.

Therapeutic Overview

Psychotherapy and Stress Reduction

Psychotherapy may be beneficial for psoriasis patients. Seng et al.²¹ found group therapy to be a useful and supportive treatment. Group therapy provided patients with knowledge about psoriasis and helped them better cope with their skin disease. Talking to other psoriasis patients enabled participants to learn how to manage disease-related stress and gain self-confidence.²¹

Case reports have described improvements in psoriasis severity with relaxation and stress reduction techniques, such as hypnosis and thermal biofeedback.^{22,23} Likewise, Price et al.²⁴ showed the potential efficacy of psychotherapy in a study of 11 patients, who completed an eight-session intervention consisting of relaxation and cognitive techniques. Patients reported a significant reduction in levels of anxiety and showed improvements in psoriasis severity based on a visual-analogue scale examining area of involvement, erythema, induration, and scaling.²⁴

Additionally, in a study of 37 patients treated with ultraviolet B (UVB) or PUVA therapy, Kabat-Zinn et al.²⁵ found that stress reduction may help accelerate the rate of clearance. Patients were randomly assigned to either an audiotape-guided, meditative stress reduction exercise during the light treatment, or a control group consisting of the light treatment alone. Study findings revealed that patients in the stress reduction group reached the clearing point (or the point at which less than 5% of the baseline level of psoriasis remained) more rapidly than controls in both UVB and PUVA therapies.²⁵

Pharmacotherapy and Stress Reduction

Pharmacotherapy may also be a helpful adjunct to psoriasis treatment. Studies have demonstrated improvements in psoriasis with oral administration of antidepressants, such as the tricyclic antidepressant (TCA) imipramine (Tofranil®), the monoamine-oxidase inhibitor (MAOI) moclobemide (Manerix®), and bupropion-SR (Wellbutrin®).²⁶⁻²⁹

Modell et al.²⁹ found that the norepinephrine-dopamine uptake inhibitor bupropion-SR may be effective in treating non-depressed individuals with psoriasis. Ten patients were given bupropion-SR monotherapy at 150 mg/day for 3 weeks, and then increased to 300 mg/day for 3 more weeks. Only one patient remained on 150 mg/day dosing for all 6 weeks. Eight out of the 10 patients showed improvement from baseline after 6 weeks of therapy, with an average body surface area reduction of about 50%. Of these eight responders, disease severity worsened (towards pre-study baseline psoriasis coverage) within 3 weeks of discontinuing bupropion-SR.²⁹

In contrast, there are also a total of six cases reporting that the selective-serotonin reuptake inhibitors (SSRIs) fluoxetine (Prozac®) and paroxetine (Paxil®) may induce or exacerbate psoriasis.³⁰⁻³²

Pharmacologic Treatment Recommendations

When pharmacologic treatment is deemed appropriate for stress reduction, SSRIs should be considered for first-line therapy. Despite the six reported cases of SSRI-associated flares of psoriasis,³⁰⁻³² SSRIs have certain merits in the treatment of psoriasis patients experiencing depression. As well, these

agents may possibly confer adjuvant benefits for non-depressed psoriatics who are stress responders. SSRIs, such as fluoxetine, paroxetine, sertraline (Zoloft®), and escitalopram (Lexapro®), are generally safe and better tolerated than other classes of antidepressants.³³

In stress responders, paroxetine may be preferential because of its anti-anxiety effects. It also offers the advantage of having minimal anticholinergic activity and no associated weight gain. Common side-effects include headache, gastrointestinal upset, and sexual dysfunction.³³

TCAs, though effective antidepressants, can be lethal in overdose. Side-effects are common and include sedation, weight gain, orthostatic hypotension, and anticholinergic effects. MAOIs may be used to treat patients whose symptoms do not respond to first-line antidepressants (also known as, refractory depression). MAOIs should be prescribed with caution because of their potentially dangerous side-effects (i.e., serotonin syndrome and hypertensive crisis). Common side-effects include orthostatic hypotension, drowsiness, weight gain, sexual dysfunction, dry mouth, and sleep dysfunction.³³

In addition, anti-anxiety medications may be helpful for short-term use in specific stressful situations for stress responders. For instance, alprazolam (Xanax®) is a rapid-acting medication, with both anti-depressant and anti-anxiety effects, that may be beneficial in these situations. Because it has a shorter and more predictable half-life, as compared with other benzodiazepines, there is less risk of accumulation in the body when used over long periods of time. However, alprazolam can be highly sedating and potentially addictive,³⁴ and therefore, treatment should be limited to short-term use on the order of a few weeks to a maximum of a few months.

Conclusion

An extensive number of clinical studies exists supporting stress as an exacerbating factor in psoriasis.⁵⁻¹² One problem is that most investigations on stress are generally retrospective, primarily based on patient recall of past events, which may or may not be an entirely reliable measure. However, there are three prospective studies confirming an association between stress and psoriasis.^{4,10}

In sum, stress appears to be an important precipitating factor in the development and exacerbation of psoriasis. Patients who are identified as stress responders may especially benefit from stress reduction through psychotherapy and/or pharmacotherapy.

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Propylene Glycol: An Often Unrecognized Cause of Allergic Contact Dermatitis in Patients Using Topical Corticosteroids

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ABSTRACT

Propylene glycol (PG) is considered to be a ubiquitous formulary ingredient used in many personal care products and pharmaceutical preparations. It is an organic compound commonly found in topical corticosteroids (CS). Cutaneous reactions to PG are mostly irritant, but allergic contact dermatitis to PG is well-documented. Cosensitization to PG and topical CS can occur, making it challenging to choose the appropriate topical CS in a PG-allergic patient. This review is aimed at guiding clinicians in the selection of a suitable topical corticosteroid when presented with patients allergic to PG.

Key words: allergic contact dermatitis, corticosteroids, propylene glycol, topical

Propylene glycol (PG) is a colorless, viscous, nearly odorless liquid that is used as an intermediate for the synthesis of other chemicals.^{1,2} It is a multifunctional excipient that is used in many products as a solvent, vehicle, humectant, or emulsifier.³ The annual PG production and global demand are rapidly increasing.³ Vehicles for topical corticosteroid preparations commonly include PG for enhancing stratum corneum penetration. In addition to topical steroids, PG can also be found in other topical pharmacologic preparations, including antibacterials, antifungals, benzoyl peroxide, and emollients.¹ Cutaneous reactions to PG have been recognized since 1952.¹

Sources of PG

Approximately half of the PG produced is used in the synthesis of other chemicals.² The other half is utilized in the manufacturing of many industrial and personal care products. PG is used as a plasticizer, solvent (in lacquers and varnishes), and as a component in antifreeze products, lubricants, cutting-fluids, and inks. It is found in many cosmetic and pharmaceutical preparations, food (for coloring, thickening, and flavoring), and household cleansers. In a recent study by the North American Contact Dermatitis Group (NACDG), personal care products were found to be the most common sources of exposure to PG (53.8%), followed by topical steroids, and other topical medicaments.³

Allergic Contact Dermatitis to PG

Cutaneous reactions to PG are classified into four groups: irritant contact dermatitis, allergic contact dermatitis (ACD), non-immunologic contact urticaria, and subjective or sensory irritation.⁴ The incidence of true ACD to PG is unknown. This is primarily attributed to the difficulty in determining the ideal concentration for patch testing that would be nonirritating, but high enough to elicit an allergic response. The majority of skin reactions to PG are irritant in nature, however, true allergic sensitization does occur. The most convincing evidence of allergic sensitization to PG is the development of systemic

contact dermatitis after giving PG orally to PG-allergic patients.⁵ The overall prevalence of allergic reactions to PG was found to be relatively low (3.5%) by the NACDG.³ The NACDG currently recommends using a 30% aqueous PG solution for patch testing.³ In our experience at the University of British Columbia Contact Dermatitis Clinic, the prevalence of positive patch test reactions to PG over a 2 year period was 1.57% (13/828 patients). It was presumed that an increased individual susceptibility to irritation may also be associated with allergic reactivity through reduction of the skin's barrier function and the release of cytokines.² To confirm an allergy to PG, it has been recommended that positive patch test reactions should be followed by serial dilution patch tests, repeat open application tests or oral challenge tests, or all three of these assessments.⁴

PG and ACD to Topical Corticosteroids

The prevalence of ACD from topical corticosteroids (CS) is unknown. ACD to topical CS should be suspected if the dermatitis worsens or does not improve during treatment. ACD can result from an allergy to the steroid molecule or to a component of the vehicle. CS are divided into four classes on the basis of structure and cross-reactivity pattern: classes A (hydrocortisone type), B (triamcinolone acetonide type), C (betamethasone type), and D.⁶ Class D is further divided into D1 (betamethasone dipropionate type) and D2 (methylprednisolone aceponate type). There are different screening markers that are used for patch testing to the corticosteroid classes. The screening markers used on the NACDG screening series are as follows: tixocortol-21-pivalate (class A), budesonide and triamcinolone acetonide (class B), clobetasol-17-propionate (class D1), and hydrocortisone-17-butyrate (class D2).⁶ Patch test reactions to class A steroids are the most common.⁷ Reactions to classes B and D steroids are less common, whereas reactions to class C steroids are extremely rare.⁷ The most common cross-reactions are between steroids in classes A and D2, followed by classes B and D2, and classes A and B.⁸

An investigation by the NACDG demonstrated that topical CS were responsible for 18.3% of the positive patch test reactions to PG.³ In a recent study, PG was found to be the most common allergen in topical CS, being present in 64% of the steroidal products.⁷ It was especially common in branded ointments and gels. Moreover, studies have reported a significant number of patients have a concomitant reaction to both topical CS and PG, which suggests the possibility of cosensitization.^{3,8}

Case Report

A 55-year-old female presented to our clinic with a history of severe recurrent eyelid dermatitis resulting in multiple visits to the emergency room and treatment with systemic steroids. Her left leg dermatitis also recently worsened. The patient’s past medical history was significant for a previously treated venous ulcer of the left leg and chronic venous insufficiency dermatitis. There was a positive family history of atopy, but she denied any personal history of atopy. She had been applying amcinonide 0.1% (Cyclocort®) and fusidic acid 2% (Fucidin®) ointments on the leg dermatitis for many years with only intermittent improvement. Patch testing was done with the 2010 NACDG screening series (Table 1). She was found to be allergic to PG, budesonide, lanolin alcohol, balsam of Peru, and glyceryl thioglycolate. We could not identify the source of PG (amcinonide 0.1% and fusidic acid 2% ointments are both PG-free), but this patient could have been sensitized to PG from her personal care products. She was most likely sensitized to budesonide from prolonged application of amcinonide 1% ointment (a class B corticosteroid). Fusidic acid 2% ointment contains lanolin, which was an additional factor for the persistence of her dermatitis. Given that she was allergic to both PG and budesonide, it would have been helpful to know which topical CS were PG-free. Ideally, we would have prescribed her a PG-free class C or D1 topical CS. Consequently, we switched her to tacrolimus 0.1% ointment (PG- and corticosteroid-free) for treating both the eyelid and leg dermatitis. Subsequently, the eyelid dermatitis cleared. Her leg dermatitis occasionally recurs secondary to underlying venous insufficiency, for which she continues compression stocking therapy.

Ingredient	Day 3 (48 hours)	Day 7
Propylene glycol	++	++
Budesonide	++	++
Lanolin alcohol	++	++
Balsam of Peru	+	+
Glyceryl thioglycolate	-	+

Table 1: Patch test results to the 2010 North American Contact Dermatitis Group screening series

Reactions were graded using a scoring system recommended by the International Contact Dermatitis Research Group: + = erythema and papules, ++ = edema or vesicles, +++ = bullae and/or erosions, - = no reaction.

The Choice of a Topical CS in a PG-allergic Patient

Given that PG is the most common allergen in topical CS, it is important to know which topical corticosteroid to prescribe to a PG-allergic patient. We have conducted a search of all topical CS available in Canada. We have excluded topical CS that contain

other active ingredients (e.g., salicylic acid). We then searched carefully for preparations that are PG-free. Ingredients of the different topical CS were checked using the *Compendium of Pharmaceuticals and Specialties (CPS) 2010* drug reference guide in addition to pharmaceutical company website searches. We have created a chart containing all PG-free topical CS available in Canada sorted on the basis of potency and structural class (Table 2 on page 7).

Conclusion

PG is found in many products. The sensitizing potential of PG is well documented, but the true incidence of its role in ACD is unknown. PG is the most common allergen in topical CS. Cosensitization to PG and topical CS is possible. If patch testing is unavailable and the physician is highly suspecting PG allergy, we recommend prescribing any PG-free topical corticosteroid. Another option is to consider tacrolimus ointment, which is a PG-free steroid-sparing agent (pimecrolimus 1% cream contains PG). Empirically, one can prescribe a PG-free class C topical corticosteroid given the rarity of ACD to class C topical CS. Ideally, patch testing should be done if the clinical picture is suggestive of allergy to PG and/or topical CS. It is important to note that the steroid formulations discussed in this paper pertain only to topical CS products available in Canada, as products from other countries may contain different compositions of non-medicinal ingredients. We hope that this review will be of benefit in guiding physicians when choosing the appropriate topical corticosteroid in patients allergic to PG.

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Structural class	Class A: Hydrocortisone type	Class B: Triamcinolone acetonide type	Class C: Betamethasone type	Class D1: Betamethasone dipropionate type	Class D2: Methylprednisolone aceponate type
Class 7: Least potent	<ul style="list-style-type: none"> Hydrocortisone 0.5%, 1% [OI] (Cortoderm®) Hydrocortisone 1%, 2.5% [CR, LO]; 2.5% [SL] (Emo-Cort®) 				
Class 6: Low potency		<ul style="list-style-type: none"> Desonide 0.05% [OI] (Desocort®) 			
Class 5: Lower mid-strength		<ul style="list-style-type: none"> Fluocinolone acetonide 0.01% [OL] (Derma-Smoother/FS®) 		<ul style="list-style-type: none"> Betamethasone valerate 0.05% [OI] (Betaderm®) Betamethasone valerate 0.05% [CR, LO] (ratio-Ectosone) Betamethasone valerate 0.1% [CR] (Prevex® B, ratio-Ectosone) Betamethasone valerate 0.1% [LO] (Betaderm®, ratio-Ectosone, Valisone®) 	<ul style="list-style-type: none"> Prednicarbate 0.1% [CR] (Dermatop®)
Class 4: Mid-strength		<ul style="list-style-type: none"> Triamcinolone acetonide 0.1% [OI, CR] (Aristocort®) Amcinonide 0.1% [CR, LO] Cyclocort®, ratio-Amcinonide) 	<ul style="list-style-type: none"> Desoximetasone 0.05% [CR] (Topicort®) Difflocortolone valerate 0.1% [CR, OC, OI] (Nerisone®) 		
Class 3: Upper mid-strength		<ul style="list-style-type: none"> Triamcinolone acetonide 0.5% [CR] (Aristocort®) 		<ul style="list-style-type: none"> Betamethasone valerate 0.1% [OI] (Betaderm®) Betamethasone dipropionate 0.05% [CR] (Diprosone®) Betamethasone dipropionate 0.05% [LO] (Diprosone®, ratio-Topisone) 	
Class 2: High potency		<ul style="list-style-type: none"> Amcinonide 0.1% [OI] (Cyclocort®, ratio-Amcinonide) 	<ul style="list-style-type: none"> Desoximetasone 0.25% [CR]; 0.05% [GL] (Topicort®) 	<ul style="list-style-type: none"> Betamethasone dipropionate 0.05% [OI] (Diprosone®, ratio-Topisone) 	
Class 1: Superpotent				<ul style="list-style-type: none"> Clobetasol propionate 0.05% [OI, LO] (ratio-Clobetasol) Clobetasol propionate 0.05% [SL] (Dermovate®) Clobetasol propionate 0.05% [SH, SP] (Clobex®) 	

Table 2: Propylene glycol-free topical corticosteroids available in Canada sorted by potency and structural class
CR = cream, GL = gel, LO = lotion, OL = Oil, OC = oily cream, OI = ointment, SH = shampoo, SL = solution, SP = spray

Update on Drugs

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Name/Company	Approval Dates/Comments
Belimumab <i>Benlysta</i> ® Human Genome Sciences GlaxoSmithKline	The US FDA approved this new first-in-class human monoclonal antibody in March 2011 for the treatment of systemic lupus erythematosus (SLE). Treatment is indicated for adult patients with active, autoantibody-positive SLE who are receiving standard therapy. The drug inhibits the biological activity of the B-lymphocyte protein (BLyS). Elevated levels of BLyS are associated with autoimmune disorders and are believed to contribute to the production of autoantibodies that attack and destroy the body's own healthy tissues. The recommended dosing regimen is 10 mg/kg by intravenous infusion at 2-week intervals for the first 3 doses and at 4-week intervals thereafter. It is the first new lupus drug to receive regulatory approval in more than 50 years.
Ipilimumab <i>Yervoy</i> ™ Bristol-Myers Squibb	The US FDA approved this human monoclonal antibody in March 2011 for the treatment of metastatic melanoma. Administered intravenously, the drug blocks a T-lymphocyte antigen (CTLA-4), altering the body's ability to fight off cancerous cells and allowing the immune system to recognize, target, and attack cells in melanoma tumors. Regulatory approval was based on a study of 676 patients with late-stage melanoma that showed better overall survival with ipilimumab compared with an experimental tumor vaccine (median survival was 10 months vs. 6.5 months). Common autoimmune side-effects included colitis, diarrhea, endocrine dysfunction, fatigue, and skin rash. Additionally, severe to fatal autoimmune reactions were observed in 12.9% of ipilimumab-treated patients. Due to the unusual and severe side-effects, approval is accompanied by an FDA-mandated Risk Evaluation and Mitigation Strategy (REMS) to inform health care professionals about these serious risks.
Imiquimod 3.75% Cream <i>Vyloma</i> ™ Graceway Pharmaceuticals	Health Canada approved this immune response modifier in March 2011 for the topical treatment of external genital warts and perianal warts in patients ≥18 years of age. Under clinical investigation, Vyloma™ showed that the once-daily treatment regimen for up to 8 weeks was safe and provided sustained efficacy.

Drug News

In March 2011, the US FDA announced the approval of an expanded age indication for the live, attenuated varicella zoster virus (VZV) vaccine (Zostavax®) for the prevention of herpes zoster infection (shingles) in individuals 50 to 59 years of age. The vaccine was originally approved in May 2006 for the prevention of herpes zoster in individuals ≥60 years of age. Approval of this expanded indication was based on findings from the Zostavax Efficacy and Safety Trial (ZEST), a multicenter placebo-controlled, double-blind study involving 22,439 subjects aged 50 to 59 years, who were randomized to receive a single dose of either the VZV vaccine (n=11,211) or placebo (n=11,228). Study participants were monitored for the development of shingles for at least 1 year. Compared with placebo, VZV vaccination reduced the risk of developing shingles by 69.8%.

More information is available at:

<http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm248390.htm>

<http://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm132831.pdf>