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An Update on New and Emerging Options for the Treatment of Vitiligo

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ABSTRACT

Vitiligo is an acquired leukoderma that results from the loss of epidermal melanocytes, and is characterized by macules and patches of depigmented skin. With a relatively high rate of prevalence, vitiligo occurs in localized, generalized, or segmental patterns; it can run a rapidly progressive course or remain stationary. The pathogenesis of vitiligo is not yet fully understood, but the autoimmune hypothesis is the most commonly accepted one, based on which, many treatment modalities have been described. Although many therapeutic options exist and new modalities are still emerging, treatment challenges persist, as not all patients respond to available therapies. Variables that affect the choice of treatment include the extent, distribution, and progression rate of the lesions. Another challenge is the lack of a standardized scoring system, which hampers the production of level 1a evidence studies for the treatment of this condition.

Key Words: Vitiligo, leukoderma, photochemotherapy, phototherapy, vitamin D_3 analogues, corticosteroids, topical immunomodulators, excimer laser, phenylalanine, Placentrex®, depigmentation

The worldwide prevalence of vitiligo is estimated to range between 0.5% and 4%.[1] These depigmented macules were first described more than 3,000 years ago in pre–Hindu Vedic and ancient Egyptian texts.[2]

The pathogenesis of vitiligo is complex and not yet fully understood, but it is believed to involve a combination of autoimmune, genetic, and environmental factors. The autoimmune hypothesis suggests that antibodies develop against melanocyte surface antigens.[3] Gauthier, et al. recently proposed the melanocytorrhagy hypothesis, which is based on an *in vivo* observation of melanocyte detachment from the basal layer, followed by transepidermal migration, which in turn triggers melanocyte death.[4] In addition, the neural, self-destruct, and biochemical hypotheses have also been proposed.[1]

Evaluation of Therapeutic Options Based on Strength of Evidence

This review will primarily discuss the more recent studies on vitiligo with a high level of evidence. Reference will be made throughout the discussion regarding the strength of evidence as defined in Table 1.

Lack of Standardized Measurements

With the absence of a standardized scoring system for vitiligo, a meta-analysis to assess different treatment options is difficult. In their efforts to fill that gap, Hamzavi, et al. developed and applied a simple clinical tool known as the Vitiligo Area Scoring Index (VASI), and used it to model the response of

vitiligo to narrowband UVB (NB–UVB) phototherapy using parametric tests. VASI scoring correlated well with both patient (P=0.05) and physician global assessments (P<0.001).[5]

Quality of Evidence	Grade of Quality	Description of Research
1	a	Systematic reviews (meta-analyses) of randomized controlled studies with high homogeneity
	b	Individual randomized controlled studies with narrow confidence intervals
	c	Randomized controlled studies, in which a disease was eradicated by a drug, or a disease, where formerly all patients failed treatment, is successful in some patients
2	a	Systematic reviews of cohort studies with high homogeneity
	b	Individual cohort studies including randomized controlled studies of lesser quality (short follow-up, large confidence intervals)
	c	Studies with statistically significant differences between compared treatments
3	a	Systematic reviews of case-control studies of high homogeneity
	b	Individual case-control studies
4		Cohort and case-control studies of poor quality
5		Expert opinion

Table 1: Levels of evidence-based medicine as developed by Sackett, et al.[6]

Also, to further assist in devising a standardized approach for measurement and evaluation, the Vitiligo European Task Force proposed a consensus definition of the disease and a methodology for assessing treatment outcomes by using a system that combines analysis of extent, stage of disease, and disease progression.[7] Presently, vitiligo studies use some form of global physician assessment, but they lack any commonly accepted systematic method for measuring treatment response.

Photochemotherapy

Photosensitizers, used in photochemotherapy, either increase the sensitivity of the skin, in the case of psoralen, or increase the sensitivity of melanocytes, as khellin does, by activating melanocytes or melanosomes, and inducing IL-1 synthesis. An evidence level 4 clinical trial showed that topical khellin plus UVA (KUVA) (n=16) and systemic psoralen plus UVA (PUVA) therapy (n=17) led to similar responses, provided that the treatment duration was long enough.[8] Another level 4 retrospective 10-year analysis of 97 patients showed that treatment with PUVA resulted in >90% repigmentation in only 8% of patients. Moreover, the repigmentation was inhomogeneous and weak.[9]

Phototherapy

Phototherapy, in the form of narrow band ultraviolet B (NB-UVB) (311nm-313nm), or broad band ultraviolet B (BB-UVB) (290nm-320nm), inhibits the induction and secretion of cytokines, and stimulates inactive melanocytes in the outer root sheath of hair follicles to proliferate and migrate into vitiligo lesions. NB-UVB is considered to be the initial treatment of choice for the treatment of moderate-to-severe vitiligo.[10] In a level 2c prospective study conducted in 2006, Parsad, et al.[11] showed that NB-UVB (n=13) was superior to PUVA (n=9) when comparing the rate of marked repigmentation to complete repigmentation in both treatment groups (41.9% and 23.6%, respectively). This result was also confirmed by Yones, et al.[12] in an evidence level 1b double-blind randomized clinical trial of 56 patients with nonsegmental vitiligo, that compared treatment with NB-UVB vs. PUVA. At the end of 48 treatments, 64% of patients in the NB-UVB group showed >50% improvement in body surface area affected, compared with 36% of patients in the PUVA group. Furthermore, patients in the NB-UVB group showed improved color-matched repigmentation, as well as a lower incidence of side-effects. In a randomized controlled study published in 2006, El Mofty, et al.[13] investigated the effects of PUVA and NB-UVB (311nm) on 15 patients; comparisons between the two modes of treatment showed no difference in either the degree of response or in the incidence of complications.

In a study by Sitek, et al.[14] to assess the stability of NB-UVB-induced pigmentation on 31 patients with generalized vitiligo, 16% experienced >75% stable repigmentation 2 years after cessation of up to 1 year of NB-UVB therapy. In an evidence level 4 clinical trial, the combination of NB-UVB and calcipotriol showed no increase in efficacy, probably due to the fact that calcipotriol is rapidly degraded (>90%) by UV irradiation.[15]

Vitamin D_3 Analogues

Calcipotriol (a vitamin D_3 analogue) inhibits T-cell activation, stimulates growth and differentiation of keratinocytes and melanocytes, induces melanogenesis by reducing the disturbed calcium influx into melanocytes, and restores calcium homeostasis. Calcipotriol, as monotherapy, showed little or no treatment response in several studies.[16] In a level 1b evidence 3-month prospective trial of 49 patients with vitiligo affecting 5% of their skin, investigators compared 0.05% betamethasone dipropionate cream, b.i.d. (group 1), with 0.005% calcipotriol ointment (calcipotriene in the US), b.i.d. (group 2), and a combination of 0.05% betamethasone dipropionate cream in the morning and 0.005% calcipotriol ointment at night (group 3).[17] No patient achieved excellent (75%) repigmentation, 25%-50% repigmentation was observed in 46.7%, 33.3%, and 46.7% of patients in groups 1, 2, and 3, respectively. Marked repigmentation (50%-75%) was achieved in 13%, 6.7%, and 26.7% of patients in groups 1, 2 and 3, respectively. In a randomized controlled clinical trial of 40 vitiligo patients, Arca, et al.[18] compared NB-UVB combined with topical 0.005% calcipotriol ointment with NB-UVB monotherapy. There was no statistically significant difference between the two groups following 30 treatments. Kullavanijaya and Lim,[19] in a prospective, nonrandomized controlled clinical trial, showed that 9 of 17 patients with symmetrical vitiligo had a better response on the side treated with NB-UVB and calcipotriol, when compared with NB-UVB alone, following a number of treatments ranging from 29 to 114. Ermis, et al.,[20] in an evidence level 1b study of 35 patients, compared the efficacy of 0.005% calcipotriol cream with placebo when used 1 hour before PUVA treatment on bilateral symmetrical lesions. The combination was more effective than PUVA alone (63% of calcipotriol-treated lesions resulted in complete repigmentation, compared with 15% of PUVA treated lesions and 7% of placebo treated lesions).

Topical Corticosteroids

Topical corticosteroids have been widely used for the treatment of vitiligo, but its use is impractical in generalized vitiligo because of associated adverse effects, such as skin atrophy, telangiectasia, and striae distensae.[21] Treatment should be discontinued if there is no clinical improvement following 2 months of therapy. In a level 1a evidence meta-analysis involving randomized controlled trials on the non-surgical treatment of localized and generalized vitiligo, Njoo, et al.[22] suggested that class 3 corticosteroids should be advised as first-line therapy for patients with localized disease. The pooled odds ratio (OR) for topical class 3 corticosteroids vs. placebo was significant [14.32; 95% confidence interval [CI], 2.45-83.72]. Topical class 3 and class 4 corticosteroids carried the highest mean success rates (OR=56%; 95% CI, 50%-62% and OR=55%; 95% CI, 49%-61%, respectively).

Systemic Corticosteroids

Systemic corticosteroids may arrest the progression of vitiligo and lead to repigmentation by immunosuppression. As clinical improvement is experienced by patients who are receiving oral corticosteroid treatment for actively spreading vitiligo, a reduction in complement-mediated cytotoxicity by autoantibodies to melanocytes, and a reduction of antibody titer to surface antigens of melanocytes are noted in their serum samples. There have been few reports on the use of systemic steroids in vitiligo therapy. In a study by Kim, et al.,[23] a low daily dose of oral prednisolone (0.3mg/kg body weight) was used in actively spreading vitiligo patients in order to minimize the side-effects. They observed an arrest in disease progression in 87.7% and repigmentation in 70.4% of 81 patients. In another study by Lee, et al.,[24] high-dose prednisolone pulse therapy, in the form of methylprednisolone sodium succinate (25mg/kg/day, maximum of 1000mg/day) mixed with 100mL of 5% dextrose, was injected intravenously on 3 consecutive days, and showed an arrest of lesion progression in 85% of patients, but a low rate of repigmentation was observed. Based on these results, Lee, et al. suggested the need for further studies on phototherapy in combination with steroid pulse treatment, in order to determine the optimal dosages/regimen to improve the rate of repigmentation. A prospective, open clinical trial involving 14 patients with progressive or static vitiligo by Seiter, et al. explored high-dose methylprednisolone (8mg/kg of body weight) intravenous pulsed therapy, administered on 3 consecutive days. The study findings included cessation of disease progression and repigmentation in 71% of patients; the rate and extent of repigmentation varied from 10% to 60% of the surface area.[25]

Topical Immunomodulators (TIM)

Topical tacrolimus was recently introduced for the treatment of vitiligo. This immunomodulator offers the advantage of prolonged treatment without the adverse effects seen in the long-term use of corticosteroids.[16] Tacrolimus and pimecrolimus act at the level of gene expression and through suppression of proinflammatory cytokines (e.g., interleukins, TNF-α and INFγ).[1] In an evidence level 2c trial, tacrolimus-treated lesions showed a mean repigmentation of 41% vs. 49% for the clobetasol-treated lesions in two symmetric vitiliginous lesions in 20 children. Regarding side-effects, atrophy developed in three of the patients treated with clobetasol.[26]

In a study by Sendur, et al.[27] 23 vitiligo patients were treated once daily with 1% pimecrolimus cream; 19 subjects completed the 6-month study. Three patients showed an excellent response (76%-100%), four had moderate response (51%-75%), six exhibited mild improvement (26%-50%) and five patients had minimal response (1%-25%); one patient had no response to the treatment. Three

patients experienced side-effects in the form of burning and stinging sensations.

Some evidence points to the synergistic activity of combination therapy with topical tacrolimus and UVB phototherapy (either NB-UVB or excimer laser).[28] However, this combination may increase the risk of skin carcinogenesis. Results of a study on hairless mice suggest that topical calcineurin inhibitors do not affect the clearance of DNA photoproducts. Moreover, the use of tacrolimus may be useful in preventing UVB-induced erythema by inhibiting early-phase events of the inflammatory process.[29]

Excimer Laser

The excimer laser has a wavelength of 308nm. Hadi, et al.,[30] conducted a retrospective study on 32 patients with 55 vitiliginous lesions. Results showed that 52.8% of the lesions developed ≥75% repigmentation, with a mean 23 excimer laser treatments. Repigmentation (75%) occurred more on the face in 71.5% of the treated areas, followed by the neck, scalp and genitalia in 60%, then the extremities with 46.7%, while no lesions on the hands and feet exhibited ≥75% repigmentation. Passeron, et al.,[31] in a level 2b evidence study, compared the efficacy of the excimer laser in combination with 0.1% tacrolimus ointment (group A) with the excimer laser as monotherapy (group B). After 24 sessions, repigmentation occurred in 100% of patients in group A, and 85% of patients in group B. In comparison with NB-UVB, phototherapy with the excimer laser has the advantage of applying targeted treatment only to the depigmented sites. However, NB-UVB, which has been studied more extensively, may be useful for the treatment of extensive vitiligo and is more advantageous when compared with the excimer laser in terms of costs, duration of treatment sessions and patient compliance.[28]

Comparison of Non-Surgical Therapies

In a meta-analysis of the literature among patient series studies on generalized vitiligo, the highest mean success rates were achieved with NB-UVB (63%; 95% CI, 50%-76%), BB-UVB (57%; 95% CI, 29%-82%), and PUVA therapy (51%; 95% CI, 46%-56%). Study findings also associated PUVA with the highest rates of side-effects.[22]

Surgical Therapy

Surgical treatment options for vitiligo offer the potential for rapid and more desirable amounts of repigmentation. The different modalities of surgical techniques include tattooing, organ-cultured fetal skin allografting, epidermal culture grafting, melanocyte culture grafting, autologous noncultured melanocyte-keratinocyte cell transplantation, epidermal grafting by the suction blister technique, thin Thiersch split skin grafting, or miniature punch grafting.[32]

Patients with stable vitiligo, who are refractory to medical therapy, are the best candidates for surgical treatment. Intractable disease activity means a higher risk of treatment failure and Koebnerization at the recipient site. Segmental vitiligo, which is characterized by a rapid progression followed by stabilization, generally responds best to surgical intervention.[33]

In surgical procedures, melanocytes are grafted from healthy skin derived either directly from cultivated melanocytes or from specimens of the epidermis.[34] Grafting melanocyte-keratinocyte suspensions in an evidence level 4 clinical trial, resulted in 95%–100% repigmentation in over half of the 142 patients in the study.[35] In epidermal blister grafting, ≥80% repigmentation was achieved in an evidence level 2a study when treatment was combined with photochemotherapy.[34] Full-thickness punch grafting, with epidermal biopsies that are 1.5mm to 2.5mm in diameter, from normally pigmented to depigmented areas, can achieve rapid and complete repigmentation (in a high percentage).[34] In cultured cell grafting, keratinocytes, along with melanocytes, are superior to pure melanocyte grafts, because melanocytes are grown in a physiologic environment.[34] In 1989, Gauthier and Surleve-Bazeille[36] introduced the use of noncultured cellular grafts that were able to treat larger skin areas with only a small piece of donor skin; however, its cellular suspension gave poorer results on curved areas. Autologous, noncultured, melanocyte-keratinocyte cell transplantation involves injecting an epidermal suspension with melanocytes and keratinocytes from normally pigmented donor skin, which is mechanically separated using a trypsin ethylenediaminetetraacetic acid (EDTA) solution, onto dermabraded, depigmented skin and covered with a collagen dressing. Mulekar[33] concluded that this form of cell transplantation achieved optimum results when used in segmental and focal vitiligo. Minigrafting is considered the easiest, fastest and least expensive method of surgical repigmentation; however, its main side-effect is cobblestoning at the donor site.[37]

Multiple procedures may be needed to achieve desirable rates of repigmentation. Relative contraindications to surgery include patients with a positive history of the Koebner phenomenon, postinflammatory hyperpigmentation, keloids, or hypertrophic scars. There is also a concern regarding the tumorigenic risk of culturing techniques, because of the presence of tumor promoters in certain culture media combined with the use of postoperative phototherapy.[37]

Other Treatment Options

Other techniques include:

- dermabrasion, in which re-epithelialization takes place from the remnants of dermal appendages;

- 5-fluorouracil, which induces the repigmentation of vitiligo by the overstimulation of follicular melanocytes that migrate to the surface during epithelialization, resulting in hyperpigmentation.

In a study by Sethi, el al.,[32] the efficacy of treatment with dermabrasion alone was 30.0% at 4 months and 63.3% at 6 months. The efficacy of dermabrasion combined with 5-fluorouracil was 56.7% at 4 months and 73.3% at 6 months.

Phenylalanine and Placentrex®

L-phenylalanine is an inhibitor of cytolitic antibodies and supports the stimulation of melanin synthesis and the migration of melanocytes from healthy to depigmented skin by solar radiation. A retrospective study of 193 patients treated with oral (50mg/kg or 100 mg/kg daily) and topical (10% gel) phenylalanine, followed by sun exposure, showed a total overall improvement rate of 56.7%, with 90.3% for the face, 42.8% for the trunk, and 37.1% for the limbs. The authors suggested that the higher percentage of total healing for the face could be due to the association of phenylalanine use and radiation from the sun.[38] Another novel agent is topical human placental extract (Placentrex®, Albert David Ltd.), which promotes melanin synthesis by supplying the amino acid, tyrosine, as well as encouraging copper tyrosinase linkage. The efficacy of dermabrasion combined with Placentrex® gel was 23.3% at 4 months and 46.7% at 6 months.[32]

Depigmentation

In patients with extensive vitiligo, depigmentation can be achieved with monobenzyl ether of hydroquinone and monomethyl ether of hydroquinone at 20% concentration, either alone or in combination with Q-switched ruby laser.[39]

Conclusion

Several factors control the choice of treatment for vitiligo. The best modality of therapy should be individualized for each patient depending on the extent, distribution and rate of progression of the lesions. After many years of research, the challenge of generating level 1a evidence studies for the treatment of vitiligo still exists, due in large part to the lack of a standardized scaling system.

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Drug Treatments for Skin Disease Introduced in 2007

Drug Class	Generic/Trade Company Names	Indication	Approving Regulatory Agency
Antiacne Agents	**Adapalene Gel 0.3%** *Differin*® Galderma Laboratories	Approval granted for a higher concentration formulation of this topical retinoid for the treatment of moderate-to-moderately severe acne.	US FDA
	Drospirenone/ Ethinyl Estradiol *Yaz*® Berlex Inc.	A new indication approved for the treatment of moderate acne vulgaris in women wanting an oral contraceptive for birth control.	US FDA
	Tretinoin 0.05% Gel *Anthralin*® Galderma Laboratories	Approved this topical retinoid for the treatment of acne vulgaris.	US FDA
Antibacterial Agents	**Daptomycin for Injection** *CUBICIN*® Cubist Pharmaceuticals	Approved for the additional indications of right-sided infective endocarditis (RIE) due to *Staphylococcus aureu*s and *Staphylococcus aureus* bacteremia, when associated with RIE or with complicated skin and soft-tissue infections.	EMEA
	Retapamulin Ointment 1% *Altabax*® GlaxoSmithKline	Approved for the topical treatment of impetigo due to susceptible strains of *Staphylococcus aureus* or *Streptococcus pyogenes*. This product is the first in a new class of prescription topical antibacterials to be used twice daily for a 5-day period in patients ≥9 months.	US FDA
	Tinidazole Tablets *Tindamax*® Mission Pharmacal	Approved for the treatment of bacterial vaginosis. This oral medication provides a shorter treatment course, requires fewer doses, as well as exhibits an improved tolerability profile than current therapies.	US FDA
Antifungal Agents	**Ciclopirox Topical Solution 8%** Perrigo Company	Approval granted for the treatment of mild-to-moderate fungal infections of the nails. This nail lacquer is considered to be the therapeutic equivalent of Penlac® (sanofi-aventis).	US FDA
	Ketoconazole 2% Foam *Extina*® Stiefel Laboratories	Approved for the topical treatment of seborrheic dermatitis in immunocompetent patients ≥12 years of age. The novel vehicle delivery system (VersaFoam® HF® Technology) has been shown to improve absorption and drug distribution.	US FDA
	Terbinafine Hydrochloride *Lamisil*® Novartis Pharmaceuticals	Approved for the treatment of tinea capitis in children ≥4 years of age. This new granular formulation, which can be sprinkled on food, is intended to improve patient compliance and treatment outcomes.	US FDA

Antihistamines	**Desloratadine** *Aerius®/ Azomyr®/ Neoclarityn®* Schering-Plough	Two new formulations of this antihistamine were approved. • orodispersible tablets for the treatment of symptoms associated with allergic rhinitis and chronic idiopathic urticaria (CIU) in adults and children ≥6 years of age; • oral solution for the treatment of symptoms associated with allergic rhinitis and CIU in adults and children ≥1 year of age.	EMEA
	Levocetirizine Dihydrochloride *Xyzal®* UCB/ sanofi-aventis	Approved for the relief of symptoms associated with seasonal and perennial allergic rhinitis and uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children ≥6 years of age.	US FDA
	Loratadine Dry Syrup 1% *Claritin®* Shering-Plough	Approved for the treatment of allergic rhinitis, urticaria and pruritus associated with skin diseases in children ≥3 years of age. The dry syrup granule formulation is presently only available in Japan.	MHLW/ KIKO Japan
Antimicrobial Agents	**Nanocrystalline Silver Cream** *NPI 32101* Nucryst Pharmaceuticals	Approved for broad spectrum protection against microbes including strains resistant to MRSA, such as *Pseudomonas aeruginosa* and *Staphylococcus aureus*.	US FDA
Antipsoriatic Agents	**Adalimumab** *HUMIRA®* Abbott Laboratories	Approved for the treatment of moderate-to-severe plaque psoriasis.	EMEA
Antiviral Agent	**Famciclovir** TEVA Pharmaceutical Industries	Approval granted to the first generic formulation of famciclovir for the treatment of herpes zoster (shingles).	US FDA
Atopic Dermatitis/ Eczema	**Clobetasol Propionate 0.05%** *Olux-E™ Foam* Stiefel Laboratories	Approved for the treatment of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses (psoriasis and eczema) in patients ≥12 years of age.	US FDA
Crohn's Disease	**Adalimumab** *Humira®* Abbott Laboratories	Approved as a treatment for reducing the signs and symptoms and inducing and maintaining clinical remission in adults with moderately-to-severely active Crohn's disease who have had an inadequate response to conventional therapy.	US FDA EMEA
	Infliximab *Remicade®* Centocor/ Schering-Plough	Approved for a new indication that includes the treatment of severe, active Crohn's disease in pediatric patients aged 6-17 years who are nonresponsive to conventional therapy (i.e., a corticosteroid, or an immunomodulator) and primary nutrition therapy, or who are intolerant to, or have contraindications for such therapies.	EMEA

Dermal Fillers	**Hyaluronic Acid Gel Particles** *Perlane*® Medicis	Approved for implantation into the deep dermis to the superficial subcutis for the correction of moderate-to-severe facial folds and wrinkles, such as nasolabial folds.	US FDA
	Hyaluronic Acid Injectable Soft Tissue Filler *ELEVESS*® Anika Therapeutics / Galderma	Approved as a soft tissue filler for the treatment of facial wrinkles and scar remediation.	US FDA
	Cross-Linked Hyaluronic Acid Injectable Gel *Juvéderm™ Ultra;* *Juvéderm™ Ultra Plus* Allergan, Inc.	Approval of label extensions following submission of new clinical data that demonstrated that duration of benefit for both products may last up to 1 year.	US FDA
HIV	**Lopinavir/ Ritonavir** *Kaletra*® Abbott Laboratories	Approved a lower-strength tablet formulation (lopinavir 100mg + ritonavir 25mg) for pediatric HIV patients weighing >15kg who are able to swallow the intact tablet.	US FDA
	Maraviroc *Selzentry*® Pfizer, Inc.	Approved for use in combination with other antiretroviral drugs for the treatment of adults with CCR5-tropic HIV-1, who have been treated with other HIV medications and who have evidence of elevated levels of HIV in their blood.	US FDA
	Raltegravir Tablets *Isentress*® Merck & Co., Inc.	Approval granted to this integrase inhibitor for the treatment of HIV-1 infection; to be used in combination therapy with other antiretroviral agents.	US FDA
Oncologic Agent	**Rose Bengal Disodium 10%** *PV-10* Provectus Pharmaceuticals	Orphan Drug designation was granted to this anti-cancer drug for the treatment of metastatic melanoma.	US FDA
Vaccines	**Cervical Cancer Vaccine** *Cervarix*® GlaxoSmithKline	Approved for the prevention of cervical cancer and precancerous lesions associated with the most common cancer causing human papillomavirus types in females 10-45 years of age.	TGA Australia
	Smallpox Vaccine *ACAM2000™* Acambis PLC	Approved for protection against smallpox. This vaccine is intended for the inoculation of high-risk individuals and could be used to protect vulnerable populations in the event of a bioterrorist attack.	US FDA
	Vaccinia Immune Globulin Intravenous (Human) Cangene Corporation	Approved for counteracting certain complications associated with smallpox vaccination.	TPD Canada

Class	Name/Company	Approval Dates and Comments
Antipsoriatic Agent	**Adalimumab** *Humira*® Abbott Laboratories	The US FDA approved this biologic agent in January 2008 for the treatment of adults with moderate-to-severe chronic plaque psoriasis who are not suitable candidates for other systemic therapies.
Antihistamine	**Loratadine** *Claritin*® Schering-Plough	The US FDA approved a labeling change for this antihistamine in January 2008 to advise consumers that this OTC formulation relieves allergy symptoms caused by both perennial and seasonal allergies.
HIV	**Etravirine** *Intelence*™ Tibotec Therapeutics	The US FDA approved this non-nucleoside reverse transcriptase inhibitor (NNRTI) in January 2008 for the treatment of HIV infection in adults who have failed other antiretroviral therapies. NNRTIs block cellular replication. For use in combination with other antiretroviral agents.

Drug News

Anti-aging Agent	In recent studies led by dermatologists David McDaniel and Zoe Draelos, the efficacy of a new antioxidant, coffeeberry (REVALÉSKIN™, Stiefel Laboratories), was assessed. Dr. McDaniel led a 6 week, double-blind study of 30 subjects aged 30-70 years with a variety of skin types. Dr. Draelos conducted a 12 week study with 50 women aged 30-50 years with mild-to-moderate photoaging. Improvement in skin texture was seen after 3 weeks. The statistically significant findings from both investigations showed improvement in overall skin appearance.
Antipsoriatic Agent	Efalizumab (Raptiva®, EMD Serono Canada Inc.) is the first biologic treatment for psoriasis to receive public reimbursement through the provincial formularies in the Canadian provinces of Nova Scotia and New Brunswick. The benefit of Exceptional Status provides drug coverage to patients with severe, debilitating psoriasis.
Antipsoriatic Agent	At the 66th annual meeting of the American Academy of Dermatology*, clinical data was presented from a multicenter, randomized, double-blind Phase II study on oral apremilast (CC-10004, Celgene Corporation) for the treatment of moderate-to-severe plaque-type psoriasis. Apremilast inhibits the production of various proinflammatory mediators such as interleukin-2 (IL-2), IL-17, and IL-23, interferon-γ, TNF-α, leukotrienes, and nitric oxide synthase, which in combination, are responsible for immune-mediated inflammatory diseases. Interim findings showed that 24.4% of subjects treated with 20mg of oral apremilast every 12 hours experienced ≥75% improvement in their symptoms, as measured by the Psoriasis Area and Severity Index (PASI) after 84 days vs. 10.3% in the placebo group ($p=0.023$). Fifty-seven percent of subjects in the active treatment group achieved a PASI 50 response rate compared with 23% of subjects receiving placebo ($p<0.001$). PASI 90 was attained by 14% in the apremilast group vs. 5.7% of those who received placebo ($p=0.113$). Substantial improvement in patient quality of life, as measured by the Dermatology Life Quality Index (DLQI), was reported by patients in the apremilast arm. Based on the favorable mid-stage data, Celgene is expanding the dosage of apremilast to 30mg and extending the treatment period up to 6 months from 84 days. The most common side-effects reported were headache, nasal inflammation, nausea, and diarrhea. *A Phase 2 Study Demonstrating the Efficacy and Safety of the Oral Therapy CC-10004 in Subjects With Moderate to Severe Psoriasis. Abstract P2614. Presented at: the 66th Annual Meeting of the American Academy of Dermatology (February 1-5, 2008) in San Antonio, TX, USA.

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