

Treatments for Scalp Psoriasis with Emphasis on Calcipotriol Plus Betamethasone Dipropionate Gel (Xamiol[®])

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ABSTRACT

Scalp psoriasis occurs in 50%-75% of patients with plaque psoriasis. It may be the only area of the body affected, or it may be associated with disease elsewhere, including psoriatic arthritis. Most cases are treated topically, usually with steroids and/or calcipotriol. In 2008, Health Canada and the US FDA approved a stable, once-daily 2-compound gel containing calcipotriol and betamethasone dipropionate (Xamiol[®], LEO Pharma; Taclonex Scalp[®], Warner Chilcott). This once-daily therapy improves patient quality of life with a quick onset of action and greater efficacy than monotherapy with either ingredient or twice daily treatment with calcipotriol 0.005% (Dovonex[®], LEO Pharma) scalp solution. The gel vehicle was developed for ease of use, improved cosmetic acceptability and absorption on the scalp. By 2 weeks, approximately 60%, and by 8 weeks, approximately 70% of patients have controlled disease (i.e., absent or very mild disease). At 8 weeks, the calcipotriol and betamethasone dipropionate gel formulation has a safety profile comparable with betamethasone dipropionate and is associated with significantly fewer adverse events than calcipotriol. Xamiol[®] may be safely used for up to 52 weeks. No cases of atrophy, striae, or steroid purpura were noted in two 52-week studies.

Keywords: calcipotriol, betamethasone dipropionate, steroid, vitamin D analogue, psoriasis, scalp psoriasis, fixed combination therapy

Scalp Psoriasis

Psoriasis affects approximately 2% of the population,¹ and in 50%-80% of cases, the scalp is affected.² Scalp involvement may occur in isolation, with plaque psoriasis located elsewhere (most common), or with erythrodermic, pustular or guttate psoriasis, and/or psoriatic arthritis.³ Single or multiple, erythematous, pruritic, scaly plaques may occur anywhere on the scalp. The entire scalp may be affected and lesions may spread onto the forehead and behind the ears. Quality of life can be severely compromised, particularly if lesions are visible, scales fall onto clothes, and when pruritus is intense. Hair loss due to telogen effluvium may rarely occur.⁴ Scaling and hair, particularly with very thick hair, may be obstacles to medications reaching the scalp.

Current Treatments for Scalp Psoriasis

Treatment is almost always topical, although systemic and biologic therapy may be necessary, particularly if there is also extensive psoriasis elsewhere on the body.³ Once-daily, efficacious treatments have been associated with greater adherence.⁵

Topical steroids are the most widely used treatment. They are available in a number of formulations including lotions,

solutions, gels, sprays, foams, shampoos, oils, ointments, and creams. In a randomized controlled trial, superpotent clobetasol propionate shampoo (Clobex[®], Galderma) was shown to control (i.e., clear/almost clear) the disease in 42.1% of the patients (compared with 2.1% using the vehicle).⁶ In a double-blind, vehicle controlled study, 26% of the patients showed complete clearance vs. only 1% of the patients applying the vehicle.⁷ Foams are well tolerated and efficacious. Of the patients in clinical trials 72%-74% were controlled with betamethasone valerate⁸ or clobetasol foam.⁹ Salicylic acid may be added for its keratolytic effects (e.g., Diprosalic[®] lotion, Schering Plough).^{3,10}

The unpleasant smell, yellow staining of white or grey hair, and mutagenic potential limit the use of tars.¹¹

Calcipotriol (Dovonex[®], LEO Pharma), a topical vitamin D derivative, may be safely used for 52 weeks.¹² One study showed that twice daily application has similar efficacy to 1% betamethasone valerate,¹³ although other studies showed that it was significantly less effective than 0.1% betamethasone 17-valerate solution,¹⁴ and 0.05% clobetasol propionate shampoo.¹⁵

Some patients are treated with a twice-daily application of calcipotriol and corticosteroids to try to improve efficacy and tolerability. However, mixing commercially available topical steroids and calcipotriol is not advised, since the pH of the resultant mixture would be different and most likely both components would be inactivated.

Two small studies showed that a stable topical ointment containing calcipotriol and betamethasone dipropionate (Dovobet®, LEO Pharma) is efficacious.^{16,17} However, the ointment base is generally not well accepted for scalp use, since it makes the hair greasy and is difficult to wash out of long hair.

Xamiol®, the Compound

Xamiol® is a lipophilic gel specially formulated for the scalp. It contains the same active ingredients as Dovobet® ointment, namely calcipotriol 0.005% and betamethasone dipropionate 0.05%.¹⁸ This shear thinning gel sets when at rest and gets thinner when shaken. It has 2 year stability at room temperature, but should be used within 3 months of opening.¹⁹ Systemic absorption is low.¹⁹

Mechanism of Action

Calcipotriol binds to the vitamin D receptor, then acts as a heterodimer with the retinoid X receptor (RXR),²⁰ normalizing differentiation and proliferation. It also reduces CD45RO+ and T suppressor cells, and induces a Th1 to Th2 switch.²¹⁻²⁴

Betamethasone dipropionate is a potent topical steroid. In the cytoplasm, steroids bind to glucocorticoid receptors, then rapidly translocate to the nucleus where they

inhibit or stimulate genes that regulate inflammation.²⁵ As a consequence, the production of cytokines, such as interleukin-1 and -8, tumor necrosis factor alpha, and gamma interferon are inhibited; nitric oxide, prostaglandins, and levels of leukotrienes are reduced.^{23,26,27} Corticosteroids can also regulate keratinocyte differentiation.²⁸ Both vitamin D and corticosteroids can increase the number of T regulatory cells that are diminished in psoriatic skin.^{29,30}

Clinical Efficacy of Xamiol®

This formulation has a quick onset of action and is an effective long-term treatment. In the phase II trial (n=218),³¹ after 2 weeks, the total sign score (TSS = redness score + thickness score + scaling score; range 0-12) decreased by 4.49 in the Xamiol® arm, and by 3.75 in the betamethasone arms (p=0.005). Moreover, 67.6% of the Xamiol® group compared with 52.7% in the betamethasone group were clear/almost clear (p=0.025). At 8 weeks, the TSS was reduced by 5.33 for the Xamiol® group vs. 4.76 for the betamethasone arm (p=0.042); 83.3% of patients in the Xamiol® group vs. 74.6% using betamethasone showed an absence of disease or very mild disease.

The 2 phase III, international, multicenter, randomized, blinded pivotal trials involved almost 3,000 patients and showed that Xamiol® was more efficacious than its individual ingredients.^{32,33} (Table 1)

Jemec et al.³² reported a reduction of 70.8% in TSS in the Xamiol® group, 57.7% in betamethasone dipropionate (p=0.12) group, 49.0% in the patients using calcipotriol (p<0.0001), and 35.6% using the vehicle (p<0.0001). The Investigator Global Assessment (IGA) was “absent/very

STUDY	Calcipotriol/ Betamethasone dipropionate O.D.	Betamethasone dipropionate O.D.	Calcipotriol O.D.	Calcipotriol scalp solution B.I.D.	Vehicle O.D.
Buckley, et al. ³¹ (n=218)	83.3%	74.6%			
Jemec, et al. ³² (n=1505)	71.2%	64.0%	36.8%		22.8%
van der Kerkhof, et al. ³³ (n=1415)	68.4%	61.0%	43.4%		
Kragballe, et al. ³⁴ (n=312)	68.6%			31.4%	
Luger, et al. ³⁶ (n=869)	55.7%		31.8%		
Tyring, et al. ³⁷ (n=175)	71.9%				40.5%

Table 1: Percent of patients with Investigator Global Assessment of absent/very mild at 8 weeks

mild” in 71.2% of the patients who were treated with Xamiol® vs.:

- 64.4% of those treated with betamethasone dipropionate (odds ratio [OR] 1.41, 95% confidence interval [CI]: 1.08-1.83, p=0.011)
- 36.8% of those treated with calcipotriol (OR 4.13, 95% CI: 3.00-5.70, p<0.0001)
- 22.8% of patients treated with the vehicle (OR: 8.65, 95% CI: 5.52-13.56, p<0.0001).

The onset of action was fast; at 2 weeks, 57.5% had absent/very mild disease on Xamiol® compared with 47.1% on betamethasone, 18.8% on calcipotriol, and 11.8% on vehicle. The amount of study medication used during the entire study was less for Xamiol® (139.1gm vs. 159.5gm for betamethasone, 155.4gm for calcipotriol, and 176.4gm for vehicle. The average weekly quantity of study medication used was 17-22gm/week.

In a study by Kragballe et al., once-daily Xamiol® was compared with twice daily Dovonex® scalp solution (n=312).³⁴ More than twice as many patients using Xamiol® had controlled disease (i.e., absent/very mild; 68.6% vs. 31.4%). At 8 weeks, 56.3% of those whose condition was very severe had controlled disease with Xamiol®, but none

did on calcipotriol. In common with Jemec’s trial, a quick onset was noted; at week 2, 49% on Xamiol® compared with 38.4% on steroids, and 15.7% on calcipotriol had absent/very mild disease. Significant improvements in quality of life, as measured by the short form-36 (SF-36) questionnaire, were noted in the mental component at weeks 2, 4, and 8, but only at week 8 for calcipotriol scalp solution.³⁵ In addition, the amount of improvement in the Skindex 16 was approximately twice as great with Xamiol®.

Two 52-week studies assessed long-term management.^{36,37} In the first study, disease was absent/very mild/mild at 92.3% of the visits in the Xamiol® arm vs. 80% in the calcipotriol arm (p<0.0001).³⁶ The withdrawal rate due to unacceptable treatment efficacy was higher in the calcipotriol arm (11.6% vs. 3.3%). The second long-term study (n=175) was conducted in patients who were Hispanic/Latino (56%) or African-American (44%).³⁷ In the initial 8-week placebo controlled portion, significantly more patients on Xamiol® than vehicle had controlled disease (71.9% vs. 40.5%, p<0.001). In patients treated with Xamiol® from the onset, the median number of visits in which patients had clear, minimal or mild disease was 100%.

STUDY	Patients with at least 1 AE	Patients with 1 AE on calcipotriol or vehicle	Patients with perilesional AEs	Adverse Drug Reactions
Buckley, et al. ³¹	35.5% Xamiol® vs. 35.5% betamethasone	-----	10.3% Xamiol® vs. 10.0% betamethasone	8.14% Xamiol® vs. 10.9% betamethasone
Jemec, et al. ³²	34.4% Xamiol® vs. 34.9% betamethasone (p=0.91)	46.2% calcipotriol (p=0.0014) vs. 40% vehicle (p=0.24)	4.7% Xamiol® vs. 5.3% betamethasone vs. 13.2% calcipotriol vs. 13.3% vehicle	7.9% Xamiol® vs. 8.4% betamethasone vs. 19.5% calcipotriol vs. 15.6% vehicle
van der Kerkhof, et al. ³³	38.7% Xamiol® vs. 41.0% betamethasone (p=0.43)	46.1% calcipotriol (p=0.04)	6.2% Xamiol® vs. 5.8% betamethasone vs. 12.8% calcipotriol	9.6% Xamiol® vs. 8.8% betamethasone vs. 18.4% calcipotriol
Kragballe, et al. ³⁴	34.5% Xamiol®	56.7% calcipotriol scalp solution (p<0.001)	3.4% Xamiol® vs. 19.2% calcipotriol scalp solution (p<0.001)	3.4% Xamiol® vs. 26.9% calcipotriol scalp solution (p<0.001)
Luger, et al. ³⁶	66.8%	71.9% calcipotriol (p=0.11)	11.9% Xamiol® vs. 21.6% calcipotriol (p<0.001)	17.2% Xamiol® vs. 29.5% calcipotriol (p<0.001)
Tyring and Bibby ³⁷	36.7% Xamiol® vs. 34.2% vehicle	-----	3.1% Xamiol® vs. 2.6% vehicle	6.3% Xamiol® vs. 7.9% vehicle

Table 2: Adverse events reported for studies comparing Xamiol® with other treatments.

Patient Information

The Xamiol® bottle should be shaken. Then part hair to expose the affected area of the scalp, then apply to dry skin and gently rub in. Wash hands after applying. To remove any excess gel vehicle from the hair, a mild, unmedicated shampoo should be applied to dry hair and left on for a few minutes. Then the hair should be washed normally. A second shampooing may be required.¹⁸

Safety of Xamiol®

There were no significant changes in serum calcium, skin atrophy, or striae in any of the trials. Table 2 summarizes adverse events in the phase II and pivotal phase III trials.

A 52-week Xamiol® vs. calcipotriol study by Luger et al.³⁶ showed similar results, although there were no differences in the rates of AEs possibly related to long-term corticosteroid use (e.g., rosacea, folliculitis, acne; 2.6% Xamiol® vs. 3.0% corticosteroids). In the Hispanic/Latino/African-American study, the Xamiol® and vehicle groups had similar AE rates (36.7% and 34.2, respectively), adverse drug reactions (6.3% and 7.9%, respectively) and perilesional/lesional adverse events (3.1 and 2.6%, respectively) at 8 weeks.³⁷

Conclusion

Xamiol® is a fast-acting, very efficacious, safe, once-daily treatment for scalp psoriasis ranging from mild to very severe. It is more efficacious than calcipotriol in the same base, or as the marketed solution (Dovonex® scalp solution), betamethasone dipropionate, or the gel vehicle. Approximately 60% of patients achieve absent or very mild disease after only 2 weeks of therapy, and 70% after 8 weeks. The safety profile is similar to that of betamethasone dipropionate and better than calcipotriol. Two 52-week studies have shown that Xamiol® can be safely used long-term. No cases of atrophy, striae, or senile purpura were noted in any of the studies.

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Use of Tacrolimus Ointment in Vitiligo Alone or in Combination Therapy

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ABSTRACT

Current treatments for vitiligo are largely unsatisfactory. Topical corticosteroids and phototherapy (narrow-band UVB and psoralen+UVA) are the most prescribed, however, these therapies are often not effective and have important side-effect, especially when used for a long time. Many studies have reported the efficacy and safety of tacrolimus ointment in adults and children with vitiligo, particularly when located on the head and neck. Successful treatment is possible when it is combined with other therapies, such as narrow-band UVB, microphototherapy, helium-neon laser, or narrow-band excimer laser.

Keywords: corticosteroids, phototherapy, tacrolimus, vitiligo

Vitiligo, an acquired pigmentary skin disorder affecting 1% of the world's population, is characterized by depigmented macules that correspond histologically with reduced or absent cutaneous melanocytes.¹ Although the mechanism of melanocyte dysfunction and disappearance is still unclear, there are 2 major theories regarding its pathogenesis: the autoimmune theory and the autotoxicity theory.² Current treatments, e.g., topical corticosteroids, narrow-band UVB (NB-UVB), and psoralen+UVA (PUVA), are the most prescribed,³ but are not often effective, and corticosteroids applied to the face may lead to cutaneous atrophy, telangiectasia, and ocular complications. NB-UVB treatment requires expensive equipment and trained personnel, and PUVA has been associated with a risk of carcinogenesis.³ Phototherapy and corticosteroids have limited effectiveness, particularly on the acral regions.⁴

Immunomodulators, such as tacrolimus ointment 0.1% and 0.03% (Protopic®, Astellas), and pimecrolimus cream 1% (Elidel®, Novartis) are approved for treating atopic dermatitis in adult patients and pediatric patients over 2 years of age.² Tacrolimus can be used as an alternative to topical steroids in many other forms of dermatitis, such as vitiligo. This ointment does not cause the atrophy, telangiectasia, or adverse ocular effects of topical corticosteroids, which has limited application to the face and intertriginous areas.¹

Tacrolimus acts on T cells and mast cells, inhibiting T cell activation and the production of proinflammatory cytokines, such as Tumor Necrosis Factor (TNF), whose levels are higher in vitiligo lesional skin.⁵ Moreover, it prevents the release of proinflammatory mediators in mast cells by degranulation.¹ Recently, the successful treatment of vitiligo with tacrolimus has been reported (See Table 1).

Xu et al.¹ studied 30 vitiligo patients who were treated with tacrolimus ointment for 4 months or more. Of these, 83.3% patients showed some repigmentation at the end of 4 months. In particular, 1 patient achieved excellent (100%) repigmentation at the end of 14 weeks, and another 2 patients exhibited 100% repigmentation at the end of 16 weeks. Of these 25 patients, repigmentation was graded as complete in 20%, moderate in 20%, mild in 23.3%, and minimal in 20%. Of the patients with segmental vitiligo of the head and neck, 80% showed the some response, but there was no statistical significance between segmental and vulgaris vitiligo. Patients who had vitiligo for more than 5 years also responded well. Repigmentation is notoriously difficult to achieve. The mean percentage of repigmentation on the head and neck was greater than that seen on the trunk and extremities. The only reported side-effect was initial burning on application in 4 patients. The study found that tacrolimus

Reference	Evidence
Xu, et al. ¹	83.3% (25/30) repigmentation: 12% excellent 20% complete 20% moderate 23.3% mild 20% minimal
Choi, et al. ²	69.3% repigmentation: (no difference of disease location or age of onset; better response in short-duration disease)
Hartmann, et al. ⁴	81% repigmentation on face 80% repigmentation on extremities (when in occlusion)

Table 1: Recent studies on the treatment of vitiligo with tacrolimus ointment

was a safe and effective therapy for vitiligo, especially when it involved the head and neck.

In 2008, Choi et al.² studied 79 patients; 52 were treated with tacrolimus and 27 with topical corticosteroids. Topical immunomodulators were found to be as effective as topical steroids and patient response was faster than that once obtained by topical steroids. The patients studied were then divided in 3 groups according to the location of vitiligo lesions: 59 had lesions on the face, 53 on the hands, and 23 on the feet. After treatment, 38 showed repigmentation on the face, 31 on the hands, and 9 on the feet. The investigators could not find any statistically significant differences in the ratio of lesions, which showed response among these 3 groups. They further divided their study into 2 groups: long-duration (>12 months) and short-duration (<12 months). The short-duration group showed a higher rate of response that was statistically significant. There was no statistical difference between the group of younger (i.e., <18 years of age) and older (i.e., >18 years of age) patients. The faster response of topical immunomodulators may be related to their effects on melanocytes, i.e., the proliferation of melanocytes is enhanced by a tacrolimus-treated keratinocyte supernatant, which is rich with stem cell factor and matrix metalloproteinase-9.² These results coincide with those of Lepe et al.⁷ who, in a study of 20 patients, documented that clobetasol and tacrolimus showed more than 75% repigmentation in 5 patients. There were no statistically significant differences between these 2 treatments ($p>0.05$).

In a placebo-controlled 12-month prospective study of 31 vitiligo patients, Hartmann et al.⁴ documented the safety and efficacy of tacrolimus, even in those with disease of long-standing duration and in those who received long-term treatment. Tacrolimus may significantly improve the quality of life of affected patients. In the region beyond the face and neck, additional occlusion with polyurethane foil or hydrocolloid dressing may significantly enhance the therapeutic results and may shorten the time until the start of repigmentation. When tacrolimus was applied occlusively, repigmentation was documented in 81% of patients with facial lesions, and in 80% of patients with lesions on the extremities.

Many studies suggest the associated use of tacrolimus with other therapeutic options to improve the rate of repigmentation.⁸⁻¹⁰ Lotti et al.⁸ studied 458 patients with vitiligo that affected less than 10% of their skin surface. A 311 nm narrow-band microphototherapy (Bio Skin[®], Cropper Medical) was given alone or in combination with topical treatment, (i.e., tacrolimus, pimecrolimus, betamethasone dipropionate 0.05%, calcipotriol, or phenylalanine cream). The investigators reported that targeted combination therapies in vitiligo were remarkably more effective than a single treatment.

Fai et al.⁹ studied 110 patients with chronic and refractory vitiligo in a period of 30 months, and suggested that the combination of topical tacrolimus with NB-UVB phototherapy as an alternative approach that could be highly effective for the treatment of refractory vitiligo located on the face, trunk, and limbs. However, long-term data and randomized controlled trials on a large number of patients are required.

The association of tacrolimus with NB-UVB excimer laser has been reported to improve the repigmentation rate, but it is associated with the possibility of unexpected burns.¹⁰ Recently, an association between helium-neon laser and topical tacrolimus has been proposed to be effective without infringing on the issue of additional photocarcinogenic risk. Since the underlying repigmentation mechanisms of these 2 modalities are different, it is reasonable to propose that combining them may produce better clinical results.¹¹

It is important to remember that NB-UVB, microphototherapy, UVB narrow-band excimer laser, and helium-neon laser still have the potential to produce skin cancer. In fact they are effective for treating vitiligo, especially when combined with tacrolimus ointment. Based on the evidence, these treatment options appear to be safe and well tolerated, even though they may have carcinogenic potential, which is extremely important for children affected by vitiligo.

Silverberg et al.¹² reported that the use of tacrolimus ointment is an effective alternative treatment for vitiligo in children, particularly involving head and neck areas. Kanwar et al. studied 25 Asian children with vitiligo (i.e., 54.5% had vitiligo vulgaris, 40.9% had focal vitiligo, and 4.5% had segmental vitiligo). In this study, application with topical 0.03% tacrolimus applied twice daily for 12 weeks was shown to be an effective and well-tolerated treatment. Response was graded as complete (i.e., >75% repigmentation) in 57.9% of the patients, moderate (i.e., 50%-75% repigmentation) in 26.3%, mild (i.e., <50% repigmentation) in 15.7%, and 3 patients had no response. Side-effects, such as pruritus and burn, which was noted in only 3 patients, were minimal.¹³

Conclusion

Tacrolimus ointment is effective and safe for treating vitiligo, especially when it is located on the head and neck, or when the disease is long-lasting. Childhood vitiligo can be successfully treated with tacrolimus, sparing the adverse events seen from topical corticosteroids. Although topical application is not associated with systemic immunosuppression, the long-term risk from the application of tacrolimus ointment to the skin is still unknown. Further studies with topical tacrolimus for the treatment of vitiligo with long-term follow-up are necessary to better evaluate the safety, efficacy, and stability of repigmentation, especially when associated with focused UVB microphototherapy.

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The Canadian Pemphigus and Pemphigoid Foundation

The Canadian Pemphigus and Pemphigoid Foundation was established in March 2009, and is a national not-for-profit organization created to help improve the quality of life of Canadians who are suffering from these diseases. Their activities focus on:

- Helping set up support groups across Canada so that patients and caregivers can learn from one another as well as medical experts in their area.
- Developing and distributing relevant information and educational materials to help patients develop effective health management strategies.
- Working with other organizations and medical professionals who share their interests in improved health management strategies and finding a cure.

Their Board of Directors is comprised of talented and committed patients and caregivers from across Canada, with some of the most knowledgeable and experienced medical professionals in Canada participating on their Medical Advisory Council. The Council is lead by Dr. Neil Shear, Chief of Dermatology – Sunnybrook Health Sciences Centre and Professor at the University of Toronto. Joining him is Dr. Scott Walsh (University of Toronto), Dr. Régine Mydlarski (University of Calgary), Dr. Jan Dutz (University of British Columbia), pharmacist Sandra Knowles (Sunnybrook Health Sciences Centre) and, more recently, Dr. Peter Chauvin, Associate Professor and Director of the Division of Oral Diagnostic Sciences - Faculty of Dentistry, McGill University. Learn more about this foundation at <http://www.pemphigus.ca/e/>.

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Update on Drugs

Name/Company	Approval Dates/Comments
Alitretinoin <i>Toctino</i> ® Basilea Pharmaceutica	The health authorities in Austria, Belgium, and Luxembourg approved this new once-daily oral treatment in March 2009 for the treatment of adults with severe chronic hand eczema unresponsive to potent topical corticosteroids.
Pralatrexate Allos Therapeutics	The US FDA received a New Drug Application in March 2009 for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma.
Benzyl Alcohol Lotion 5% Sciele Pharma	The US FDA approved this new prescription non-neurotoxic medication in April 2009 for the treatment of head lice in patients 6 months of age and older. This product kills head lice by asphyxiation without potential neurotoxic side-effects.
Botulinum Toxin – Type A <i>Azzalure</i> ® Galderma/Ipsen	The French regulatory authority, the Agence Française de Sécurité Sanitaire des Produits de Santé, approved this neurotoxin in March 2009 for aesthetic use in the treatment of frown lines.

Drug News

The Genentech unit of Roche Holding AG reported in April 2009, that it is pulling the psoriasis treatment Efalizumab (Raptiva®) off the US market because of links to an often fatal brain infection. The drug was approved by the US FDA for patients with chronic moderate-to-severe plaque psoriasis and this move comes only about 6 months after the drug's labeling was updated to carry warnings of links to progressive multifocal leukoencephalopathy. The company said no new prescriptions should be written, and the drug will no longer be available at all after June 8, 2009. Genentech says patients should talk with their doctors before stopping treatment with the drug, because abruptly halting it can lead to sudden worsening of their psoriasis.

Health Canada and Allergan are informing healthcare professionals about important safety information related to botulinum toxin – type A and the potential risk of serious adverse effects of muscle weakness remote to the injection site. Key safety updates within the new product monographs for this neurotoxin include:

- Patients may experience muscle weakness remote to the injection site. Possible symptoms include muscle weakness, dysphagia, aspiration pneumonia, speech disorders, and respiratory depression. These reactions can be fatal.
- Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise.
- Botulinum toxin – type A should only be given by physicians with appropriate qualifications and experience in the use of this product. The revised product monographs emphasize the need to follow the recommended dosage and frequency of administration.
- Patients with a history of underlying neurological disorders, dysphagia and/or aspiration should be treated with extreme caution.

Any case of serious suspected distant toxin spread or other serious or unexpected adverse reactions in patients receiving botulinum toxin – type A should be reported to Allergan or Health Canada.