Chemical compatibility of calcipotriene 0.005% foam in combination with tazarotene:

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Objectives: Combination therapy is an effective approach to the treatment of skin disease, and studies have shown that topical combination therapy with a vitamin D3 analogue and a corticosteroid are an effective approach for treating mild to moderate psoriasis. It is believed that this combination approach enhances the efficacy of the vitamin D3 analogue and limits the toxicity of the corticosteroid. A new calcipotriene foam formulation has been developed using a novel vehicle technology that collapses to deliver calcipotriene through the skin. Because the compatibility of products not only depends on the active ingredients, but also the inactive ingredients present in the respective products, it is critical to understand whether a vehicle influences the chemical stability of the active ingredients. The objective of these studies was to evaluate the chemical compatibility of calcipotriene 0.005% foam (CAL foam) with available corticosteroid products: desonide 0.05% foam (DES foam), clobetasol propionate 0.05% EF foam (CP foam) and clobetasol propionate 0.05% spray (CP spray).

Methods: Equal amounts (400-500 mg) of CAL foam and DES foam, CP foam, or CP spray were sealed in a glass container and stored at 40°C for 6, 15, 24, 32, and 48 hours. Concentrations of calcipotriene, desonide, and clobetasol propionate were determined by ultra performance liquid chromatography (UPLC) after each time-point and compared to that of an unstressed freshly mixed sample (control).

Results: The potencies of calcipotriene remained at >97% relative to control samples, thus calcipotriene is chemically stable for up to 48 hours at 40°C after CAL foam is mixed with either DES foam, CP foam or CP spray. Likewise, the potency of desonide and clobetasol propionate remained at >97% relative to control samples, thus desonide and clobetasol propionate are also chemically stable for up to 48 hours at 40°C after CAL foam is mixed with either DES foam, CP foam, or CP spray.

Conclusion: These results show that calcipotriene foam is chemically compatible when used concomitantly with either desonide foam or with clobetasol propionate in either DES foam or EF foam formulation. This study provides the clinician with the confidence to use this new calcipotriene foam formulation in combination with available topical steroid foams and sprays.

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Long-term safety of adalimumab: An analysis of all adalimumab exposure in all moderate to severe psoriasis clinical trials

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Objective: To assess the long-term safety data of all adalimumab-treated patients in all phase II, II/III, III, Illb, and IV clinical trials in moderate to severe psoriasis.

Methods: Safety data from all patients treated with at least 1 dose of adalimumab in any of the 15 clinical trials in moderate to severe psoriasis were pooled through November 6, 2008. Patients treated through November 6, 2009, respectively, to create two overlapping datasets. Most patients received 40 mg adalimumab every other week, begun either 1 week after an initial dose of 80 mg or after a period of placebo treatment. Adverse events (AEs) that occurred up to 70 days after the final dose of adalimumab were analyzed. Standardized incidence ratios (SIR) were determined by ultra performance liquid chromatography (UPLC) after each time-point and compared to that of an unstressed freshly mixed sample (control).

Results: One thousand three hundred ten patients were enrolled from September 26, 2008 to November 30, 2009, of which 1255 have received ≥1 dose of ADA. The demographic distribution includes 58% male; median age 46 (range 18-91); median weight 86.2 kg (range 43.1-193.0). Median registry exposure is 174 days (range, 14-676). Of dosed patients, 8% (0.6%) have discontinued the registry, most frequently because of withdrawal of consent. A total of 1% (15/1235) of patients reported ≥1 SAE. One patient died after experiencing systemic inflammatory response syndrome, aspiration pneumonia, and congestive cardiac failure. Serious infections of special interest occurred in two patients (candidiasis and urosepsis). One patient, who at enrollment had a negative purified protein derivative test, developed disseminated TB after 16 weeks of treatment. Malignancies were reported in nine patients (0.7%): seven were nonmelanoma skin cancer and two were melanomas (1 invasive melanoma). One patient reported lupus-like syndrome, allergic reaction, demyelinating disorder, congestive heart failure, and stroke. For this interim analysis, 49.6% of 1235 patients had reached 3 months in the study; of observed patients, 46.6% (286/610) had a PGA of ‘clear or minimal,’ and mean change from baseline DLQI was -5.1 (97% confidence interval 0.001). There were no events of hepatitis B reactivation, 1 lymphoma, and no melanoma in situ and 1 invasive melanoma. One patient each reported lupus-like syndrome, aspiration pneumonia, and congestive cardiac failure. Serious infections and malignancies (excluding NMSC) were 0.006/0.007. The 2008 and 2009 incidence rates were identical for nonmelanoma skin cancer (NMSC) (0.007), demyelinating disorder (0.002), on patient-reported outcomes (PROs).

Results: AE rates from pooled results for all adalimumab-treated patients in all moderate to severe psoriasis clinical trials were low and generally stable over time.

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