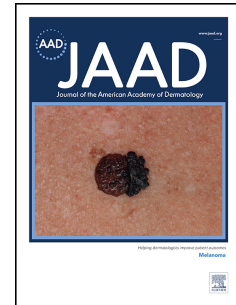


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References for Common Contact Allergens Present in Prescription Topical Corticosteroids

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Title: References for Common Contact Allergens Present in Prescription Topical Corticosteroids
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To the Editor:

Contact sensitization is a requisite for the development of allergic contact dermatitis (ACD). This process may occur more readily on an impaired skin barrier, particularly for weak sensitizers.¹ Therefore, patients with eczematous dermatoses treated with a topical corticosteroid (TC) can experience worsening to the very medication meant to help. In these situations, selection of an appropriate TC can be challenging. Patch testing data suggest sensitization to inactive ingredients in prescription TCs occurs more frequently than to the active ones,^{2,3} and use of specific inactive ingredients can vary by the TC active ingredient, vehicle, and even manufacturer. In a prior study of over 5000 patch tests, the positivity rate for propylene glycol (PG), a common TC ingredient, was 4.0% (100% PG concentration), compared to 0.8% (budesonide), 0.2% (hydrocortisone butyrate), 0.2% (clobetasol-17-propionate), and 0.1% (desonide) for prescription TCs.³ Studies of patch test positivity to sorbitan sesquioleate, another common TC ingredient have ranged from 0.6% to 10.7%.⁴

The aim of our study was to identify common contact allergens within prescription TCs across several different corticosteroid active ingredients, vehicles, and manufacturers, and provide a resource for prescribers to select appropriate TCs for patients sensitized to common allergens present within these medications. We obtained ingredient lists from manufacturers for the ointment and cream formulations of 13 commonly prescribed TCs and analyzed their inactive ingredients for contact allergens currently on patch testing core series (American Contact Dermatitis Society [ACDS] or North American Contact Dermatitis Group [NACDG]).³

We reviewed 120 prescription TCs (**Table 1**). PG was the most commonly identified potential allergen among inactive ingredients, present in 62/120 (51.2%). Inactive ingredients present in ointments varied less frequently between manufacturers compared to creams. Nevertheless, when prescribing TCs we recommend including a note to the pharmacist indicating ingredients to avoid (e.g. PG) and specify at least one manufacturer that produces an appropriate version (e.g. dispense EXAMPLE manufacturer or an alternative with the exact same active and inactive ingredients).

As a supplemental reference, we also reviewed inactive ingredients present in topical prescription alternatives to TCs. These products may be preferred in certain scenarios (e.g. for corticosteroid-sparing agents and/or cases of corticosteroid allergy; **Table 2**).

Several resources are currently available to aid in selection of TCs or TC-sparing agents for patients with ACD. These include The National Library of Medicine's DailyMed, The Contact Allergen Management Program (CAMP), and SkinSAFE Products. The DailyMed website is challenging to navigate and use of its search function for individual products is often inadequate. CAMP and Skin Safe generate a personalized database of products, including TCs, based on an individual's identified contact allergens. While these systems are tremendously helpful, they require membership to the ACDS (CAMP) or paid subscription (SkinSAFE Products) and many TC prescribers do not have accounts.

To address some of these challenges identified in prescribing TCs for patients with ACD, we will create a routinely updated, publicly available reference on inactive ingredients in TCs, similar to

Table 1 (Twitter/Instagram @DrAriGoldminz and @MiaMologousis). Additional vehicle options will also be included in this reference.

References:

1. Goossens RA. Allergic contact dermatitis from the vehicle components of topical pharmaceutical products. *Immunol Allergy Clin North AM*. 2014;34(3):663-670. doi:10.1016/j.iac.2014.04.010
2. Coloe J, Zirwas MJ. Allergens in corticosteroid vehicles. *Dermatitis*. 2008;19(1):38-42. doi:10.2310/6620.2008.07054
3. DeKoven JG, Warshaw EM, Zug KA, et al. North American Contact Dermatitis Group Patch Test Results: 2015-2016. *Dermatitis*. 2018;29(6):297-309. doi:10.1097/DER.0000000000000417
4. de Groot A, Gilissen L, Geier J, Orton D, Goossens A. Adding sorbitan sesquioleate to the European baseline series: Necessary, reasonable, or unavoidable? *Contact Dermatitis* 2019;81(3):221-225. doi:10.1111/cod.13332
5. Sheman A, Roszko K. Contact allergy to propylene glycol and cross reactions. *Dermatitis*. 2018;29(6):350-351. doi:10.1097/DER.0000000000000416

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Potency	Topical Corticosteroid	Manufacturers Assessed	Propylene Glycol (PG)	Sorbitan/Sorbitol/Polysorbate ^a	Sorbic Acid	Parabens	Lanolin	Cetearyl/Cetyl/Stearyl Alcohol	Beeswax/White Wax	Coconut Derivatives	Methylchlorisothiazolinone/ methylisothiazolinone (MI/ MCI)	Diazolidinyl Urea	Isopropyl Myristate	Edetate Disodium ^c	Benzyl Alcohol
Class I (Superpotent)	Clobetasol propionate 0.05% ointment	⁹ Taro, Teligent, Akorn/Hi-Tech, Encube, Lupin, Glenmark, Cadila/Zydus, Sandoz/Fougera, Cosette/G&W	<i>Taro, Teligent, Akorn/Hi-Tech, Encube, Lupin, Glenmark, Cadila/Zydus, Sandoz/Fougera, Cosette/G&W</i>	<i>Taro, Teligent, Akorn/Hi-Tech, Encube, Lupin, Glenmark, Cadila/Zydus, Sandoz/Fougera, Cosette/G&W</i>	–	–	–	–	–	–	–	–	–	–	–
	Clobetasol propionate 0.05% cream	⁹ Taro, Teligent, Sola, Akorn/Hi-Tech, Lupin, Glenmark, Cadila/Zydus, Sandoz/Fougera, Teva/Actavis	<i>Taro, Teligent, Sola, Akorn/Hi-Tech, Lupin, Glenmark, Cadila/Zydus, Sandoz/Fougera, Teva/Actavis</i>	<i>Teligent, Sola, Akorn/Hi-Tech, Cadila/Zydus, Taro, Lupin, Glenmark, Sandoz/Fougera, Teva/Actavis</i>	–	<i>Teligent, Sola, Akorn/Hi-Tech, Cadila/Zydus, Taro, Lupin, Glenmark, Sandoz/Fougera, Teva/Actavis</i>	<i>Teligent, Sola, Akorn/Hi-Tech, Cadila/Zydus, Taro, Lupin, Glenmark, Sandoz/Fougera, Teva/Actavis</i>	<i>Taro, Teligent, Sola, Akorn/Hi-Tech, Lupin, Glenmark, Cadila/Zydus, Sandoz/Fougera, Teva/Actavis</i>	<i>Taro, Lupin, Glenmark, Sandoz/Fougera, Teva/Actavis, Teligent, Sola, Akorn/Hi-Tech, Cadila/Zydus</i>	–	–	–	–	–	–
	Betamethasone dipropionate 0.05% (augmented) ointment	⁵ Merck, Prasco, Teligent, Sandoz/Fougera, Teva/Actavis	<i>Merck, Prasco, Teligent, Sandoz/Fougera, Teva/Actavis</i>	–	–	–	–	–	<i>Merck, Prasco, Teligent, Sandoz/Fougera, Teva/Actavis</i>	–	–	–	–	–	–
	Halobetasol propionate 0.05% ointment	⁵ Teligent, Sola, Taro, Perrigo, Cosette/G&W	<i>Teligent, Sola, Taro, Perrigo, Cosette/G&W</i>	<i>Teligent, Sola, Taro, Perrigo, Cosette/G&W</i>	–	–	–	–	<i>Teligent, Sola, Taro, Perrigo, Cosette/G&W</i>	<i>Teligent, Sola, Taro, Perrigo, Cosette/G&W</i>	–	–	–	–	–
	Halobetasol propionate 0.05% cream	⁴ Taro, Perrigo, Sandoz/Fougera, Cosette/G&W	–	–	–	–	–	<i>Teligent, Sola, Taro, Perrigo, Cosette/G&W</i>	–	–	<i>Taro, Perrigo, Sandoz/Fougera, Cosette/G&W</i>	<i>Taro, Perrigo, Sandoz/Fougera, Cosette/G&W</i>	–	–	–
Class II (High Potency)	Betamethasone dipropionate 0.05% (augmented) cream	⁴ Taro, Merck, Perrigo, Sandoz/Fougera	<i>Taro, Merck, Perrigo, Sandoz/Fougera</i>	<i>Taro, Merck, Perrigo, Sandoz/Fougera</i>	–	–	–	<i>Taro, Merck, Perrigo, Sandoz/Fougera</i>	<i>Taro, Merck, Perrigo, Sandoz/Fougera</i>	–	–	–	–	–	–
	Betamethasone dipropionate 0.05% ointment	² Sandoz/Fougera, Teligent	–	–	–	–	–	–	–	–	–	–	–	–	–
	Desoximetasone 0.25% ointment	⁹ Taro, Teligent, Akorn/Hi-Tech) Glenmark, Cadila/Zydus, Teva/Actavis, Sandoz/Fougera, Perrigo, Lupin	–	–	–	–	–	–	<i>Taro, Teligent, Akorn/Hi-Tech^d, Glenmark, Cadila/Zydus, Teva/Actavis, Sandoz/Fougera^d, Perrigo, Lupin^d</i>	–	–	–	–	–	–
	Desoximetasone 0.25% cream	⁴ Taro, Teva/Actavis, Perrigo, Lupin	–	–	–	–	<i>Taro, Teva/Actavis, Perrigo, Lupin</i>	<i>Taro, Teva/Actavis, Perrigo, Lupin</i>	–	–	–	–	<i>Taro, Teva/Actavis, Perrigo, Lupin</i>	<i>Teva/Actavis, Taro, Perrigo, Lupin</i>	–
Class III (Medium to High Potency)	Betamethasone dipropionate 0.05% cream	⁶ Taro, Glenmark, Cadila/Zydus, Sandoz/Fougera, Teva/Actavis, Cosette/G&W	<i>Taro, Glenmark, Teva/Actavis, Cadila/Zydus, Sandoz/Fougera, Cosette/G&W</i>	<i>Glenmark, Taro, Teva/Actavis, Cadila/Zydus, Sandoz/Fougera, Cosette/G&W</i>	–	–	–	<i>Taro, Cadila/Zydus, Sandoz/Fougera, Teva/Actavis, Cosette/G&W, Glenmark</i>	<i>Glenmark, Taro, Teva/Actavis, Cadila/Zydus, Sandoz/Fougera, Cosette/G&W</i>	–	–	–	–	–	–
Class IV/V (Medium Potency)	Desoximetasone 0.05% ointment	³ Taro, Teligent, Lupin	–	–	–	–	–	–	–	–	–	–	–	–	–
	Desoximetasone 0.05% cream	² Taro, Lupin	–	–	–	–	<i>Taro, Lupin</i>	<i>Taro, Lupin</i>	–	–	–	–	<i>Taro, Lupin</i>	<i>Taro, Lupin</i>	–
	Fluocinolone acetonide 0.025% ointment	³ Teligent, Sandoz/Fougera, Cosette/G&W	–	–	–	–	–	–	–	–	–	–	–	–	–
	Fluocinolone acetonide 0.025% cream	² Teligent, Cosette/G&W	<i>Teligent, Cosette/G&W</i>	<i>Cosette/G&W, Teligent</i>	<i>Cosette/G&W, Teligent</i>	<i>Teligent, Cosette/G&W</i>	<i>Cosette/G&W, Teligent</i>	<i>Teligent, Cosette/G&W</i>	<i>Teligent, Cosette/G&W</i>	–	–	–	–	<i>Teligent, Cosette/G&W</i>	–
	Hydrocortisone valerate 0.2% ointment	³ Taro, Glenmark, Cosette/G&W	<i>Taro, Glenmark, Cosette/G&W</i>	–	–	<i>Taro, Glenmark, Cosette/G&W</i>	–	<i>Taro, Glenmark, Cosette/G&W</i>	–	–	–	–	–	–	–
	Hydrocortisone valerate 0.2% cream	⁵ Taro, Lupin, Perrigo, Glenmark, Cosette/G&W	<i>Taro, Lupin, Perrigo, Glenmark, Cosette/G&W</i>	–	<i>Perrigo, Taro, Lupin, Glenmark, Cosette/G&W, Perrigo</i>	–	<i>Taro, Lupin, Perrigo, Glenmark, Cosette/G&W</i>	–	–	–	–	–	–	–	–
	Mometasone furoate 0.1% ointment	⁴ Merck, Perrigo, Glenmark, Cosette/G&W	– ^d	–	–	–	–	–	<i>Merck, Perrigo, Glenmark, Cosette/G&W</i>	–	–	–	–	–	–
	Mometasone furoate 0.1% cream	⁴ Taro, Merck, Glenmark, Cosette/G&W	<i>Taro, Merck^e, Glenmark^e, Cosette/G&W^e</i>	–	–	–	–	<i>Taro, Cosette/G&W, Merck, Glenmark</i>	<i>Merck, Taro, Glenmark, Cosette/G&W</i>	–	–	–	–	–	–
	Triamcinolone acetonide 0.1% ointment	⁵ Taro, Perrigo, Teligent, Sandoz/Fougera, Cosette/G&W	–	–	–	<i>Taro, Perrigo, Teligent, Sandoz/Fougera, Cosette/G&W</i>	–	–	–	<i>Taro, Perrigo, Teligent, Sandoz/Fougera, Cosette/G&W</i>	–	–	–	–	–
Class VI (Low Potency)	Triamcinolone acetonide 0.1% cream	⁷ Taro, Teligent, Perrigo, Glenmark, Sandoz/Fougera, Crown, Cosette/G&W	<i>Taro, Perrigo, Crown, Cosette/G&W, Teligent, Glenmark, Sandoz/Fougera</i>	<i>Taro, Teligent, Perrigo, Glenmark, Sandoz/Fougera, Cosette/G&W, Crown</i>	<i>Crown, Perrigo, Cosette/G&W, Taro, Teligent, Perrigo, Glenmark, Sandoz/Fougera</i>	<i>Cosette/G&W, Taro, Teligent, Perrigo, Glenmark, Sandoz/Fougera, Crown</i>	<i>Cosette/G&W, Taro, Teligent, Perrigo, Glenmark, Sandoz/Fougera, Crown</i>	<i>Taro, Teligent, Perrigo, Glenmark, Sandoz/Fougera, Cosette/G&W, Crown</i>	–	–	–	–	–	–	<i>Teligent, Glenmark, Sandoz/Fougera, Taro, Perrigo, Crown, Cosette/G&W</i>
	Alclometasone dipropionate 0.05% ointment	³ Taro, Glenmark, Sandoz/Fougera	– ^d	–	–	–	–	–	<i>Taro, Glenmark, Sandoz/Fougera</i>	–	–	–	–	–	–
	Alclometasone dipropionate 0.05% cream	³ Taro, Glenmark, Sandoz/Fougera	<i>Taro, Glenmark, Sandoz/Fougera</i>	–	–	–	–	<i>Taro, Glenmark, Sandoz/Fougera</i>	–	–	–	–	–	–	–
	Desonide 0.05% ointment	⁷ Taro, Teligent, Akorn/Hi-Tech, Encube, Perrigo, Glenmark, Sandoz/Fougera	–	–	–	–	–	–	–	–	–	–	–	–	–
	Desonide 0.05% cream	⁵ Taro, Perrigo, Glenmark, Teva/Actavis, Cosette/G&W	<i>Teva/Actavis, Glenmark, Taro, Perrigo, Cosette/G&W</i>	<i>Teva/Actavis, Taro, Perrigo, Glenmark, Cosette/G&W</i>	<i>Teva/Actavis, Taro, Perrigo, Glenmark, Cosette/G&W</i>	<i>Perrigo, Glenmark, Cosette/G&W, Taro, Teva/Actavis</i>	–	<i>Taro, Perrigo, Glenmark, Cosette/G&W, Teva/Actavis^f</i>	<i>Taro, Perrigo, Glenmark, Teva/Actavis, Cosette/G&W</i>	–	–	–	–	–	–
	Hydrocortisone 2.5% ointment	² Sandoz/Fougera, Perrigo	–	–	–	–	–	–	–	–	–	–	–	–	–
Class VI (Low Potency)	Hydrocortisone 2.5% cream	⁵ Teva/Actavis, Sandoz/Fougera, Perrigo, Ani, Taro	<i>Teva/Actavis, Perrigo, Ani, Taro, Sandoz/Fougera</i>	<i>Teva/Actavis, Sandoz/Fougera, Taro, Ani, Perrigo</i>	<i>Teva/Actavis, Ani, Taro, Sandoz/Fougera</i>	<i>Teva/Actavis, Perrigo, Taro, Sandoz/Fougera, Ani</i>	<i>Taro, Teva/Actavis, Perrigo, Ani, Sandoz/Fougera</i>	<i>Teva/Actavis, Sandoz/Fougera, Perrigo, Ani, Taro</i>	<i>Teva/Actavis, Sandoz/Fougera, Perrigo, Ani, Taro</i>	–	–	–	<i>Teva/Actavis, Sandoz/Fougera, Perrigo, Ani, Taro</i>	–	<i>Sandoz/Fougera, Teva/Actavis, Perrigo, Ani, Taro</i>

Table 1. Information obtained directly from manufacturer's website or from a company representative. Key inactive ingredients listed include those present or related to allergens on the American Contact Dermatitis Society Group and/or North American Contact Dermatitis Group core allergen series. While not specifically tested on these standard series, white wax and edetate disodium were included in the analysis given their potentials to cross react with beeswax and ethylenediamine dihydrochloride, respectively. Formulations containing a particular allergen are represented in *italics*, and those without are in **bold**. "–" represents those TCs for which no formulations contained the given allergen.

^a Polysorbate, tested on the NAC-80, is a potential cross-reactor with sorbitol and sorbitans.

^b Some versions contain white wax, a potential cross-reactor with beeswax, a propolis-related substance.

^c Edetate disodium is a potential cross-reactor with ethylenediamine dihydrochloride.

^d Some versions contain medium chain triglycerides (MCTs). MCTs are derived from the processing of coconut or palm kernel oil, which may be relevant for patients with coconut contact allergy. However, cross-reactivity between MCTs and coconut contact allergens has not been confirmed in the literature.

^e Some versions also contain propylene glycol derivatives (e.g. hexylene glycol and propylene glycol stearate), which are structurally similar to propylene glycol but not confirmed to be cross-reactors.⁵

^f Contains stearic acid, which is used to prepare, but is an unknown cross-reactor of, stearyl alcohol.

Table 2. Key Inactive Ingredients in Topical Non-Corticosteroid Prescription Alternatives Related to Top Contact Allergens

Topical Non-Corticosteroid	Manufacturers Assessed	Propylene Glycol (PG)	Cetearyl/Cetyl/Stearyl Alcohol	Beeswax/White Wax ^a	Coconut Derivatives	Diazolidinyl Urea	Toophenol	Edetate Disodium ^b	Benzyl Alcohol
Calcipotriene 0.005% cream	3 Glenmark, Prasco, Sandoz/Fougera	–	<i>Sandoz/Fougera, Glenmark, Prasco</i>	–	<i>Glenmark^c, Prasco, Sandoz/Fougera</i>	<i>Prasco, Sandoz/Fougera, Glenmark</i>	<i>Prasco, Glenmark, Sandoz/Fougera</i>	<i>Prasco, Sandoz/Fougera, Glenmark</i>	<i>Sandoz/Fougera, Glenmark, Prasco</i>
Calcipotriene 0.005% ointment	Glenmark, Prasco, Taro	<i>Glenmark, Prasco, Taro</i>	–	–	–	–	<i>Glenmark, Prasco, Taro</i>	<i>Glenmark, Prasco, Taro</i>	–
Tacrolimus 0.1% ointment	3 Astellas Pharma, Glenmark, Sandoz/Fougera	–	–	<i>Astellas Pharma, Glenmark, Sandoz/Fougera</i>	–	–	–	–	–
Pimecrolimus 1% cream	3 Bausch Health, Teva/Actavis, Glenmark	<i>Bausch Health, Teva/Actavis, Glenmark</i>	<i>Bausch Health, Teva/Actavis, Glenmark</i>	–	– ^c	–	–	–	<i>Bausch Health, Teva/Actavis, Glenmark</i>
Crisaborole 2% ointment	1 Pfizer	<i>Pfizer</i>	–	–	–	–	–	<i>Pfizer</i>	–

Table 2. Information obtained directly from manufacturer's website or from a company representative. Key inactive ingredients listed include those present or related to allergens on the American Contact Dermatitis Society Group and/or North American Contact Dermatitis Group core allergen series. While not specifically tested on these standard series, white wax and edetate disodium were included in the analysis given their potentials to cross react with beeswax and ethylenediamine dihydrochloride, respectively. Formulations containing a particular allergen are represented in *italics*, and those without are in **bold**. "–" represents those TCs for which no formulations contained the given allergen.

^a Some versions contain white wax, a potential cross-reactor with beeswax, a propolis-related substance.

^b Edetate disodium is a potential cross-reactor with ethylenediamine dihydrochloride.

^c Some versions contain medium chain triglycerides (MCTs). MCTs are derived from the processing of coconut or palm kernel oil, which may be relevant for patients with coconut contact allergy. However, cross-reactivity between MCTs and coconut contact allergens has not been confirmed in the literature.