Therapeutic Class Overview
Antipsoriatic Agents

INTRODUCTION

- The goal of treatment for patients with psoriasis is to control the disease. There are three main treatment modalities available at present for the treatment of psoriasis: topical agents, phototherapy, and systemic agents. Topical therapies are the mainstay for mild disease either as monotherapy or in combination, and topical therapies are also commonly used in conjunction with phototherapy, traditional systemic agents, or biologic agents for moderate to severe disease. Phototherapy, photochemotherapy, and traditional systemic agents are generally used for moderate or severe disease and in situations in which topical therapy is ineffective or otherwise contraindicated (Menter et al, 2011; Feldman 2017).
- Topical corticosteroids (e.g., betamethasone, clobetasol, triamcinolone, etc.) are the cornerstone of treatment for the majority of patients with psoriasis. Their effectiveness in treating psoriasis is due to anti-inflammatory, antiproliferative, immunosuppressive, and vasoconstrictive effects. Drawbacks associated with topical corticosteroid treatment are local cutaneous side effects and more serious systemic side effects that are associated with long-term use over a large body surface area (Menter et al, 2011). Due to these side effects, several agents have been developed and tested as monotherapy or in combination with topical corticosteroids in the hopes of reducing the duration of corticosteroid treatment.
- Other topical antipsoriatic agents include anthralin, calcitriol, calcipotriene, and tazarotene. These agents are available in a variety of vehicles. Early forms of treatment also included coal tar. In the United States, coal tar use has declined due to lack of standardization of available compounds and the development of other agents with less cosmetic issues such as odor and staining.
- Oral antipsoriatic systemic agents are typically reserved for moderate to severe psoriasis and are often combined with other therapies. Acitretin, a topical retinoid, modulates the cellular differentiation of the epidermis and is known to have immunomodulatory and anti-inflammatory activity (Menter et al, 2009[b]). Acitretin is most effective as a maintenance therapy, usually after the disease has been stabilized, or in combination with other treatments such as phototherapy (Villasenor-Park et al, 2012). Methoxsalen is a naturally occurring photosensitivity agent (psoralen) that enhances skin reactivity to ultraviolet light A (UVA). The combination of psoralen and UVA is referred to as photochemotherapy or PUVA. PUVA is an option for psoriasis that does not respond to topical medications alone or for lesions that are too extensive for topical treatment (Menter et al, 2010).
- Agents included in this review are the topical and oral antipsoriatics, which are listed in Table 1. Biologics (i.e., adalimumab, adalimumab-adbm, adalimumab-atto, brodalumab, etanercept, etanercept-szzs, guselkumab, infliximab, infliximab-abda, infliximab-dyyb, infliximab-qbtx, ixekizumab, secukinumab, and ustekinumab) that are used to treat psoriasis and other inflammatory/immunologic diseases are not included in this review. Topical corticosteroids are also not included in this review.
- Medispan Class: Antipsoriatics, Antipsoriatic – Systemic, and Topical Steroid Combinations

Table 1. Medications Included Within Class Review

Generic	Brand	Manufacturer	FDA Approval Date	Generic Availability
Topical Agents				
Anthralin	DRITHO-CREME® HP cream	Summers	-*	-
	ZITHRANOL® shampoo	Elorac	-*	-
Calcipotriene	DOVONEX® cream	Leo Pharma	07/22/1996	✔
	SORILUX® foam	Stiefel	10/06/2010	-
	Topical ointment	Glenmark Generics	03/24/2010	✔
	Topical scalp solution	various	03/03/1997	✔
Calcitriol	VECTICAL® ointment	Galderma	01/23/2009	✔
Tazarotene**	TAZORAC® cream	Allergan	09/29/2000	✔
	TAZORAC® gel		06/13/1997	-
Calcipotriene/ Betamethasone dipropionate	ENSTILAR® foam	Leo Pharm	10/16/2015	-
	TACLONEX® suspension		05/09/2008	-
	TACLONEX® ointment		01/09/2006	✔
Oral Systemic Agents				
Acitretin	SORIATANE® capsules	Stiefel	10/28/1996	✔
Methoxsalen	OXSORALEN-ULTRA® capsules	Valeant	10/30/1986	✔

*Anthralin products are unapproved marketed drugs that have not been formally evaluated by the Food and Drug Administration (FDA) as it was initially marketed before the Federal, Food, Drug, and Cosmetic Act was passed.
**Tazarotene 0.1% topical foam (FABIOR®) is approved for the treatment of acne. The AVAGE® brand of tazarotene 0.1% topical cream is approved for cosmetic indications.

(DRUGS@FDA.com, 2018; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2018; Clinical Pharmacology, 2018)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Drug(s)	Psoriasis (Quiescent or Chronic)	Severe Psoriasis	Plaque Psoriasis	Photo-chemotherapy	Acne Vulgaris
Topical Agents					
Anthralin (DRITHRO-CREME, ZITHRANOL)	✔				
Calcipotriene (DOVONEX, SORILUX, Calcipotriene ointment)			✔ *		
Calcitriol (VECTICAL)			✔ **		
Tazarotene (TAZORAC)			✔		✔ †
Calcipotriene/ betamethasone dipropionate (ENSTILAR foam)			✔		
Calcipotriene/ betamethasone dipropionate (TACLONEX suspension)			✔ ‡		
Calcipotriene/ betamethasone dipropionate (TACLONEX ointment)			✔ ‖		
Oral Systemic Agents					
Acitretin (SORIATANE)		✔			
Methoxsalen (OXSORALEN-ULTRA)				✔ ¥	

*SORILUX indicated for plaque psoriasis of scalp and body in patients 18 years or older; Calcipotriene Topical Solution, 0.005% (Scalp Solution) is indicated for the treatment of chronic, moderately severe psoriasis of the scalp.
**Mild to moderate plaque psoriasis in adults 18 years and older.
†TAZORAC 0.1% cream and gel
‡TACLONEX suspension indicated for plaque psoriasis of the scalp and body in patients 18 years and older. Additionally, the suspension is indicated for plaque psoriasis of the scalp in patients ages 12 to 17 years.
‖TACLONEX ointment is indicated for plaque psoriasis in patients 12 years of age and older. Limitations of use: Do not use on face, axillae or groin and do not use if skin atrophy is present at the treatment site.
¥For control of severe, recalcitrant, disabling psoriasis not adequately responsive to other forms of therapy and when the diagnosis has been supported by biopsy.

(Prescribing Information: Calcipotriene ointment, 2015; Calcipotriene solution, 2015; DOVONEX, 2017; DRITHOCREME, 2014; ENSTILAR, 2017; OXSORALEN-ULTRA, 2015; SORIATANE, 2017; SORILUX, 2016; TACLONEX ointment, 2017; TACLONEX suspension, 2017; TAZORAC cream, 2017; TAZORAC gel, 2017; VECTICAL, 2012; ZITHRANOL, 2011)

Information on indications, mechanism of action, pharmacokinetics, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

- Various strengths and formulations of anthralin or dithranol have been evaluated (Fredriksson, 1983; Jones et al, 1985). Results from these trials support efficacy of anthralin in the treatment of psoriasis with no significant differences identified between dosage strength, formulation, or administration.
- Topical calcipotriene has demonstrated favorable efficacy in treating psoriasis in several studies with marked improvements in clearing of psoriatic lesions occurring in approximately 50 to 70% of patients (Highton et al 1995; Dubertret et al, 1992; Thaci et al, 2001). Treatment success was reported in patients with psoriasis who were treated with topical calcipotriene foam in two eight-week, multicenter, randomized, double-blind, vehicle-controlled clinical trials (Feldman et al, 2012; Feldman et al, 2013).
- For the treatment of plaque psoriasis, topical calcipotriene has demonstrated favorable efficacy when combined with betamethasone, psoralen plus ultraviolet A (PUVA), and methotrexate (Buckley et al, 2008; De Jong et al, 2003; Kragballe et al, 2009; Luger et al, 2008; Ortonnne et al, 2009; Ozkan et al, 2012; Torras et al, 2014; van de Kerkhof et al, 2009). The combination of calcipotriene plus betamethasone has demonstrated superior efficacy when compared to monotherapy with either calcipotriene or betamethasone or placebo in several clinical trials (Buckley et al, 2008; Douglas et al, 2002; Guenther et al, 2002; Jemec et al, 2008; Kaufman et al, 2002; Kragballe et al, 2004; Kragballe et al, 2009; Luger et al, 2008; Ortonne et al, 2009; Papp et al, 2003; Parslew et al, 2005; Singh et al, 2000; van de Kerkhof et al, 2005; van de Kerkhof et al, 2009; van de Kerkhoff et al, 2004).
- The efficacy of calcitriol ointment for the treatment of mild to moderate plaque psoriasis was demonstrated in two double-blind, randomized controlled studies involving 839 patients. Calcitriol applied twice daily for eight weeks was significantly more effective than the vehicle. Additionally, there were no clinically relevant changes in calcium homeostasis or other routine laboratory parameters in calcitriol-treated patients (Lebwohl et al, 2007).
- Head-to-head trials comparing the vitamin D analogues have been conducted. Ortonne et al found calcitriol to be significantly better tolerated than calcipotriol in sensitive skin fold areas (Ortonne et al, 2003). In another 12-week, randomized trial in patients with chronic plaque psoriasis, calcitriol demonstrated similar efficacy to calcipotriol and had a significantly better safety profile (Zhu et al, 2007).
- Head-to-head trials comparing therapies from different medication classes for the treatment of psoriasis also exist. Veronikis et al compared calcipotriene to coal tar and found that both agents were effective in the treatment of plaque psoriasis with no significant differences found between treatment groups (P value not reported) (Veronikis et al, 1999). Calcipotriol solution has been compared to clobetasol shampoo, with clobetasol being found to be significantly more efficacious in terms of total severity score measures as well as global severity score ($P<0.05$ for all) (Reygagne, 2005).
- Tazarotene was shown to be more effective than placebo in treating plaque psoriasis (Weinstein et al, 1997). Results demonstrated that both tazarotene 0.1% and 0.5% gel were significantly more effective than placebo in reducing the severity of signs and symptoms of target lesions ($P<0.05$). A second, placebo-controlled trial with the same methodology found similar results (Weinstein et al, 2003). Topical tazarotene in combination with a low-, mid-, and high-potency topical corticosteroid has been evaluated in patients with mild to moderate plaque psoriasis (Guenther et al, 2000; Lebwohl et al, 1998). While all treatments were effective, the tazarotene and topical corticosteroid combination produced significantly higher treatment success rates at weeks two, eight, and 12 vs tazarotene monotherapy (all $P<0.05$). Bowman et al compared the combination of tazarotene gel plus calcipotriene ointment to clobetasol ointment in patients with stable psoriasis and found

that both treatments were effective in reducing scaling, plaque elevation, and overall lesion severity with no significant differences between the two groups (P=0.93, P=0.76, and P=0.29, respectively) (Bowman et al, 2002).

- Acitretin has been shown to be effective in the treatment of patients with moderate to severe psoriasis in open-label studies and controlled clinical trials (Olsen et al, 1989; Tosti et al, 2009). In combination with calcipotriol, acitretin demonstrated improved clinical outcomes compared to acitretin alone or placebo (Rim et al, 2003; van de Kerkhof et al, 1998). Acitretin in combination with phototherapy can enhance treatment efficacy for patients with moderate to severe chronic plaque psoriasis that does not clear using UVB, PUVA, or acitretin alone. Compared with acitretin or UV light monotherapy, the combination regimen enhances efficacy and limits treatment frequency, duration, and cumulative doses (Lebwohl et al, 2001).
- Several large multicenter trials have demonstrated the efficacy of oral methoxsalen with UVA (PUVA) in psoriasis, indicating clearance of lesions in 70% to 89% of patients (Henseler et al, 1981; Roenigk et al, 1979; Melski et al, 1977). Two systematic reviews of the large majority of PUVA studies verified these findings demonstrating that between 70% and 100% of patients treated with PUVA achieved clearing of psoriasis lesions (Griffiths et al, 2000; Spuls et al, 1997).
- The Agency for Healthcare Quality and Research (AHRQ) published a comparative effectiveness review of the biologic systemic agents compared to nonbiologic systemic agents or phototherapy on an individual drug level for the treatment of chronic plaque psoriasis. A total of five randomized clinical trials and four observational studies were identified. In summary, limited data exist that compare agents. Existing data were considered to be low strength of evidence, which in general favored the biological agents over the non-biologic agents (Lee et al, 2012).
- A Cochrane Review was conducted to compare the effectiveness, tolerability, and safety of topical treatments for chronic plaque psoriasis, relative to placebo, and to similarly compare vitamin D analogues (alone or in combination) with other topical treatments. A total of 177 randomized controlled trials with 34,808 participants were included. When used on the body, most vitamin D analogues were significantly more effective than placebo. Dithranol, combined treatment with vitamin D/corticosteroid, and tazarotene all performed significantly better than placebo. Head-to-head comparisons of vitamin D for psoriasis of the body against potent or very potent corticosteroids had mixed findings. For both the body and scalp psoriasis, combined vitamin D and corticosteroid treatment performed significantly better than vitamin D alone or corticosteroid alone. When applied to psoriasis of the scalp, vitamin D was significantly less effective than both potent corticosteroids and very potent corticosteroids. Vitamin D generally performed better than coal tar, but findings compared to dithranol were mixed. For both body and scalp psoriasis, potent corticosteroids were less likely than vitamin D to cause local adverse events, such as burning or irritation. No comparison of topical agents found a significant difference in systemic adverse effects (Mason et al, 2013).
- In addition to its FDA approval for the treatment of psoriasis, tazarotene, a topical retinoid agent, is also FDA-approved for the treatment of acne vulgaris. In a placebo-controlled trial by Bershad et al, tazarotene 0.1% gel was compared with tazarotene 0.1% gel plus a vehicle gel, or vehicle gel alone (Bershad et al, 2002). The primary efficacy endpoint, reduction in acne vulgaris lesions, was significant in both tazarotene treatment groups compared to the vehicle group (P=0.002). Clinical trials comparing tazarotene to other topical retinoid agents have shown conflicting results, with tazarotene being at equivalent or more effective than other topical retinoids (Pariser et al, 2008; Tanghetti et al, 2010).
- The current guidelines for the management of psoriasis and psoriatic arthritis from the American Academy of Dermatology (AAD) recommend topical agents for mild to moderate psoriasis. Topical agents are also used adjunctively with ultraviolet light or systemic medications for resistant lesions or more severe disease. Topical corticosteroids are recommended as first-line treatment for most patients. Other topical agents included in the guidelines are vitamin D analogues, tazarotene, tacrolimus, pimecrolimus, anthralin, coal tar, and combination products. Combination products include corticosteroid and salicylic acid, corticosteroid and vitamin D analogue, corticosteroid and tazarotene, and tacrolimus and salicylic acid. When used in conjunction with ultraviolet radiation B or psoralen and UVA phototherapy or biologics, acitretin is effective for psoriasis and the treatment of choice in human immunodeficiency virus-positive patients with severe psoriasis due to its lack of significant immunosuppression (Gottlieb et al, 2008; Menter et al, 2009[a]; Menter et al, 2009[b]; Menter et al, 2010; Menter et al, 2011).
- In a 2013 position paper published by the AAD, psoriasis patients with moderate to severe psoriasis may avoid stepwise-therapy (i.e., first phototherapy, then oral systemic therapies, followed by biologic therapies) and be moved to later line therapy based on disease severity (AAD, 2013). Treatment needs vary depending on the severity of disease, body location of disease, characteristics of the psoriasis being treated including lesion thickness, degree of erythema and amount of scaling, as well as patient preferences.

- Topical retinoids such as tazarotene are also effective in the treatment of acne vulgaris. Guidelines do not recommend one retinoid over another but do generally recommend these agents as a first-line combination option (Thiboutot et al, 2009; Eichenfield et al, 2013).
    - According to the AAD, topical retinoids (e.g., tretinoin, adapalene, tazarotene) are recommended among the first-line treatment options for the management of acne (strength of recommendation: A [based on consistent and good-quality patient-oriented evidence]; level of evidence I [good-quality patient-oriented evidence, i.e., evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life], and II [limited-quality patient-oriented evidence]) (Zaenglein et al, 2016). Topical retinoids are important in addressing the development and maintenance of acne and are recommended as monotherapy in primarily comedonal acne, or in combination with topical or oral antimicrobials in patients with mixed or primarily inflammatory acne lesions. The guidelines do not prefer one topical retinoid over another.
        - There are several head-to-head studies with retinoid products. Some support greater efficacy of tazarotene over adapalene and tretinoin, and adapalene over tretinoin, but the concentrations and formulations were varied. Overall, the limitations of the existing studies prohibit direct efficacy comparisons of topical retinoids.
    - According to the Medical Letter, topical retinoids can be used alone or in combination with antibiotics to treat both inflamed and noninflamed acne lesions, or for maintenance treatment of acne (Medical Letter, 2016).

SAFETY SUMMARY

- Topical calcipotriene is contraindicated in individuals with hypersensitivity to any components of the preparation. Additionally, calcipotriene administration in patients with vitamin D toxicity or hypercalcemia is also contraindicated. Calcipotriene should not be used for the treatment of the face, and the scalp solution is contraindicated in acute psoriatic eruptions. The most common adverse effects of calcipotriene are local effects including burning, pruritus, edema, peeling, stinging, dryness, skin irritation, and erythema. Contact dermatitis has been reported to occur with use of topical calcipotriene. Systemic side effects of vitamin D analogs, including hypercalcemia, are rare unless patients apply more than the recommended dosage of 100 g per week (Clinical Pharmacology, 2018).
- There are no known contraindications to topical calcitriol. Among patients receiving laboratory monitoring, hypercalcemia was observed in 24% (18/74) of patients exposed to active drug and in 16% of (13/79) patients exposed to vehicle. This increase in calcium and albumin-adjusted calcium levels was <10% above the upper limit of normal. The effects of calcitriol on calcium metabolism have not been evaluated for treatment durations of >52 weeks. Additionally, increased absorption of calcitriol may occur with the use of occlusive dressings. Avoid exposure of treated areas to artificial or natural sunlight. The safety and efficacy of topical calcitriol in patients with disorders of calcium metabolism and patients with erythrodermic, exfoliative, or pustular psoriasis have not been evaluated. The most common adverse effects include hypercalciuria, pruritus, and lab test abnormalities (not otherwise specified).
- There are no known contraindications to calcipotriene/betamethasone suspension, ointment, or foam. Caution should be used with all formulations in patients with elevated serum calcium levels. Additionally, hypothalamic-pituitary-adrenal axis suppression has occurred due to systemic absorption of the topical corticosteroid. Avoid exposure of treated areas to artificial or natural sunlight. Local adverse reactions such as atrophy, irritation, and allergic contact dermatitis are more likely to occur with occlusive use. Common adverse effects include pruritus, worsening of psoriasis, erythema, and burning sensation.
- Topical tazarotene is contraindicated in patients who are pregnant or who have a documented hypersensitivity reaction to any component of the formulation. Tazarotene should not be used on eczematous skin as severe irritation may occur. Additionally, increased photosensitivity may occur with concurrent administration of fluoroquinolones, phenothiazines, sulfonamides, tetracyclines, and thiazides. Patients should be cautioned to take protective measures (e.g., sunscreens, protective clothing) against exposure to sunlight or ultraviolet light (e.g., tanning beds) until tolerance is determined. Excessive pruritus, burning, skin redness or peeling may occur. Discontinue tazarotene until skin integrity is restored, or reduce the dosing interval or switch to a lower concentration. The most common adverse effects include burning, erythema, and pruritus.
- Topical anthralin is contraindicated in acute or actively inflamed psoriatic eruptions. Additionally, the agent should not be used if there is a hypersensitivity to the active ingredient or any of its components. The most common side effects of anthralin are skin irritation and staining of lesional and adjoining skin, nails, and clothing.

- Acitretin is teratogenic and its use, therefore, is limited to male and female patients of nonchildbearing potential. Acitretin should only be considered for women of childbearing potential with severe psoriasis unresponsive to other therapies or whose clinical condition contraindicates the use of other treatments. Other contraindications for acitretin include severe liver or kidney impairment, chronic elevation of lipid profile, and use in combination with methotrexate or tetracyclines. Potential adverse effects of acitretin include dry skin and mucus membranes, alopecia, skin peeling, pruritus, cheilitis, rhinitis, hyperlipidemia, liver toxicity, and teratogenicity. Periodic monitoring of bones, lipid profile, and eyes is recommended.
- Methoxsalen is contraindicated with a history of light sensitivity, melanoma, invasive squamous cell carcinoma or aphakia. Skin irritation, including severe edema, erythema, blistering, and exfoliative dermatitis, can occur during PUVA therapy. Pruritus and other dermatological effects may occur as well. Nausea occurs in 10% of patients receiving methoxsalen, and central nervous system (CNS) effects including depression, dizziness, and headache have been reported. Patients who have received PUVA therapy should be monitored throughout their lives for the development of cutaneous malignancies.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
Topical Therapy				
DRITHO-CREME (anthralin)	Cream: 1%	Treatment of psoriasis (quiescent or chronic): Cream: Apply once a day to psoriatic lesions for 5 to 10 minutes using the lowest strength possible for at least one week; may increase contact time up to 20 to 30 minutes as tolerated		Avoid spreading cream onto the forehead; remove by washing or showering. For scalp psoriasis, comb hair to remove scalar debris; wet and part hair; rub cream into lesions.
ZITHRANOL (anthralin)	Shampoo: 1%	Scalp Psoriasis: Apply onto wet scalp 3 to 4 times per week. Leave on scalp for 3 to 5 minutes and then rinse thoroughly.		
DOVONEX (calcipotriene)	Cream: 0.005%	Plaque psoriasis: Apply a thin layer to affected area 1 to 2 times per day and rub in completely.	Safety and effectiveness of DOVONEX cream have been demonstrated in patients treated for 8 weeks.	
SORILUX (calcipotriene)	Foam: 0.005%	Plaque psoriasis: Apply a thin layer twice daily to the affected areas and rub in gently and completely.		Avoid contact with the face and eyes. Not for oral, ophthalmic, or intravaginal use.
Calcipotriene ointment	Ointment: 0.005%	Plaque psoriasis: Apply a thin layer to affected area 1 to 2 times per day and rub in gently and completely.		
Calcipotriene scalp solution	Solution: 0.005%	Severe Psoriasis of the scalp: Comb hair to remove scaly debris and apply twice daily,	Safety and efficacy have been	Do not spread to forehead. Keep well away from

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
		only to lesions, and rub in gently and completely.	demonstrated in patients treated for 8 weeks.	eyes. Avoid applying to uninvolved scalp margins.
VECTICAL (calcitriol)	Ointment: 3 mcg/g	Plaque psoriasis: Apply to affected areas twice daily, morning and evening.	The maximum weekly dose should not exceed 200 g.	Not for oral, ophthalmic, or intravaginal use.
ENSTILAR (calcipotriene/ betamethasone dipropionate)	Foam: 0.005%/ 0.064%	Plaque psoriasis: Apply to affected area once daily for up to 4 weeks.	Do not use more than 60 g every 4 days.	Do not use with occlusive dressings unless directed by a physician. Not for oral, ophthalmic, or intravaginal use. Avoid use on face, groin, axillae, or if skin atrophy is present at treatment site.
TACLONEX (calcipotriene/ betamethasone dipropionate)	Ointment: 0.005%/ 0.064% Topical Suspension: 0.005%/ 0.064%	Ointment: Psoriasis: Apply to affected areas once daily for up to 4 weeks. Topical Suspension: Plaque Psoriasis: Apply to affected areas once daily for up to 8 weeks.	Maximum weekly dose should not exceed 100 g for patients ≥18 years of age. For patients 12 to 17 years of age, maximum weekly use should not exceed 60 g. Treatment of >30% of body surface area is not recommended.	Do not use on face, axillae, or groin. Do not use with occlusive dressings unless directed by a physician. Do not use if skin atrophy is present at treatment site. Shake topical suspension before use. Not for oral, ophthalmic, or intravaginal use.
TAZORAC (tazarotene)	Cream: 0.05%, 0.1% Gel: 0.05%, 0.1%	Psoriasis: Cream, gel: Apply a thin film to affected area once daily in the evening. Acne vulgaris for ages ≥12 years old: Cream (0.1%), gel (0.1%): Apply a thin film to affected area once daily in the evening.	Psoriasis: Start with 0.05% cream/gel, then increase to 0.1% if tolerated and medically indicated. Treatment of >20% of body surface area is not recommended	Not for oral, ophthalmic, or intravaginal use. Avoid contact with eyes, mouth, or other mucous membranes. Apply to dry skin and at least an hour after using

Drug	Dosage Form: Strength	Usual Recommended Dose	Other Dosing Considerations	Administration Considerations
			(gel only).	emollients.
Oral Agents				
SORIATANE (acitretin)	Capsules: 10 mg, 17.5 mg, 25 mg	Psoriasis: Initiate at 25 to 50 mg per day, given as a single dose with the main meal. Maintenance doses of 25 to 50 mg per day may be given dependent upon response to initial treatment.		
OXSORALEN (methoxsalen)	Capsules: 10 mg	Psoriasis: Take 2 hours before UVA exposure with food or milk according to following table: <30 kg: 10 mg 30-50 kg: 20 mg 51-65 kg: 30 mg 66-80 kg: 40 mg 81-90 kg: 50 mg 91-115 kg: 60 mg >115 kg: 70 mg	If weight changes during treatment, no change in dose is usually required. The number of doses per week will be determined by the schedule of UVA exposures. Dosages may be increased by 10 mg after the 15th treatment.	

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
Topical Therapy					
DRITHO-CREME, ZITHRANOL (anthralin)	No data	Safety and efficacy have not been established.	No data	No data	Pregnancy category C* Unknown whether excreted in breast milk; discontinue nursing or discontinue drug
DOVONEX, SORILUX, calcipotriene ointment, calcipotriene scalp solution (calcipotriene)	DOVONEX, calcipotriene scalp solution: No differences in adverse events for subjects >65 years. However, greater sensitivity cannot be ruled out.	Safety and efficacy have not been established.	No data	No data	DOVONEX: Unclassified† Only use if potential benefit justifies risk to fetus

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
	SORILUX: Trials did not include sufficient numbers of subjects >65 years. Calcipotriene ointment: Severity of skin-related adverse events showed a significant difference for subjects >65 years.				SORILUX, calcipotriene ointment, calcipotriene scalp solution: Pregnancy category C* Unknown whether excreted in breast milk; use with caution.
VECTICAL (calcitriol)	Trials did not include sufficient numbers of subjects >65 years.	Safety and efficacy have not been established.	No data	No data	Pregnancy category C* Unknown whether excreted in breast milk; use with caution.
ENSTILAR, TACLONEX (calcipotriene/ betamethasone)	No differences in safety and effectiveness for subjects >65 years; however, greater sensitivity cannot be ruled out.	Safety and efficacy have not been established in children <12 years (suspension, ointment).	No data	No data	Pregnancy category C* Unknown whether excreted in breast milk; use with caution. Do not apply to breast when nursing.
TAZORAC (tazarotene)	Cream: No overall differences in safety or effectiveness were observed between subjects >65 years and younger subjects; however, greater sensitivity of some older individuals cannot be ruled out. Gel: Subjects >65 years of age had more adverse events and lower treatment success rates after 12 weeks.	Safety and efficacy have not been established in patients with psoriasis under the age of 18 years and patients with acne under the age of 12 years.	No data	No data	Unclassified† Contraindicated in pregnancy due to the risk of fetal malformation. Unknown whether excreted in breast milk; use with caution.
Oral Therapy					
SORIATANE (acitretin)	Trials did not include sufficient numbers of	Safety and efficacy have not been	Plasma concen-	Elevations of liver function	Pregnancy category X*

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy and Nursing
	subjects >65 years. Initial dose should be at the low end of the dosing range.	established.	trations significantly lower in end-stage renal failure.	tests (AST, ALT or LDH) were experienced by 1 in 3 patients. Perform LFTs prior to initiation and at 1- and 2-week intervals until stable.	Do not use prior to or during nursing.
OXSORALEN (methoxsalen)	Trials did not include sufficient numbers of subjects >65 years. Initial dose should be at the low end of the dosing range. Use with caution, especially those with a pre-existing history of cataracts, cardiovascular conditions, kidney and/or liver dysfunction, or skin cancer.	Safety in children has not been established.	No data	Treat with caution since hepatic biotransfor-mation is necessary for drug urinary excretion.	Pregnancy category C* Unknown whether excreted in breast milk; discontinue nursing or discontinue drug.

* Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
Pregnancy Category X = Contraindicated in pregnant women due to evidence of fetal abnormalities from adverse effects data from investigational or marketing experience. Risks of use of the drug in pregnant women clearly outweigh potential benefits.
†In accordance with the FDA's Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

CONCLUSION

- Numerous topical and systemic therapies are available for the treatment of psoriasis. Topical treatment is considered to be the safest option and is widely used for mild psoriasis, followed by systemic and phototherapies, which are used for moderate to severe psoriasis. Selection of medication must take into account severity of disease, thickness and scaling of the lesions, relevant comorbidities, patient preference, efficacy, and evaluation of individual patient response (AAD, 2013; Hsu et al, 2012; Menter et al, 2009[b]).
- Topical corticosteroids are the cornerstone of treatment for the majority of patients with psoriasis. Drawbacks associated with topical corticosteroid treatment are local cutaneous side effects and more serious systemic side effects that are associated with long-term use over a large body surface area (Menter et al, 2011). Several agents have been developed and tested as monotherapy or in combination with topical corticosteroids in the hopes of reducing the duration of corticosteroid treatment.
- The vitamin D analogs, calcipotriene and calcitriol, are other first-line topical agents with proven efficacy in the treatment of psoriasis. Although less effective than topical corticosteroids, they are often used in combination with topical corticosteroids to enhance efficacy and reduce the risk of atrophy, especially over the long term. One potential advantage of calcitriol is that there are no known contraindications for use, whereas calcipotriene (alone, but not in combination with betamethasone) is contraindicated in patients with hypercalcemia and vitamin D toxicity and in acute or actively inflamed psoriatic lesions. Another possible advantage of calcitriol is that it has been shown to be better

tolerated in sensitive skin fold areas as well as associated with less stinging, burning, edema and erythema (Weinstein et al, 2003; Zhu et al, 2007).

- The combination of calcipotriene and betamethasone (ENSTILAR and TACLONEX) has been evaluated in several studies for the treatment of psoriasis compared to placebo and to its individual components. Overall, results indicated that the combination product was more effective in reducing psoriasis area and severity index scores, and it increased the percentage of patients with clear or almost clear disease compared to either agent alone or placebo (Douglas et al, 2002; Guenthe et al, 2002, Kaufman et al, 2002; Kragballe et al, 2004; Papp et al, 2003; Parslew et al, 2005; Singh et al, 2000; van de Kerkhof et al, 2004; van de Kerkhof et al, 2005). The combination is available as a suspension, ointment, and foam.
- Tazarotene is the only retinoid agent that is FDA-approved for the treatment of psoriasis. Clinical trials have demonstrated its efficacy alone as well as in combination with other antipsoriatic agents. Guidelines recommend its use as an adjunct to topical corticosteroids (Menter et al, 2009[b]). No significant differences were observed between calcipotriene or calcitriol and tazarotene in several head-to-head studies (Guenther et al, 2000; Schiener et al, 2000; Tzung et al, 2005). Other topical preparations, including anthralin, have taken on more secondary roles and are particularly challenging as they stain clothing and skin.
- Of the systemic therapies, acitretin is the least effective as monotherapy and is therefore often used in conjunction with ultraviolet B or psoralen plus UVA phototherapy. Acitretin does not lead to immunosuppression or the associated risk of infection like biologic agents. Guidelines recommend the use of acitretin in combination with phototherapy as first-line treatment for psoriasis when not contraindicated, before resorting to other agents including methotrexate, cyclosporine, or biologic treatments (Lebwohl, 2001; Menter et al, 2009; Menter et al, 2010). Acitretin should not be used in women of childbearing potential.
- Methoxsalen and ultraviolet light (PUVA) is an effective method of treating psoriasis. PUVA is indicated in patients with moderate to severe psoriasis that is unresponsive to other forms of therapy or for lesions that are too extensive for topical treatment (Menter et al, 2010).
- In a position paper published by the AAD, psoriasis patients with moderate to severe psoriasis may avoid stepwise-therapy (i.e., first phototherapy, then oral systemic therapies, followed by biologic therapies) and be moved to later line therapy based on disease severity (AAD, 2013). Consensus guidelines agree that the decision for treatment should be based on efficacy, potential adverse effects, prior treatments, patient preference, duration and severity of disease, medical risk factors**,** co-morbidities, and potential impact on quality of life (AAD, 2013).
- Topical retinoids such as tazarotene are also effective in the treatment of acne vulgaris. Guidelines do not recommend one retinoid over another but do generally recommend these agents as a first-line combination option (Thiboutot et al, 2009; Zaenglein et al, 2016; Eichenfield et al, 2013).

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