

## Acne Vulgaris

Acne Vulgaris (AV) is an inflammatory dermatosis affecting the hair follicles and sebaceous glands of the skin. It is characterized by open comedones (blackheads), closed comedones (whiteheads), papules, pustules, cysts and/or nodules.<sup>[Zaenglein,2016;p947,col2,para5(entire);p948,col2,para1,ln1-2;p947,col2,para6,ln1-2]</sup> AV is the most common of all skin conditions, affecting approximately 50 million adolescents, young adults, and adults in the United States.<sup>[Zaenglein,2016;p947,col2,para6,ln1-3;p948,col1,para1,ln1-3]</sup> AV is associated with various sequelae, including long-term or permanent skin scarring, poor self-esteem, anxiety, and depression. Thus, the physical and psychological morbidity can be profound.<sup>[Zaenglein,2016;p948,col1,para1,ln5-7;p962,col1,para4,ln1-4]</sup>

Although it is advisable for patients with AV to be treated under the supervision of a board-certified dermatologist, consumers may seek recommendations from the pharmacist on OTC products to help treat their acne. As there are a wide variety options available, a pharmacist is uniquely positioned to help consumers select the most appropriate product(s) that can be used either alone or alongside prescription products to improve outcomes for patients with AV.

## Evolving Landscape of Available Acne Treatment Strategies

Over the past decade, the FDA has expanded the list of ingredients that can be used in OTC acne products.<sup>[Draelos,2012;p287,col1,para1(entire);col2,para1,ln1-4]</sup> Benzoyl peroxide (BPO) in strengths up to 10% and salicylic acid (SA) in strengths up to 2% has been permitted since in 2011.<sup>[FDA\_Guidance\_2011]</sup> In 2016, adapalene 0.1% gel was the first retinoid to become available as an OTC prescription.<sup>[Tolaymat,2021;p1,Indications,para2(entire)]</sup>

The American Academy of Pediatrics (AAP) and American Academy of Dermatology (AAD) both endorse the use of BPO and topical retinoids in the first-line setting for mild and severe acne.<sup>[Eichenfield,2013;pS176,figure1;pS177,figure2;pS178,figure3;S168,col3,bullet1;Zaenglein,2016;p948,figure1;p949,table3]</sup> Examples of OTC products include CeraVe®'s Acne Foaming Cleanser (4% BPO)<sup>[CeraVe\_website]</sup> and La Roche-Posay®'s Effaclar® Acne Treatment (5.5% micronized BPO + 0.4% lipohydroxy acid [LHA]).<sup>[LaRochePosay\_Website]</sup> La Roche-Posay®'s Effaclar® once daily topical retinoid contains 0.1% adapalene.

OTC products marketed for acne treatment that contain its more lipophilic derivative, LHA, include La Roche-Posay®'s Effaclar® Acne Treatment (2% SA + 0.05% micro-exfoliating LHA)<sup>[LaRochePosay\_Website]</sup>, Effaclar® Acne Treatment (0.5% SA + 2% glycolic acid),<sup>[LaRochePosay\_Website]</sup> CeraVe® Acne Control Cleanser (2% SA + 0.5% glycolic acid),<sup>[DataOnFile\_CeraVe]</sup> and CeraVe® Acne Control Gel (2% SA + 5.5% glycolic acid).<sup>[DataOnFile\_CeraVe]</sup>

## The Compromised Skin Barrier in AV

Patients with AV often have a compromised skin barrier, characterized by reduced total ceramides and increased trans-epidermal water loss.<sup>[Lain,2020;p1070,col2,para2,ln1-3;p1070,col1,para3,ln1-23;p1073,col1,para3,ln1-3]</sup>

Prescription and OTC acne medications can have a drying effect, which can create, or further contribute to, a compromised skin barrier.<sup>[Jordan,2016;p1172,col2,para2,ln1;ln4;ln6-7;p1170,col2,para2,ln1-4;p1170,col2,para3,ln4;p1171,col1,para1,ln1;p1171,col1,para2(entire)]</sup><sup>[Lynde,2014;p22,col2,para2,ln4-5;p23,col1,para1(entire)]</sup><sup>[Lain,2020;p1070,col1,para3,ln3-5;p1073,col1,para3,ln1;ln4-5]</sup> A compromised skin barrier in the setting of AV can exacerbate acne lesions,

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contribute to poor medication adherence, and lead to suboptimal outcomes. [Lynde,2014;p23,col1,para2,ln19-21;p20,col2,para2(entire);p21,col1,para1,ln1-2;p23,col1,para2,ln21-26;p24,table7;p23,col1,para2,ln1-3;p22,col2,para1,ln1-3;p20,col2,para1,ln15-19] [Lain,2020;p1070,col2,para2,ln3-4;p1070,col1,para3,ln6-8]

## Benefits of Adjunctive Products in the Setting of AV

Adjunctive cleansers, moisturizers, and other topical products available OTC can be recommended for use alongside 1 or more prescription acne products to facilitate or expedite acne lesion clearance, reduce irritation and inflammation, and improve patient adherence. [Lynde,2014;p21,col1,para1,ln12-15;p24,col1,para3(entire);col2,para1(entire);p24,col1,para2(entire)] [Lain,2020;p1070,col1,para3,ln8-10;p1070,col2,para2,ln12-13]

### Lipid-free cleansers

The AAP recommends twice-daily washing with a gentle, soap-free cleanser due to its low potential for irritancy. [Eichenfield,2013;pS168,col1,para2,ln11-13] [Lain,2020;p1070,col1,para1,ln1-2] Lipid-free cleansers that do not alter the pH of the skin are useful adjunctive therapies for patients who are experiencing adverse drying or peeling effects from prescription acne products. [Lain,2020;p1070,col2,para3,ln5-16] CeraVe® Hydrating Cleanser, CeraVe® Foaming Cleanser, and Cerium™ cleansers are all lipid-free cleansers that utilize combinations of water, glycerin, sodium lauryl sulfate, and stearyl alcohol to gently cleanse the skin without irritation and are suitable for sensitive skin. [Lain,2020;p1071,table1-2]

Patients with AV should be encouraged to avoid harsh mechanical cleansing techniques that can irritate their skin and exacerbate a condition. [Eichenfield,2013;pS181,col2,para3(entire)] Cleansing with mild, lipid-free cleansers using gentle motions should be recommended. [Jordan,2016]

### Ceramide-containing moisturizers

Evidence suggests that moisturizers do not adversely affect the efficacy of topical acne products, reduce the signs and symptoms of retinoid dermatitis, prevent trans-epidermal water loss, reduce skin irritation, and promote better patient satisfaction. [Draelos,2006;p276,col1,para2,ln10-20;para3,ln3-16;p277,col2,para1,ln2-3;p22,ln1-8;para3,ln1-4] [Tanghetti,2008;col6,conclusions,para2(entire)] [Munehiro,2012;p173,col1,para2,ln2-7,col2,para1,ln1-2;para2,ln5-8;ln12-13]

A variety of experts have recommended that adjunctive therapy with ceramide-containing moisturizers be considered in patients being treated for AV. [Lain,2020;p1073,col1,para1,ln10-11;col2,para1,ln1;p1072,table3] Ceramides produce phytosphingosine, which has been shown to have strong antimicrobial and anti-inflammatory effects (both in vitro and in vivo) and improve skin care in patients with AV. [Lynde,2014;p21,col1,para1,ln9-11;col2,para1(entire);p24,table7;p21,col2,para2,ln1-3;p22,col2,para1,ln15-18] The antimicrobial and anti-inflammatory effects of phytosphingosine may enhance or complement existing acne therapies. [Lynde,2014;p24,table7;p21,col2,para2,ln1-3]

Moisturizers can offset the negative effects of prescription therapies such as erythema (redness), irritation, inflammation, and/or xerosis (itching). [Lain,2020;p1072,col1,para1,ln1-6]

Non-comedogenic OTC moisturizers such as CeraVe®'s AM Facial Moisturizing Lotion with Sunscreen (SPF 30) and CeraVe®'s PM Facial Moisturizing Lotion are oil free and formulated with 3 essential ceramides to help re-establish a healthy skin barrier without exacerbating acne lesions. [CeraVe\_website]

Formulations with an SPF have the added benefit of protecting against acne medication-induced photosensitivity.<sup>[CeraVe\_website]</sup> La Roche-Posay®'s Anthelios™ Clear Skin Oil Free Sunscreen with SPF 60 is sunscreen suitable for acne-prone skin that can be used alone or under a separate moisturizer.<sup>[LaRochePosay\_website]</sup>

### *BPO + Clindamycin vs BPO + LHA as Adjunct to 0.025% Tretinoin*

A 12-week, multi-center, randomized, double-blind study of 60 adult patients aged 18 to 50 with mild to moderate acne evaluated the effectiveness of 2 different topical combination products used as adjunctive therapy to a nightly application of generic prescription 0.025% tretinoin.<sup>[Draelos,2012;p288,col1,para4,ln1-5,para5,ln1-2;ln8-16]</sup> The 2 products evaluated were a prescription product (5% BPO + 1% clindamycin) and an OTC product (5.5% micronized BPO + 0.4% micro-exfoliating LHA; currently marketed as La Roche-Posay's Duaclear Duo Dual Action Acne Treatment). Patients were randomized to one of the 2 treatment regimens (n = 34 and n = 26, respectively).

Compared with baseline acne assessment scores, both treatments resulted in statistically significant ( $P < .05$ ) reductions in acne lesion counts (inflammatory + non-inflammatory) at weeks 4, 8, and 12. Those who received the OTC regimen (BPO + LHA) achieved a statistically significant reduction in the number of pustules (assessed clinically) at week 2 ( $P < .05$ ). The same statistically significant reduction from baseline to week 2 was also observed in those who received the prescription product (BPO + clindamycin).<sup>[Draelos,2012;p289,col1,para1,ln1-3;p288,col1,para4,ln1-5,para5,ln1-2;ln8-16;col2,para3,ln4-8para4,ln1-4]</sup>

While both treatment groups experienced increases in dryness and peeling compared to their group's respective baseline, those who received BPO + LHA did not experience a significant increase in erythema compared to baseline, while those in the BPO + clindamycin group did ( $P = .042$ ).<sup>[Draelos,2012;p290,col1,para1(entire)]</sup>

### **Role of the Pharmacist**

Consumers may be seeking a recommendation for 1 or more OTC products to use either alone or in combination with a prescription product. Pharmacists should first ascertain if the consumer is already on a therapeutic regimen for their AV, and if so, what products they are currently using. Adding certain OTC products to a prescription regimen could be overly irritating, further compromise the skin's barrier,<sup>[Lain,2020;p1073,col1,para3,ln1;ln4-5]</sup> and / or render some prescription products inactive. For example, OTC BPO products inactivate generic prescription tretinoin products if they are applied to the face at the exact same time.<sup>[Zaenglein,2016;p952,col1,para4,ln9-16]</sup> Therefore, one should be applied at night and the other in the morning.

A pharmacist's support in providing education and awareness of appropriate adjunctive OTC options can help to increase medication adherence and maximize the likelihood for acne clearance.

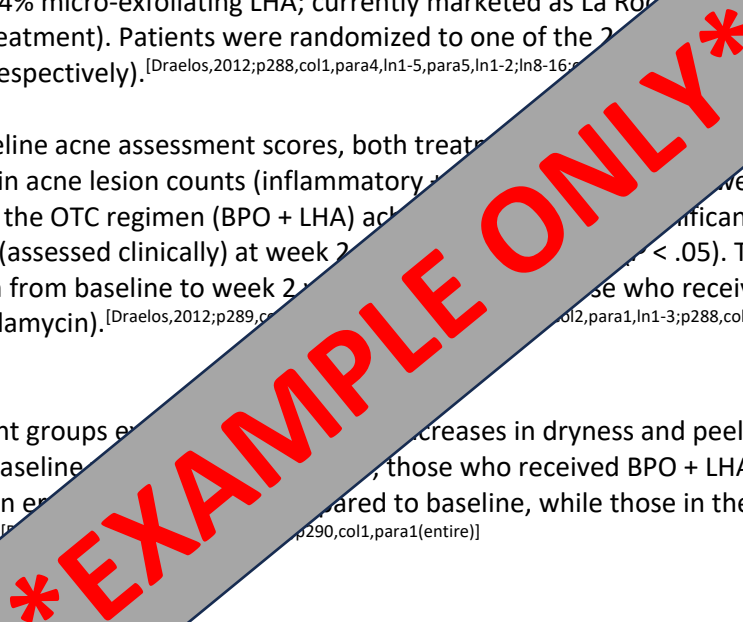
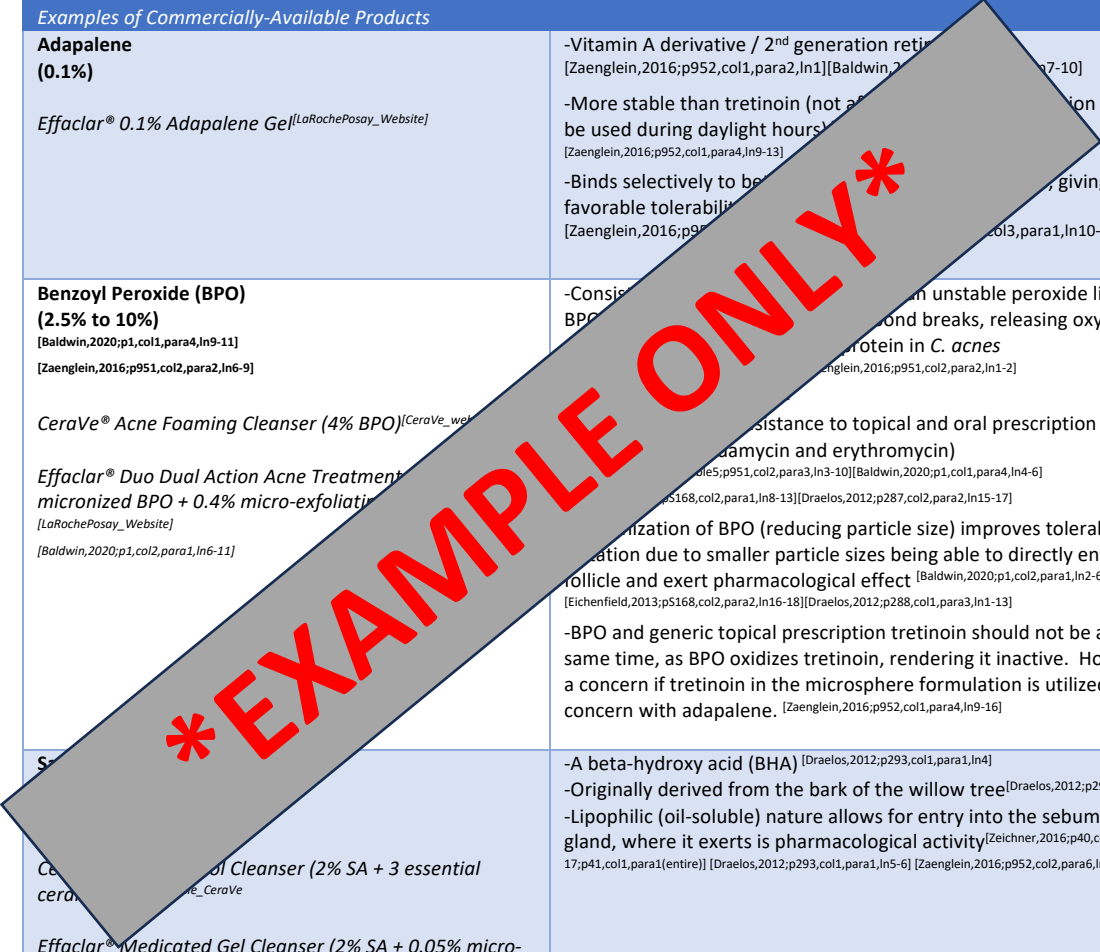


Table. Active Ingredients Utilized in OTC Acne Products

Active Ingredient (Strengths Available OTC)	Description / Mechanism of Action / Pearls
<i>Examples of Commercially-Available Products</i>	
<p><b>Adapalene</b> <b>(0.1%)</b></p> <p><i>Effaclar® 0.1% Adapalene Gel</i><sup>[LaRochePosay_Website]</sup></p>	<p>-Vitamin A derivative / 2<sup>nd</sup> generation retinoid [Zaenglein,2016;p952,col1,para2,ln1][Baldwin,2020;p1,col1,para4,ln9-11]</p> <p>-More stable than tretinoin (not a photosensitizer, can be used during daylight hours) [Zaenglein,2016;p952,col1,para4,ln9-13]</p> <p>-Binds selectively to beta-catenin, giving it a more favorable tolerability [Zaenglein,2016;p952,col1,para4,ln9-13]</p>
<p><b>Benzoyl Peroxide (BPO)</b> <b>(2.5% to 10%)</b></p> <p>[Baldwin,2020;p1,col1,para4,ln9-11] [Zaenglein,2016;p951,col2,para2,ln6-9]</p> <p><i>CeraVe® Acne Foaming Cleanser (4% BPO)</i><sup>[CeraVe_Website]</sup></p> <p><i>Effaclar® Duo Dual Action Acne Treatment (micronized BPO + 0.4% micro-exfoliating LHA)</i><sup>[LaRochePosay_Website]</sup></p> <p>[Baldwin,2020;p1,col2,para1,ln6-11]</p>	<p>-Consists of two benzoyl peroxide molecules in an unstable peroxide linkage; when the bond breaks, releasing oxygen free radicals, which oxidize the protein in <i>C. acnes</i> [Zaenglein,2016;p951,col2,para2,ln1-2]</p> <p>-Provides resistance to topical and oral prescription antibiotics used in combination (clindamycin and erythromycin) [Zaenglein,2016;p951,col2,para3,ln3-10][Baldwin,2020;p1,col1,para4,ln4-6]</p> <p>-Micronization of BPO (reducing particle size) improves tolerability and lessens irritation due to smaller particle sizes being able to directly enter the hair follicle and exert pharmacological effect [Baldwin,2020;p1,col2,para1,ln2-6;ln9-11] [Eichenfield,2013;pS168,col2,para2,ln16-18][Draelos,2012;p287,col2,para2,ln15-17]</p> <p>-BPO and generic topical prescription tretinoin should not be applied at the same time, as BPO oxidizes tretinoin, rendering it inactive. However, this is not a concern if tretinoin in the microsphere formulation is utilized, nor is it a concern with adapalene. [Zaenglein,2016;p952,col1,para4,ln9-16]</p>
<p><b>Salicylic Acid (SA)</b></p> <p><i>CeraVe® Acne Foaming Cleanser (2% SA + 3 essential ceramides)</i><sup>[CeraVe_Website]</sup></p> <p><i>Effaclar® Medicated Gel Cleanser (2% SA + 0.05% micro-exfoliating LHA)</i><sup>[LaRochePosay_Website]</sup></p> <p><i>Effaclar® Clarifying Solution (0.5% SA + 2% glycolic acid)</i><sup>[LaRochePosay_Website]</sup></p>	<p>-A beta-hydroxy acid (BHA) [Draelos,2012;p293,col1,para1,ln4]</p> <p>-Originally derived from the bark of the willow tree [Draelos,2012;p293,col1,para1,ln2-4]</p> <p>-Lipophilic (oil-soluble) nature allows for entry into the sebum-rich sebaceous gland, where it exerts its pharmacological activity [Zeichner,2016;p40,col3,para2,ln16-17;p41,col1,para1(entire)] [Draelos,2012;p293,col1,para1,ln5-6] [Zaenglein,2016;p952,col2,para6,ln1]</p>
<p><b>Lipohydroxy Acid (LHA)</b></p> <p><i>Effaclar® Medicated Gel Cleanser (2% SA + 0.05% micro-exfoliating LHA)</i><sup>[LaRochePosay_Website]</sup></p> <p><i>Effaclar® Duo Dual Action Acne Treatment (5.5% micronized BPO + 0.4% micro-exfoliating LHA)</i><sup>[LaRochePosay_Website]</sup></p>	<p>-A beta-hydroxy acid (BHA) [Draelos,2012;p293,col1,para2,ln2-3]</p> <p>-A more lipophilic derivative of SA, giving it increased comedolytic activity [Draelos,2012;p293,col1,para2,ln4-10] [Zeichner,2016;p41,col1,para2,ln1-3-4;col1,para1,ln4-7]</p>



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