



# Acne Vulgaris Medicament Management in Indonesia and the Efficacy of Various Therapeutic Regimens

Maria Clarissa Wiraputranto<sup>1</sup>, Irma Bernadette S. Sitohang<sup>1\*</sup>, Windy Keumala Budianti<sup>1</sup>, Adhimukti T. Sampurna<sup>1</sup>

Department of Dermatology and Venereology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia

## Abstract

**Edited by:** Ksenija Bogojeva-Kostovska  
**Citation:** Wiraputranto MC, Sitohang IBS, Budianti WK, Sampurna AT. Acne Vulgaris Medicament Management in Indonesia and the Efficacy of Various Therapeutic Regimens. Open Access Maced J Med Sci. 2023 Apr 14; 11(F):245-252. https://doi.org/10.3889/oamjms.2023.11576  
**Keywords:** Acne vulgaris; Efficacy; Guidelines; Grading system; Management  
**\*Correspondence:** Irma Bernadette S. Sitohang, Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia. E-mail: irma\_bernadette@yahoo.com  
**Received:** 26-Feb-2023  
**Revised:** 13-Mar-2023  
**Accepted:** 04-Apr-2023  
**Copyright:** © 2023 Maria Clarissa Wiraputranto, Irma Bernadette S. Sitohang, Windy Keumala Budianti, Adhimukti T. Sampurna  
**Funding:** This article was funded by Ministry of Research, Technology, and Higher Education of the Republic of Indonesia, grant No. NKB-933/UN2.RST/HKP.05.00/2022  
**Competing Interests:** The authors have declared that no competing interests exist  
**Open Access:** This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

**BACKGROUND:** Acne vulgaris (AV) is an inflammatory disease of the pilosebaceous unit with various pleomorphic lesions. In Indonesia, AV is the third most common case that makes patients come to seek treatment at the Hospital. The diagnosis can be established clinically and the AV grading system can be used to assess the severity. Until now, there are many AV grading systems and guidelines for AV. At Dr. Cipto Mangunkusumo Hospital uses Lehmann's grading system.

**AIM:** The aims of this review were to summarize the current guidelines for AV therapy in Indonesia and assess the efficacy of various therapeutic regimens.

**METHODS:** We conducted a comprehensive literature search using the search engines PubMed, Scopus, Research Gate, and Google Scholar in the time frame 2015 until 2022 with a total of 431 articles, and 29 studies met the inclusion criteria. The studies reported a total of 8245 participants.

**RESULTS AND DISCUSSION:** AV management may differ according to the conditions of each country. There are two therapeutic modalities for AV medication management, topical and systemic. The choice of therapy must be adjusted to the patient's needs, AV severity, and drug efficacy, taking into account the risk and benefit factors of the drug, as well as psychosocial factors.

**CONCLUSION:** Management of AV is still a challenge because the therapy in different countries is not the same. It is necessary to know the etiopathogenesis, understand patient's condition and the severity of AV, also know the efficacy of AV therapy, and consider treatment recommendations based on existing guidelines so that the treatment results can be achieved optimally.

## Introduction

Acne vulgaris (AV) is a disorder that occurs in the pilosebaceous units in the form of chronic inflammation with pleomorphic lesions, consisting of comedones, papules, pustules, and nodes [1], [2], [3]. The facial area is the most common location for AV, other predilections are the back, chest, shoulders, and upper arms [1], [3], [4]. The prevalence of AV is estimated to be around 85% of cases in the adolescents and young adults population aged 12–25 years [1]. AV severity peaks at the age of 16–19 years for boys or 14–17 years for girls [3]. The prevalence of AV during adolescence is higher in boys, while in adulthood it is higher in women [1]. Based on gender, men tend to experience more severe AV. Acne has no racial predilection but Asians and Africans tend to have more severe AV, while mild AV is more common in the white population [1], [4], [5].

From 2017 to 2019 before the Coronavirus pandemic, the prevalence of AV at the Cosmetic Dermatology Polyclinic, Department of Dermatology and Venereology, Dr. Cipto Mangunkusumo National Central General Hospital (RSCM), Jakarta was 2,697 cases. The incidence of AV in 2019 was around 46% of the number of

new cases at the Cosmetic Dermatology Polyclinic. The number of moderate AV cases and severe AV cases is more than 50% of the total AV cases [6]. There are various triggering factors for AV, such as genetic factors, stress, diet, use of cosmetics, drugs, and lifestyle [1], [2], [7]. Acne is a complex and multifactorial inflammatory disease. Currently, there are four main factors related to the pathogenesis of AV: Follicular epidermal hyperproliferation, sebum production (hyperseborrhea and diseborrhea), *Cutibacterium acnes* (*C. acnes*) colonization, and the inflammatory process. Each of these processes is interrelated and influenced by hormonal and immune responses [1], [7], [8]. This literature review aimed to summarize the current guidelines for AV therapy in Indonesia and assess the efficacy of various therapeutic regimens, both topical and systemic, as a reference for the selection of AV therapy in outpatient services.

## Methods

We conducted a comprehensive literature search with the appropriate keywords, namely

“AV,” “efficacy,” “guidelines,” “grading system,” and “management” using databases from PubMed, Research Gate, and Google Scholar. Studies that eligible for inclusion were reviews, systematic reviews and randomized controlled trials related to medication management of AV that according to AV guidelines from 2015 until 2022, and articles were written in English and Indonesian. For inclusion criteria, the articles must contain the following data

1. The participants diagnosed with AV
2. All grades of AV severity were included in the study
3. Treatment using topical, systemic or adjuvant therapy in the AV guidelines
4. There is evidence of the efficacy of topical, systemic or adjuvant therapy.

We excluded the case series, studies using new therapies outside of acne guidelines, and articles that not fully accessible. The full citation screening process is detailed using the flow chart in Figure 1. The eligible articles reported a total of 8245 participants. All authors significantly contributed to this paper. Data was collected by three authors and when there was disagreement, it was resolved by discussion and consensus by the fourth author. All authors giving final approval of the version to be published and agreeing to take responsibility for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are properly investigated and resolved. Additional publications obtained from the bibliography of related articles were also considered.

## Results and Discussion

### AV grading system

AV grading is the severity of AV disease, but until now there is no universally agreed AV grading system [3], [7]. Various grading systems used can be based on the type, number, extent of lesions, and inflammation [3]. In Indonesia, the recommended grading system is The Global Acne Grading System (GAGS) and Lehmann's grading system [7], but based on the 2015 Indonesian Acne Expert Meeting (IAEM), Lehmann's grading system is more recommended in clinical practice because it is faster and easy to use during routine visits. It divides the severity of AV to mild, moderate, and severe based on the number of comedones, inflammatory lesions (papules/pustules, nodules/cysts), and the total number of lesions. If there are <20 comedones, <15 papules/pustules, no nodules/cysts, and a total number of lesions <30, it is categorized as mild AV. In moderate AV, the number of comedones is between 20 and 100, papules/pustules 15–50, and nodules/cysts <5, with a total lesion count of 30–125. Whereas in severe AV the number of

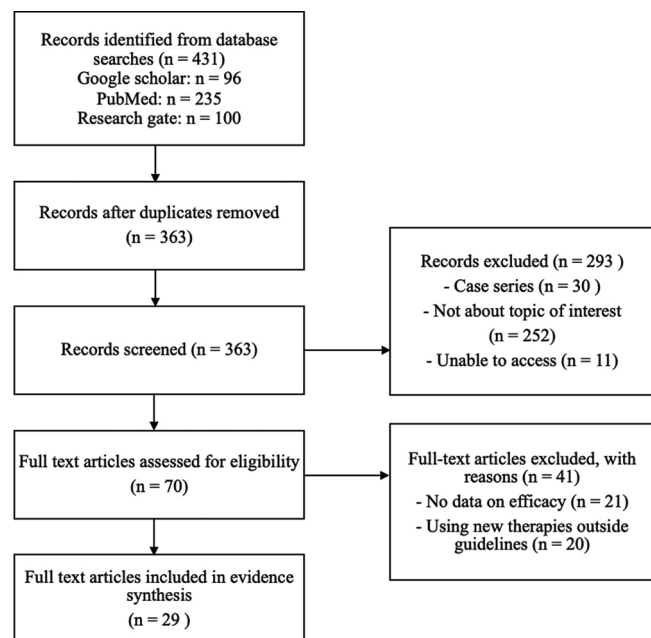


Figure 1: Flow chart

comedones is more than 100, papules/pustules more than 50, nodules/cysts more than 5, and the total number of lesions is more than 125. The use of GAGS is considered more suitable for research because it is more complicated by the division of the area and the factor of the value of the lesion in that area [3].

### Treatment

AV management aims to improve patient's facial appearance, avoid acne scars and overcome psychosocial problems [9], [10]. Treatment regimens need to adjust to the etiopathogenesis and mechanism of action of AV therapy so that there is a maximum therapeutic response. Management should start from the time the acne appears to prevent permanent sequelae [1]. The most common mechanism of action of treatment for AV is to improve the pattern of keratinization of the follicles, decrease the activity of the sebaceous glands, reduce the population of follicular bacteria, especially *C. acnes*, and use anti-inflammatory agents [1], [9]. In general, topical drugs for the treatment of AV have a good safety profile and become the first-line treatment for mild to moderate AV, and can be used as combination therapy for severe AV. Systemic therapy is usually used for the initial treatment of moderate to severe AV as well as AV refractory to topical therapy [9]. To assess the effectiveness of an AV therapeutic intervention, the minimum required duration is 6–8 weeks [3], [10], unless the patient has allergies or intolerable side effects [10].

Management of AV is sometimes quite challenging and requires a long time of therapy [11] because its management in different countries is not the same, there is often a difference of expert opinion in diagnosis and therapy [7]. Many dermatologists

from various educational centers around the world held a meeting to formulate the Global Alliance to Improve Outcomes in Acne (GA) as an international AV management recommendation and the results were published in 2003, revised in 2009, and completed in 2018. AV based on GA divides the severity into mild, moderate, severe, and very severe. The treatment of choice for mild comedonal AV is topical retinoids, while the papular/pustular type uses a fixed combination (combination of adapalene 0.3% and benzoyl peroxide [BPO] 2.5%). In moderate AV type papular/pustular to nodular can use a fixed combination with additional hormonal therapy and/or oral antibiotics. In severe (nodular) to very severe (nodular and/or acne conglobata) AV, oral isotretinoin may be added [12].

Even though, there are international recommendations, several other countries have their guidelines to adjust the conditions in their respective countries. Dermatologists who are members of the Indonesian Cosmetic Dermatology Study Group of the Indonesian Society of Dermatology and Venereology (INSDV/PERDOSKI) held an IAEM to develop guidelines for AV management in Indonesia. This meeting was held because the experts concluded that the situation and condition of AV in Indonesia were different compared to other countries, for example, related to climate differences and diverse population characteristics, and it was hoped that there would be uniformity in the aspects of diagnosis and management of AV [3]. The results of the 2015 IAEM became the basis for drafting the AV guidelines in Indonesia [13]. At RSCM, Jakarta also has the latest AV guideline in 2022 [14] which was made in reference to many other guidelines [3], [13], [15], [16], [17]. The comparison of AV management guidelines in Indonesia will be discussed below:

#### a. Mild AV

Based on the 2015 IAEM and Perdoski Guidelines, mild AV therapy is divided into 3 main lines. First-line topical therapy can use retinoid acid (RA), salicylic acid, or BPO creams. Second line, azelaic acid (AA) and or BPO. While the third line can use RA and or BPO, as well as topical antibiotics [3], [13]. In the AV guidelines at RSCM, mild AV is divided into comedonal and papular/pustular types. The first line used for the comedonal type is RA cream or RA gel and BPO. Papular/pustular types can use the same regimen but supplement with topical antibiotics. For the second line can use adapalene or tazarotene gel, and can be given AA cream for papular/pustular types [14].

#### b. Moderate AV

Moderate AV therapy is currently using a combination of topical and systemic therapy. In the 2015 IAEM and Perdoski guidelines, first-line to third-line topicals are the same as mild AV but can be supplemented with intralesional corticosteroid injections. For systemic therapy can use doxycycline or

erythromycin [3], [13]. Moderate AV in RSCM, is divided into papular/pustular and nodular types. RA cream/gel, or a combination of RA gel and BPO can be used as the first-line topical therapy for papular/pustular and nodular types. Second-line topical therapy for papular/pustular types uses adapalene or tazarotene gel in combination with BPO. The nodular type therapy is the same as the papular/pustular type topical therapy, but BPO can be replaced with AA. The first-line systemic therapy options available at RSCM AV guideline 2022 are doxycycline 50–100 mg (twice daily), clindamycin 150–300 mg (2–3 times daily), lymecycline 50–300 mg (once daily), or minocycline 50–100 mg (twice daily). Second-line antibiotics that can be an option include erythromycin 500 mg (twice daily), and trimethoprim-sulfamethoxazole 160/800 mg (twice daily). For the nodular type, use the same choice of antibiotics or use oral isotretinoin 0.1–2 mg/kg BW up to a cumulative dose of 120–150 mg/kg BW. In general, antibiotics that are often used in RSCM are doxycycline, clindamycin, or erythromycin [14].

#### c. Severe AV

The first-line topical therapy for severe AV based on the 2015 IAEM and Perdoski guidelines, can use topical antibiotics and or BPO. The second and third lines are similar to topical therapy for moderate AV. For first-line systemic therapy, we can use azithromycin, erythromycin, or quinolone antibiotics. Second-line systemic therapy may include antiandrogens for women and oral isotretinoin for men [3], [13]. Based on the AV guideline in RSCM, topical therapy for severe AV can use a combination of RA cream or gel and BPO. As for systemic therapy, high-dose oral antibiotics can be used (minimum for 6–8 weeks, maximum for 12–18 weeks) or oral isotretinoin. Regarding the use of oral isotretinoin, until now it has not been approved by the Food and Drug Administration (FDA) Republic of Indonesia but is still included in the guidelines because it is related to drug entry through a special access scheme [14].

### **Efficacy of various therapeutic regimens**

In the management of AV, clinicians have various therapeutic recommendations that can be used according to patient needs. The following will discuss the efficacy of these therapies both topically and systemically.

#### 1. Topical therapies

##### a. Topical retinoid (level of evidence [LoE] 1A)

Topical retinoids are effective first-line therapy against comedonal and inflammation AV [18]. These drugs can help normalize follicular keratinization and reduce keratinocyte cohesiveness, thereby reducing follicular occlusion and comedone formation as well as reducing inflammatory and noninflammatory lesions [18], [19]. Currently, the United States FDA has approved three types of topical retinoids, adapalene,

tazarotene, and tretinoin [11]. However, the only topical retinoids available in Indonesia are tretinoin and adapalene [19]. Usually given once a day at night [20]. The efficacy of topical retinoids increases according to the magnitude of the concentration. There is a study on tretinoin therapy with concentrations of 0.1% and 0.025% for 12 weeks, reducing microcomedones by 80% and 35%, respectively [21]. The first results of treatment can be seen after 2–3 weeks, but improvement is usually gradual and most patients need 2–4 months to achieve positive results. Common side effects of using tretinoin are skin irritation, dry skin, erythema, and peeling skin [20], [22], [23]. Topical adapalene is recommended as the first-line choice because of its better skin tolerance than other topical retinoids [20]. Kolli *et al.*, [19] compiled a systematic review of the efficacy of various topical retinoids as follows:

- Adapalene versus tazarotene

One study concluded that 0.1% tazarotene cream caused a greater reduction in the number of noninflammatory lesions than 0.1% adapalene gel for 12 weeks, but this was not statistically significant ( $p = 0.107$ ). In addition, tazarotene also showed a greater reduction in the total number of AV lesions compared to adapalene (82% vs. 64%;  $p < 0.02$ ). Another study suggested that 0.1% tazarotene gel plus 1% clindamycin gel was superior to 0.1% adapalene gel and 1% clindamycin gel for 4 weeks (reduction in the number of lesions 17.54 vs. 11.03;  $p = 0.007$ ). Other studies found no statistically significant difference or were inferior [19].

- Adapalene versus tretinoin

There is one randomized double-blind study comparing adapalene 0.1%, adapalene 0.3%, tretinoin 0.05%, or placebo for 12 weeks. After being observed, tretinoin 0.05% showed a better reduction in the number of lesions compared to adapalene 0.3%, adapalene 0.1%, and placebo (76.7% vs. 66.4% vs. 57.8% vs. 21.8%;  $p < 0.001$ ) [19].

- Tretinoin versus tazarotene

A randomized, blinded study comparing 0.04% tretinoin microsphere gel with 0.05% tazarotene cream in mild-moderate AV. After 12 weeks of observation, the inflammatory lesions diminished more rapidly with the use of tretinoin than tazarotene (4.41 vs. 3.95;  $p < 0.001$ ). There was a decrease in the number of noninflammatory lesions from baseline to week 12 for the tretinoin-treated group (92.65%;  $p = 0.002$ ) and tazarotene (79.55%;  $p = 0.0078$ ) [19].

b. Topical antimicrobial

### **BPO (LoE 1A)**

BPO is the recommended choice of topical antimicrobial because it is proven to be able to eliminate *C. acnes* and has a mild comedolytic ability [20], [23].

BPO is effective as monotherapy, but is often used in conjunction with topical retinoids or topical antibiotics and has been shown to provide better results. The most common side effects are concentration-dependent irritation, erythematous and dry skin, desquamation, and a burning sensation [10], [20], [23]. The following are the results of a Cochrane systematic review in 2020 on BPO:

- BPO versus adapalene:

Total AV lesions count achieved a greater reduction in long-term and short-to-medium-term reduction in noninflammatory lesions with BPO as monotherapy compared to adapalene [24]. However, other studies say the efficacy of BPO is the same as adapalene [16]. When the combination of BPO and clindamycin is compared with adapalene and clindamycin; the decrease in the number of total lesions, non-inflammatory lesions, and AV inflammatory lesions was not statistically significant [24].

- BPO versus topical antibiotics:

The use of topical BPO and clindamycin as monotherapy for medium and short term, can reduce non-inflammatory lesions by approximately 40% and 30%, respectively. A similar effect was observed in the reduction of inflammatory lesions (31% vs. 35% for the medium-term and 24% vs. 22% for the short term). However, there was no statistically significant difference as well as the results of using BPO compared to topical erythromycin as monotherapy [24].

### **AA (LoE 1B)**

The FDA approved AA 20% cream as an alternative treatment for AV, either through monotherapy or in combination with other drugs. AA has comedolytic, antibacterial, and mild anti-inflammatory agents. The recommended dose is twice a day. The advantage of AA 20% is that it is safe in pregnancy and effective in the treatment of post-inflammatory dyspigmentation. Usually, AA is well tolerated, but side effects such as burning, stinging, skin redness, and risk of hypopigmentation can occur in dark-skinned patients [10], [11]. The efficacy of AA in AV lesions is comparable to adapalene, whereas tretinoin is still superior to AA [16].

c. Combination therapy

Currently, there are topical drugs in fixed combinations, namely adapalene with BPO (LoE 1A), BPO with clindamycin (LoE 1A), and clindamycin with tretinoin (LoE 1A). The fixed combination of BPO and adapalene provided significantly greater efficacy from the 1<sup>st</sup> week of therapy. There were three 12 week studies of patients 12 years of age or older with moderate AV, which demonstrated a significantly higher therapeutic success rate when using the fixed combination adapalene 0.1%/BPO 2.5% (A/BPO) gel compared to adapalene 0.1% or

BPO 2.5% gel only. There are other preparations with a higher concentration, 0.3% adapalene with 2.5% BPO [18], [25]. Osman-Ponchet *et al.*, [25] reported that the fixed combination of 0.3% A/BPO made absorption into the skin more optimal. This combination showed a higher clinical success rate and good efficacy in all AV severity grades [18], [21], [24]. The use of A/BPO can often reduce the need for antibiotics and can prevent the possibility of antimicrobial resistance [21].

The combination of 5% BPO gel with 1.2% clindamycin phosphate and the combination of 0.025% tretinoin gel and 1.2% clindamycin phosphate also gave good results, compared to monotherapy alone [24]. Meanwhile, the efficacy between combination therapies was more or less similar [16]. Combination therapy has a rapid onset of action because it can reduce lesions in the 1<sup>st</sup> week and has shown long-term efficacy and tolerability [18].

## 2. Systemic antibiotic therapy

### a. Tetracyclines (LoE 1A)

Of all the oral antibiotics used in the management of AV, the tetracycline group is the longest used and is used for systemic therapy of moderate to severe AV [26]. Tetracyclines, doxycycline, and minocycline belong to this group [11]. Doxycycline is recommended as the first-line oral antibiotic. It is contraindicated in children under 8 years old, pregnant and breastfeeding women. Another alternative is tetracycline but must be taken on an empty stomach and the food consumed should not contain iron and calcium, because it is less practical so tetracycline is not considered first-line therapy [18]. Minocycline can also be an alternative because research shows that it is as effective as tetracycline and doxycycline in reducing AV inflammation [16], [18]. It should be noted that the severe side effects of minocycline are on the central nervous system and are associated with lupus and autoimmune hepatitis [18]. Various studies were conducted to determine the efficacy of which drug is better in the treatment of AV, but there is little evidence that one type of antibiotic is superior to another [27]. Sitohang *et al.*, [28] conducted a research at RSCM regarding the susceptibility of *C. acnes* cultures to antibiotics. The results obtained that most of *C. acnes* cultures were still susceptible to doxycycline and minocycline. However, about the 10% were found to be resistant to erythromycin, clindamycin, and tetracyclines.

### b. Macrolides

Erythromycin (LoE 1A) and azithromycin (LoE 1B) are macrolide antibiotics that can also be used for systemic AV therapy [22]. Erythromycin has a similar efficacy as tetracycline in the treatment of inflammatory AV and is safe for use in younger patients [16], [18]. In pregnant women with severe AV, erythromycin may be considered [18]. Azithromycin is a derivative of erythromycin and is used to treat serious systemic infections. The use of azithromycin for AV only in certain

cases, for example in patients who are contraindicated with tetracycline. It is also quite safe for pregnant and breastfeeding women [26], [29]. Kim *et al.*, [30] conducted a meta-analysis of randomized controlled trials on the efficacy of azithromycin versus doxycycline in the management of AV. The study showed that daily doxycycline therapy and pulsed dose therapy of azithromycin had similar efficacy in the treatment of moderate to severe AV at 12 weeks, with no significant difference between groups. However, the doxycycline daily therapy group reported more severe side effects than the azithromycin pulsed dose therapy group.

### c. Trimethoprim-sulfamethoxazole (TMP-SMX) (LoE 2B)

TMP-SMX can be used as an alternative when other antibiotics are contraindicated or refractory to other AV therapies. Data regarding the use of TMP-SMX in treating AV are limited [26], [27]. There was a study regarding the efficacy in a randomized, double-blind manner. In this study, there was a significant reduction in acne scores (based on the number and severity of lesions) by 62% after 5 weeks of treatment with TMP/SMX compared to baseline ( $p < 0.001$ ) and the placebo group ( $p < 0.001$ ) [27]. Serious side effects that can occur are Stevens-Johnson syndrome/toxic epidermal necrolysis, and bone marrow suppression [26].

### d. Clindamycin (LoE 2B)

The use of oral clindamycin is effective compared to placebo in AV therapy. A double-blind, placebo-controlled trial found clinical improvement in AV of at least 50% with a reduction in the number of papules and pustules compared with baseline. After 13 weeks of therapy, the patients had clinical improvement of 86% treated with clindamycin and 38% treated with placebo ( $p < 0.005$ ). The clindamycin and placebo groups experienced a 50% and 21% reduction in comedone counts ( $p < 0.05$ ) and a 78% and 26% decrease in inflammatory lesions ( $p < 0.01$ ). Commonly reported side effects are nausea, vomiting, and diarrhea [27].

## 3. Oral isotretinoin therapy (LoE 1A)

Isotretinoin is a retinoic acid derivative widely used in the treatment of AV nodulocystic [1], [18], [22], [31]. The use of oral isotretinoin has been approved by the United States FDA for the treatment of severe recalcitrant AV and for patients with moderate AV that is resistant to treatment or relapses rapidly after discontinuation of oral antibiotic therapy [2], [18], [22], [31]. This therapy gives excellent results and in almost all cases of AV experience resolution and remission in the long term [1]. Isotretinoin can reduce sebum production and colonization of *C. acnes*, enhance anti-inflammatory effects, and has a strong comedolytic effect [2], [32]. Therefore, isotretinoin is considered to be the only treatment modality that has implications for the overall pathogenesis of acne [32].

The most common side effects are xerosis, xerophthalmia, cheilitis, and headache. It can resolve

without sequelae after discontinuation of the drug [2], [10], [11], [15]. Lipid and liver function tests are recommended at baseline and after maximum dose therapy is reached [2], [9], [33]. A possible risk of inflammatory bowel disease has also been reported but is not currently supported by recent data [2], [11], [33]. One side effect that is considered serious is the possible association between isotretinoin and depression or suicide but the relationship is currently contradictory [2], [31], [33], [34]. Beside its efficacy, it is important to remember that it is teratogenic. This drug belongs to category X in pregnancy. Isotretinoin is also contraindicated in patients who are still breastfeeding, impaired liver and kidney function, uncontrolled hyperlipidemia, and have a history of hypersensitivity to isotretinoin or its components [9], [32].

### Adjuvant therapy

The adjuvant therapy is additional therapy or treatment given in conjunction with AV main therapy to accelerate healing or improve skin conditions during treatment [3]. Other benefits are helping reduce side effects from treatment (e.g. irritation and dryness), providing a synergistic effect when used in conjunction with main treatment, reducing adverse sequelae, and improving quality of life [18]. Adjuvant therapy may include many modalities. The first is dermo-cosmeceuticals (eg cleansers, moisturizers, topical sebum control agents, keratolytic, antimicrobials, anti-inflammatory agents, sunscreens and camouflages) [7], [18], [35], [36]. Goh *et al.*, [37] suggested that the appropriate use of cleansers, moisturizers, and photoprotective for acne can complement the therapeutic management thereby reducing the side effects of therapy and improving adherence and treatment results. Several topical sebum control agents, for example nicotinamide, anti-bacterial adhesive and zinc pyrrolidone carboxylic acid when combined with adapalene can reduce non-inflammatory lesions within 2 weeks of therapy according to a study by Sitohang *et al.*, [38].

The second is comedones extraction, which is commonly used for comedonal acne [7]. However, Sitohang *et al.*, [39] conducted a study comparing the extraction of acne lesions (inflammatory and non-inflammatory lesions) with oral doxycycline in patients with moderate AV. The results showed that acne lesion extraction was more effective than oral antibiotics after 6 weeks of therapy ( $p < 0.043$ ). An interesting study conducted by Sutarjo *et al.*, [40] showed that potassium hydroxide examination from the extraction of acne lesions found *Malassezia* spp. in AV lesions on the face, with a higher number of spores found in non-inflammatory lesions than in inflammatory lesions. However, the use of antifungals for adjuvant therapy still needs further research. Other adjuvant therapy are corticosteroid [7], [18], [22], chemical surgery [7], [18], [22], as well as light and laser-based

therapies [7], [18], [22]. Most AV patients were found to have vitamin D insufficiency-deficiency as stated by Saptarini *et al.*, [41] but administration of vitamin D supplement as adjuvant therapy for lesion improvement requires further research.

### Maintenance therapy

Maintenance therapy is an action or therapy to reduce and prevent AV recurrence after the main therapy is discontinued [7], [22]. Maintenance therapy is usually continued for 3–12 months [22]. The use of antibiotics as maintenance therapy is not recommended because they do not prevent the development of microcomedones and pose a risk of resistance [7], [18]. In Indonesia, maintenance therapy is based on recommendations from the 2015 IAEM, i.e. the need for communication, information, and education; skin care; 0.01–0.025% topical retinoids; dermo-cosmeceuticals [3]. Education is very important to increase patient compliance with maintenance therapy.

### Conclusion

AV management should be started as early as possible to avoid complications, such as acne scarring. Until now, there is no uniform therapy guidelines throughout the world because AV management between countries can differ according to the conditions of each country. It is necessary to know the etiopathogenesis, understand patient's condition and severity of AV. Also, it is necessary to consider the efficacy of AV therapy and treatment recommendations based on existing guidelines. These various guidelines can help dermatologists in the management of AV so that they can obtain better results.

### References

1. Goh C, Cheng C, Agak G, Zaenglein AL, Graber EM, Thiboutot DM, *et al.* Acne vulgaris. In: Kang S, Amagai M, Bruckner A, editors. *Fitzpatrick's Dermatology*. 9<sup>th</sup> ed. New York: McGraw-Hill; 2019. p. 1391-418.
2. Zaenglein AL. Acne vulgaris. *N Engl J Med*. 2018;379(14):1343-52. <https://doi.org/10.1056/nejmcp1702493> PMID:30281982
3. Wasitaatmadja SM, Arimuko A, Norawati L, Bernadette I, Legiawati L. *Acne Treatment Guidelines in Indonesia*. [Pedoman Tata Laksana Akne di Indonesia]. 2<sup>nd</sup> ed. Jakarta: Centra Communications; 2016. p. 1-13.
4. Sutaria AH, Masood S, Schlessinger J. *Acne Vulgaris*. Treasure Island: StatPearls Publishing; 2022. Available from: <https://www.ncbi.nlm.nih.gov/books/nbk459173/?report=printable> [Last

- accessed on 2022 Jul 12].
5. Heng AH, Chew FT. Systematic review of the epidemiology of acne vulgaris. *Sci Rep*. 2020;10(1):5754. <https://doi.org/10.1038/s41598-020-62715-3>  
PMid:32238884
  6. Department of Dermatology and Venereology. Patient Visit Data of Cosmetic Dermatology Division, Polyclinic Dermatology and Venereology Department RSUPN Dr. Cipto Mangunkusumo in 2017-2019 [Data Kunjungan Pasien Poliklinik Divisi Kosmetik Departemen Dermatologi dan Venereologi RSUPN Dr. Cipto Mangunkusumo Tahun 2017-2019]; 2019. p. 1-10.
  7. Wasitaatmadja SM. Acne. [Akne]. Jakarta: Badan Penerbit Fakultas Kedokteran Universitas Indonesia; 2018. p. 1-199.
  8. Cong TX, Hao D, Wen X, Li XH, He G, Jiang X. From pathogenesis of acne vulgaris to anti-acne agents. *Arch Dermatol Res*. 2019;311(5):337-49. <https://doi.org/10.1007/s00403-019-01908-x>  
PMid:30859308
  9. Leung AK, Barankin B, Lam JM, Leong KF, Hon KL. Dermatology: How to manage acne vulgaris. *Drugs Context*. 2020;10:1-18. <https://doi.org/10.7573/dic.2021-8-6>  
PMid:34691199
  10. Ogé LK, Broussard A, Marshall MD. Acne vulgaris: Diagnosis and treatment. *Am Fam Physician*. 2019;100(8):475-84.  
PMid:31613567
  11. Tan AU, Schlosser BJ, Paller AS. A review of diagnosis and treatment of acne in adult female patients. *Int J Womens Dermatol*. 2018;4(2):56-71. <https://doi.org/10.1016/j.ijwd.2017.10.006>  
PMid:29872679
  12. Thiboutot DM, Dréno B, Abanmi A, Alexis AF, Araviiskaia E, Cabal MI, et al. Practical management of acne for clinicians: An international consensus from the Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol*. 2018;78(2 Suppl 1):S1-23.e1. <https://doi.org/10.1016/j.jaad.2017.09.078>  
PMid:29127053
  13. Indonesian Society of Dermatology and Venereology (PERDOSKI). Acne vulgaris. In: Siswati AS, Rosita C, Triwahyudi D, Budianti KB, Mawardi P, Dwiyana RF, et al., editors. *Clinical Practice Guidelines for Indonesian Dermatologist and Venereologists*. [Panduan Praktis Klinis Bagi Dokter Dermatologi dan Venereologi Indonesia]. Jakarta: PP PERDOSKI; 2021. p. 343-6.
  14. Department Dermatology and Venereology. *Clinical Practice Guidelines for Acne Vulgaris RSCM*. [Panduan Praktis Klinis Akne Vulgaris RSCM]. Jakarta: RSCM; 2022. p. 5-26.
  15. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-73.e33. <https://doi.org/10.1016/j.jaad.2015.12.037>  
PMid:26897386
  16. Nast A, Dréno B, Bettoli V, Mokos ZB, Degitz K, Dressler C, et al. European evidence-based (S3) guideline for the treatment of acne update 2016-short version. *J Eur Acad Dermatol Venereol*. 2016;30(8):1261-8. <https://doi.org/10.1111/jdv.13776>  
PMid:27514932
  17. Goh CL, Abad-Casintahan F, Aw DC, Baba R, Chan LC, Hung NT, et al. South-East Asia study alliance guidelines on the management of acne vulgaris in South-East Asian patients. *J Dermatol*. 2015;42(10):945-53. <https://doi.org/10.1111/1346-8138.12993>  
PMid:26211507
  18. Oon H, Wong SN, Chen WA, Cheong WK, Goh CL, Tan HH. Acne management guidelines by the dermatological society of Singapore. *J Clin Aesthet Dermatol*. 2019;12(7):34-50.  
PMid:31531161
  19. Kolli SS, Pecone D, Pona A, Cline A, Feldman SR. Topical retinoids in acne vulgaris: A systematic review. *Am J Clin Dermatol*. 2019;20(3):345-65. <https://doi.org/10.1007/s40257-019-00423-z>  
PMid:30674002
  20. Otlewska A, Baran W, Batorycka-Baran A. Adverse events related to topical drug treatments for acne vulgaris. *Expert Opin Drug Saf*. 2020;19(4):513-21. <https://doi.org/10.1080/14740338.2020.1757646>  
PMid:32347138
  21. Leyden JJ, Stein-Gold L, Weiss J. Why topical retinoids are mainstay of therapy for acne. *Dermatol Ther (Heidelb)*. 2017;7(3):293-304. <https://doi.org/10.1007/s13555-017-0185-2>  
PMid:28585191
  22. Ju Q, Fan WX, Gu J, Hao F, He L, Li HJ, et al. Chinese guidelines for the management of acne vulgaris: 2019 update. *Int J Dermatol Venereol*. 2019;2(3):129-38. <https://doi.org/10.1097/JD9.0000000000000043>
  23. Marson JW, Baldwin HE. An overview of acne therapy, part 1: Topical therapy, oral antibiotics, laser and light therapy, and dietary interventions. *Dermatol Clin*. 2019;37(2):183-93. <https://doi.org/10.1016/j.det.2018.12.001>  
PMid:30850041
  24. Yang Z, Zhang Y, Mosler EL, Hu J, Li H, Zhang Y, et al. Topical benzoyl peroxide for acne. *Cochrane Database Syst Rev*. 2020;3(3):CD011154. <https://doi.org/10.1002/14651858.CD011154.pub2>  
PMid:32175593
  25. Osman-Ponchet H, Sevin K, Gaborit A, Wagner N, Poncet M. Fixed-combination gels of adapalene and benzoyl peroxide provide optimal percutaneous absorption compared to monad formulations of these compounds: Results from two *in vitro* studies. *Dermatol Ther (Heidelb)*. 2017;7(1):123-31. <https://doi.org/10.1007/s13555-016-0159-9>  
PMid:27900658
  26. Baldwin H. Oral antibiotic treatment options for acne vulgaris. *J Clin Aesthet Dermatol*. 2020;13(9):26-32.  
PMid:33133338
  27. Bienenfeld A, Nagler AR, Orlow SJ. Oral antibacterial therapy for acne vulgaris: An evidence-based review. *Am J Clin Dermatol*. 2017;18(4):469-90. <https://doi.org/10.1007/s40257-017-0267-z>  
PMid:28255924
  28. Sitohang IB, Fathan H, Effendi E, Wahid M. The susceptibility of pathogens associated with acne vulgaris to antibiotics. *Med J Indones*. 2019;28(1):21-7. <https://doi.org/10.13181/mji.v28i1.2735>
  29. Kardeh S, Saki N, Jowkar F, Kardeh B, Moein SA, Khorraminejad-Shirazi MH. Efficacy of azithromycin in treatment of acne vulgaris: A mini review. *World J Plast Surg*. 2019;8(2):127-34. <https://doi.org/10.29252/wjps.8.2.127>  
PMid:31309049
  30. Kim JE, Park AY, Lee SY, Park YL, Whang KU, Kim HJ. Comparison of the efficacy of azithromycin versus doxycycline in acne vulgaris: A meta-analysis of randomized controlled trials. *Ann Dermatol*. 2018;30(4):417-26. <https://doi.org/10.5021/ad.2018.30.4.417>  
PMid:30065581
  31. Mohiuddin AK. A comprehensive review of acne vulgaris. *J Clin Pharm*. 2019;1:17-45. <https://doi.org/10.15226/2378-1726/6/2/00186>
  32. Sitohang IB. Isotretinoin for treating acne vulgaris. *Int J Appl Pharm*. 2021;13(2):20-5. <https://doi.org/10.22159/ijap.2021v13i2.40045>
  33. Vallerand IA, Lewinson RT, Farris MS, Sibley CD, Ramien ML, Bulloch AG, et al. Efficacy and adverse events of oral isotretinoin for acne: A systematic review. *Br J Dermatol*. 2018;178(1):76-85. <https://doi.org/10.1111/bjd.15668>  
PMid:28542914

34. Li C, Chen J, Wang W, Ai M, Zhang Q, Kuang L. Use of isotretinoin and risk of depression in patients with acne: A systematic review and meta-analysis. *BMJ Open*. 2019;9(1):e021549. <https://doi.org/10.1136/bmjopen-2018-021549>  
PMid:30670500
35. Conforti C, Giuffrida R, Fadda S, Fai A, Romita P, Zalaudek I, et al. Topical dermocosmetics and acne vulgaris. *Dermatol Ther*. 2021;34(4):e14436. <https://doi.org/10.1111/dth.14436>  
PMid:33084158
36. Araviiskaia E, Estebanz JL, Pincelli C. Dermocosmetics: Beneficial adjuncts in the treatment of acne vulgaris. *J Dermatolog Treat*. 2021;32(1):3-10. <https://doi.org/10.1080/09546634.2019.1628173>  
PMid:31211609
37. Goh CL, Wu Y, Welsh B, Abad-Casintahan MF, Tseng CJ, Sharad J, et al. Expert consensus on holistic skin care routine: Focus on acne, rosacea, atopic dermatitis, and sensitive skin syndrome. *J Cosmet Dermatol*. 2022;22(1):45-54. <https://doi.org/10.1111/jocd.15519>  
PMid:36409588
38. Sitohang IB, Yahya YF, Simanungkalit R, Winarni DR, Madjid A. Efficacy and tolerability of topical nicotinamide plus antibacterial adhesive agents and zinc-pyrrolidone carboxylic acid versus placebo as an adjuvant treatment for moderate acne vulgaris in Indonesia: A multicenter, double-blind, randomized, controlled trial. *J Clin Aesthet Dermatol*. 2020;13(7):27-31.  
PMid:32983333
39. Sitohang IB, Soebaryo RW, Kanoko M. Acne lesion extraction versus oral doxycycline for moderate acne vulgaris: A randomized clinical trial. *J Clin Aesthet Dermatol*. 2021;14(6):E61-5.  
PMid:34804358
40. Sutarjo AS, Sitohang IB, Wahid MH, Widaty S. Comparison of *Malassezia* spp. Proportions in inflammatory and non-inflammatory facial acne vulgaris lesions. *Int J Appl Pharm*. 2020;12(3):7-11. <https://doi.org/10.22159/ijap.2020.v12s3.39454>
41. Saptarini D, Witjaksono F, Sitohang IB. Correlation study of acne vulgaris and serum Vitamin D levels in adolescents. *Int J Appl Pharm*. 2020;12(3):19-21. <https://doi.org/10.22159/ijap.2020.v12s3.39462>