Raising knowledge about the types of acne and the choice of appropriate treatment.

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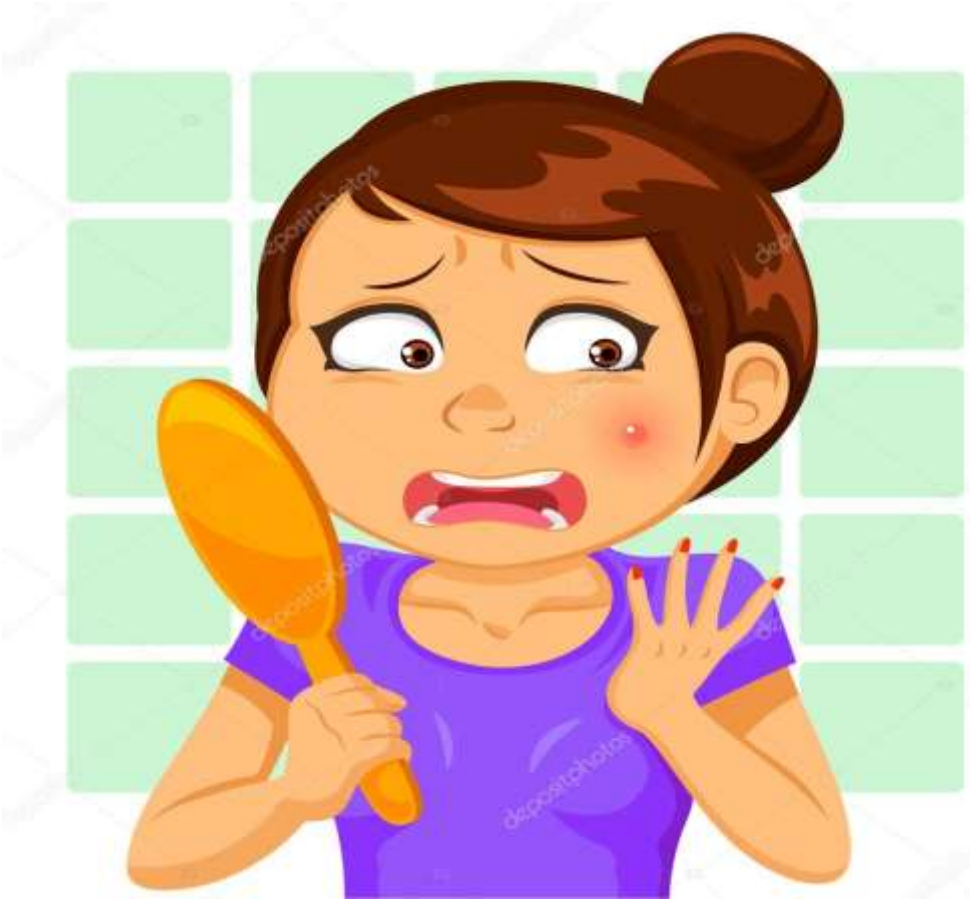
Clinical pharmacy



INTRODUCTION

- Acne vulgaris is an inflammatory skin disorder of the pilosebaceous units of the skin.

- Although most commonly seen on the face, acne can also present on the chest, back, neck, and shoulders.

- Acne is not just a self-limiting disorder of teenagers. The clinical course of acne can be prolonged or recur, resulting in long-term physical complications, such as extensive scarring and psychological distress.

Epidemiology and etiology

- Acne vulgaris is the number one skin disease in the United States.
- Acne affects approximately 85% of adolescents and adults aged 12 to 25 years.
- Acne is more likely to occur in **males during adolescence** and **females during adulthood**.
- Individuals with **a positive family history** of acne have been shown to develop more severe cases of acne at an earlier age.

Epidemiology and etiology

- The link between diet and acne has continued to be controversial, with emerging evidence suggesting a link to foods with high glycemic indexes as well as dairy products (ie, skim milk)—partially due to the hormones in the milk; however, no specific dietary changes are recommended in the management of acne.

- Local irritation from **occlusive clothing** or **athletic equipment**, **oil-based cosmetics** or **beauty products**, **prolonged sweating or environments of high humidity**, and **a variety of medications** may also worsen acne.

Epidemiology and etiology

- Increased **androgen levels**, especially during puberty, can cause an increased size of the sebaceous gland and production of abnormally high levels of sebum within those glands.

- **Keratinization**, the sloughing of epithelial cells in the hair follicle, is also a natural process. In acne, however, hyperkeratinization occurs resulting in an increased adhesiveness of the sloughed cells.

PATHOPHYSIOLOGY

- An initial acne lesion invisible to the naked eye, called a microcomedo, forms as a result of the increased cell division and cohesiveness.

- Subclinical microcomedo formation is a precursor for noninflammatory acne lesions called comedos.
  - **A closed comedo** or **"whitehead"** appears when accumulation of epithelial cells and sebum partially obstruct the follicular opening.
  - If the follicular opening is dilated, the keratin buildup can darken and form an **open comedo** or **"blackhead."**

PATHOPHYSIOLOGY

- Propionibacterium acnes, an anaerobic organism, is also found in the normal flora of the skin.

- This bacteria proliferates in the mixture of sebum and keratinocytes and can result in an inflammatory response producing more severe acne lesions such as **papules**, **pustules**, and **nodules**.

- Inflammatory lesions may result in scarring if treated inadequately.

Clinical Presentation and Diagnosis of Acne

Clinical Presentation

- Acne lesions are most often seen on the face but can also present on the chest, back, neck, and shoulders and are described as either noninflammatory or inflammatory.

Clinical Presentation

- **Inflammatory Lesions**
  - **Papules:** Solid, elevated lesion less than 0.5 cm in diameter.
  - **Pustules:** Vesicles filled with purulent fluid less than 0.5 cm in diameter.
  - **Nodules:** Warm, tender, firm lesions greater than 0.5 cm in both width and depth.
  - **Cysts:** Nodules that harden into larger, pus-filled lesions.
  - **Scars :** Inflammatory acne can result in permanent scarring that ranges from small, depressed pits to large, elevated blemishes.
  - **Hyperpigmentation:** Inflammatory acne may result in hyperpigmentation of the skin that can last for weeks to months.

Clinical Presentation

- **noninflammatory Lesions**
  - Closed comedo or "**whitehead**": A partially plugged follicle containing sebum, keratinocytes, and bacteria that remains beneath the surface of the skin. Closed comedos usually appear as small white bumps about 1 to 2 mm in diameter.
  - Open comedo or "**blackhead**": A partially plugged, dilated follicle containing sebum, keratinocytes, and bacteria approximately 2 to 5 mm in diameter that protrudes from the surface of the skin and appears black or brown in color.

Pimple Types

Papules.

Blackheads.

Whiteheads.

Nodules.

Pustules.

Cysts.

Diagnosis

- The diagnosis of acne vulgaris is clinical.
- Lesion cultures may be warranted when treatment regimens fail to rule out Gram negative folliculitis and other skin infections.
- Endocrinological laboratory evaluation is only recommended for patients who have acne and additional signs of androgen excess.
- No standard acne grading scale has been identified. While several grading scales exist, most clinicians describe acne as **mild** (non-inflammatory lesions), **moderate** (many inflammatory lesions), or **severe** (numerous severe inflammatory lesions and evidence of scarring).

TREATMENT

- Although traditionally thought of as a self-limiting disorder, acne can have patterns of **recurrence**.

- Because acne cannot be cured, proper treatment must involve both short-term and long-term strategies.

- Goals of therapy are to
  - Reduce the number and severity of existing lesions
  - Prevent the development of new lesions and recurrence
  - Prevent long-term disfigurement and permanent scarring,
  - And encourage treatment adherence.

General Approach to Treatment

- Acne treatment regimens should be based on
  - acne severity
  - and type of acne lesion.
- Other factors such as
  - response to previous treatment,
  - patient preference,
  - cost,
  - and adherence should also be considered.

General Approach to Treatment

- Topical therapy is considered **first line** for **mild** acne with oral therapies added to topical therapy in **moderate-to-severe** acne.

- Using multiple topical agents that target different aspects of acne pathogenesis is **more effective, reduces adverse effects, and minimizes treatment resistance.**

- Topical therapies should be applied to the entire area affected by acne to prevent new lesions from developing.

General Approach to Treatment

- Optimal management includes **aggressive induction** treatment and **maintenance** therapy to prevent recurrence.
- Improvement of symptoms following induction therapy occurs gradually, sometimes taking 6 to 8 weeks for results to be physically apparent.
- Patients need to be educated on continual treatment compliance during this time and should not get discouraged if acne lesions appear to worsen before getting better.

General Approach to Treatment

- Maintenance therapy should begin after 12 weeks of induction therapy and is continued for 3 to 4 months in most clinical trials.

- Due to frequent acne recurrences, clinical experience indicates that a longer duration of maintenance therapy may be beneficial for most patients.

Nonpharmacologic Therapy

- There is significant variance in the clinical benefit of many nonpharmacologic interventions for acne vulgaris.
- Patients should be counseled to avoid aggressive skin washing and to use a mild, noncomedogenic facial soap twice daily.
- Manipulating or squeezing lesions should also be avoided to minimize scarring.
- The use of an oil-free, noncomedogenic moisturizer daily may improve the tolerability of topical drug therapy.

Pharmacologic Therapy

	Mild	Moderate	Severe
1st Line Treatment	Benzoyl Peroxide (BP) or Topical Retinoid -or- Topical Combination Therapy** BP + Antibiotic or Retinoid + BP or Retinoid + BP + Antibiotic	Topical Combination Therapy** BP + Antibiotic or Retinoid + BP or Retinoid + BP + Antibiotic -or- Oral Antibiotic + Topical Retinoid + BP -or- Oral Antibiotic + Topical Retinoid + BP + Topical Antibiotic	Oral Antibiotic + Topical Combination Therapy** BP + Antibiotic or Retinoid + BP or Retinoid + BP + Antibiotic -or- Oral Isotretinoin
Alternative Treatment	Add Topical Retinoid or BP (if not on already) -or- Consider Alternate Retinoid -or- Consider Topical Dapsone	Consider Alternate Combination Therapy -or- Consider Change in Oral Antibiotic -or- Add Combined Oral Contraceptive or Oral Spironolactone (Females) -or- Consider Oral Isotretinoin	Consider Change in Oral Antibiotic -or- Add Combined Oral Contraceptive or Oral Spironolactone (Females) -or- Consider Oral Isotretinoin

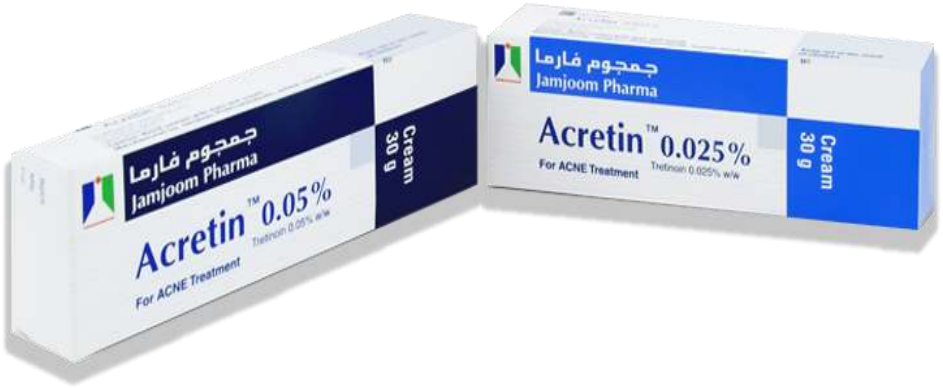
Pharmacologic Therapy

- **Topical Agents :**
- **Retinoids:** Topical retinoids are the foundation of first-line therapy for induction and maintenance regimens in all forms of acne.

- Although success is seen with monotherapy in comedonal acne, using topical retinoids in combination with benzoyl peroxide, topical antibacterial agents, or oral antibacterial agents is preferred for inflammatory acne lesions.

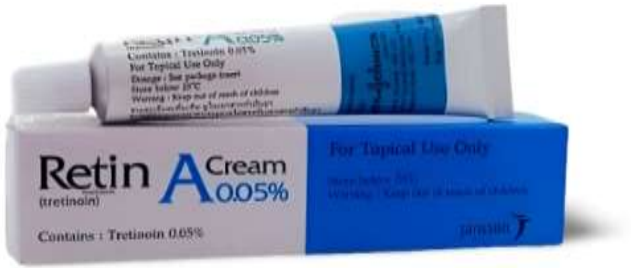
Topical Agents :

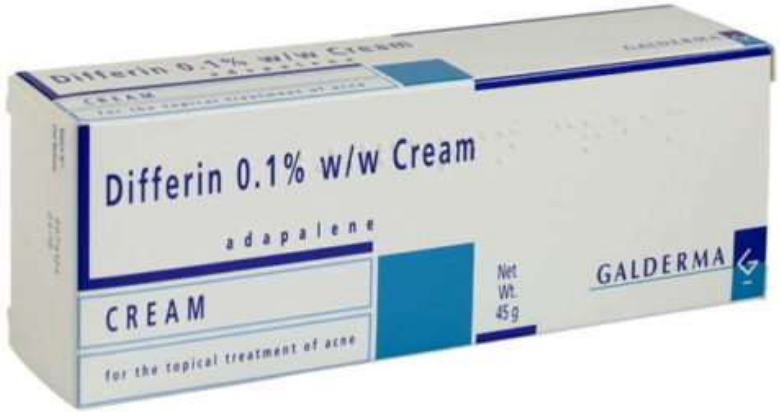
- Available **topical retinoids** include tretinoin, adapalene, tazarotene, and trifarotene.
- **Adapalene**: available by prescription and over the counter, is considered the drug of first choice because it has similar efficacy and a lower incidence of adverse effects.
- Microsphere gel **(Retin-A Micro**) or a polyolprepolymer-2 gel or cream **(Avita)** gradually release the active ingredient over time and may also cause less initial skin discomfort.
- Topical retinoid products with a foam vehicle have a more favorable tolerability profile than comparable gel formulations.


جمجوم فارما
Jamjoom Pharma
Acretin™ 0.05%
Tretinoin 0.05% w/w
For ACNE Treatment
Cream
30 g
جمجوم فارما
Jamjoom Pharma
Acretin™ 0.025%
Tretinoin 0.025% w/w
For ACNE Treatment
Cream
30 g


NDC 0378-6141-44
AVITA
20g
(tretinoin) Cream 0.025%


NDC 0378-6141-44
AVITA
20g
For Topical Use Only
(tretinoin) Cream 0.025%
Rx only


Retin A Cream 0.05%
(tretinoin)
Contains : Tretinoin 0.05%
For Topical Use Only


Differin 0.1% w/w Cream
adapalene
CREAM
for the topical treatment of acne
Net Wt. 45 g
GALDERMA

Topical Agents :

- Topical retinoids should be applied once daily at bedtime, beginning with a low-potency formulation.
- Increased strengths are then initiated according to treatment results and tolerance.
- Patients should be advised that a worsening of acne symptoms generally occurs in the first few weeks of therapy, with lesion improvement occurring in 3 to 4 months.
- The safety and efficacy of topical retinoids in children younger than 12 years of age and in pregnant women is not well established.

Topical Agents :

- Erythema, dryness, scaling, stinging/burning, pruritus, initially may worsen acne (in first 2-4 weeks)
- Possibly teratogenic
- Photosensitivity

Topical Agents :

- **Benzoyl peroxide:** is easy to use and is recommended as an alternative to, or in combination with, topical retinoids, topical antibacterial agents, or oral antibacterial agents in the treatment of acne of all severities.

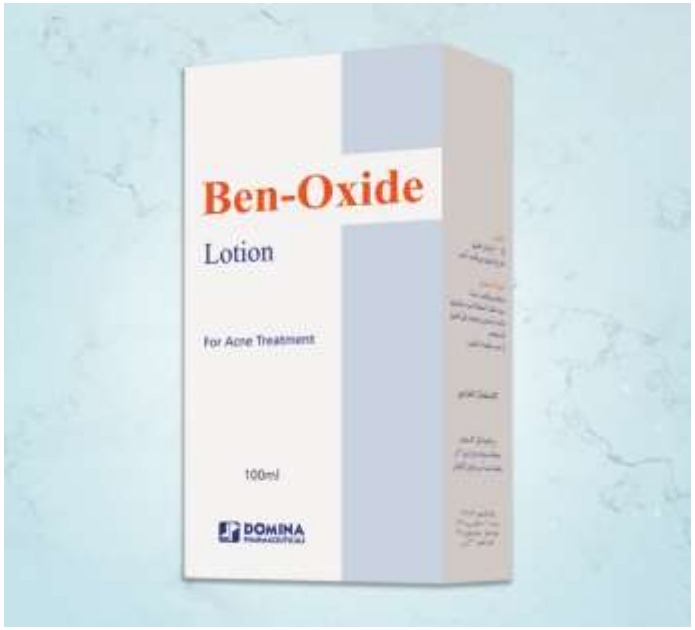
- Benzoyl peroxide is available with or without a prescription and remains the most commonly purchased over-the-counter topical treatment for acne.

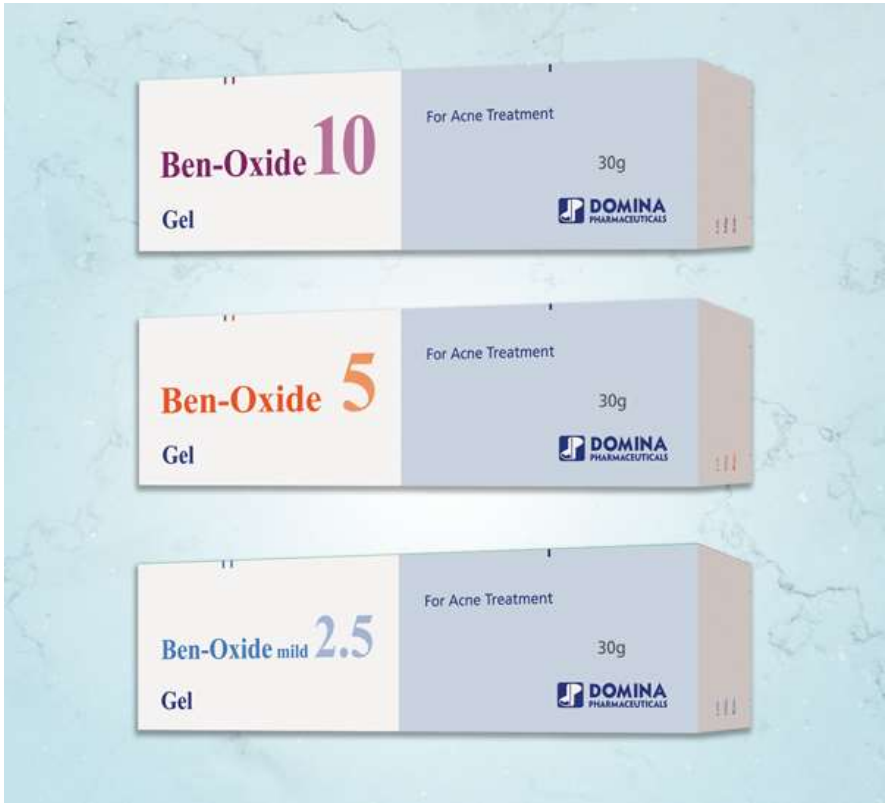
- Some data suggests that lower strengths offer similar efficacy to higher strengths.

- Beginning benzoyl peroxide treatment regimen with the lowest strength and titrating to higher effective strengths over several weeks, if needed, will reduce the incidence of localized adverse effects.

Topical Agents :

- A typical regimen for benzoyl peroxide is to apply the product to clean, dry skin no more than two times a day.
- Gel preparations are the most potent dosage form. Patients with dry or overly sensitive skin should try a cream, lotion, or facial wash first.
- If severe irritation or an allergic reaction develops, benzoyl peroxide should be discontinued.
- Patients should avoid contact with hair and dyed fabric, which may be bleached by benzoyl peroxide products.


Ben-Oxide
Lotion
For Acne Treatment
100ml
DOMINA


Ben-Oxide 10
Gel
For Acne Treatment
30g
DOMINA
Ben-Oxide 5
Gel
For Acne Treatment
30g
DOMINA
Ben-Oxide mild 2.5
Gel
For Acne Treatment
30g
DOMINA

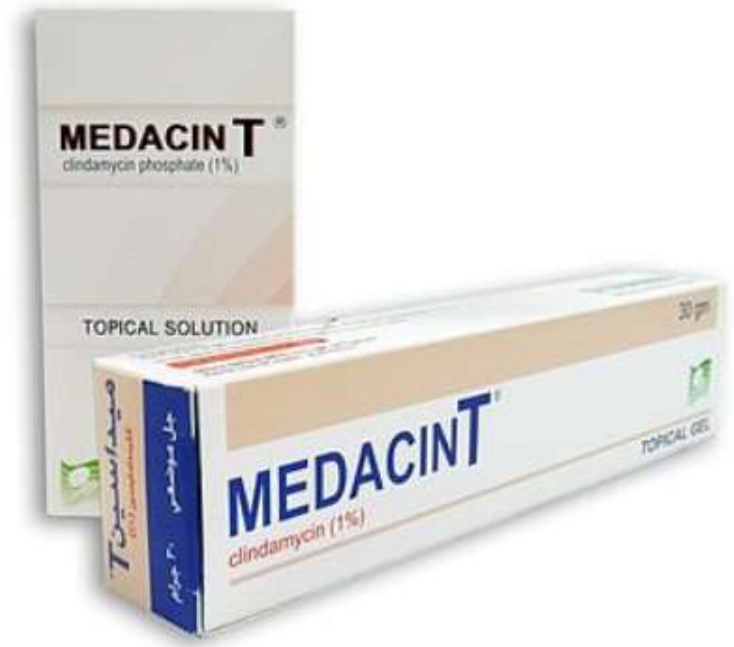
Topical Agents :

- **Antibacterials:** Topical antibacterials directly suppress P. acnes and are first-line agents used in combination with benzoyl peroxide for the treatment of mild-to-moderate inflammatory acne.

- To reduce the likelihood of bacterial resistance, topical antibiotics should be combined with benzoyl peroxide and never be used as monotherapy or as long-term maintenance therapy.

Topical Agents :

- **Clindamycin** is currently the preferred topical antibiotic for acne therapy due to increased bacterial resistance to erythromycin preparations.



Topical Agents :

- Topical **minocycline** was recently approved, but long-term safety and efficacy studies are needed to determine place in therapy

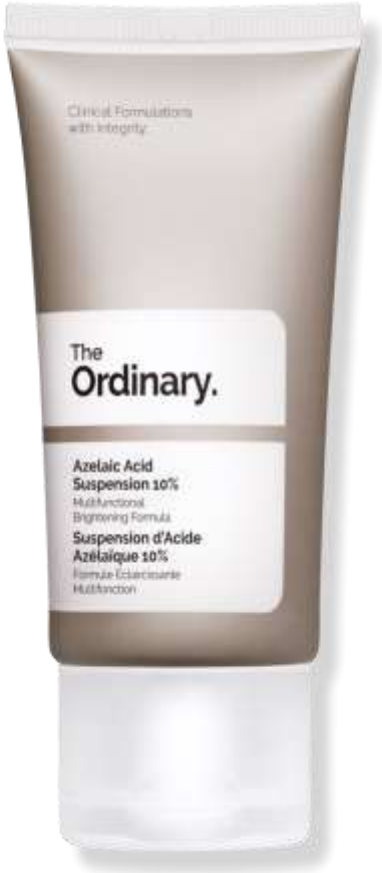
- Applied once or twice daily for 3 months, these agents are available in various formulations and combinations with benzoyl peroxide and topical retinoids.

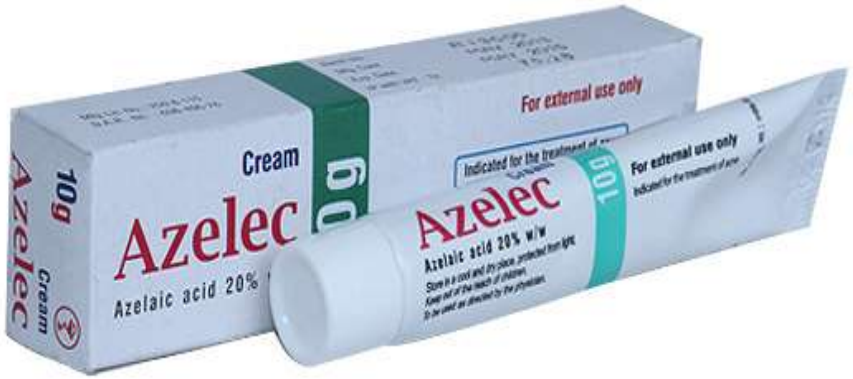
Topical Agents :

- **Azelaic Acid:** With antibacterial and anti-inflammatory properties, and the ability to stabilize keratinization.

- **Azelaic acid** is an effective alternative in the treatment of mild-to-moderate acne in patients who cannot tolerate benzoyl peroxide or topical retinoids.
- It can also even out skin tone and may prove effective in patients who are prone to postinflammatory hyperpigmentation resulting from acne.

- **Azelaic acid 20% cream** should be applied twice daily, with improvement of symptoms seen within 4 weeks.


Clinical Formulations
with Integrity
The
Ordinary.
Azelaic Acid
Suspension 10%
Multifunctional
Brightening Formula
Suspension d'Acide
Azélaïque 10%
Formule Éclaircissante
Multifonction

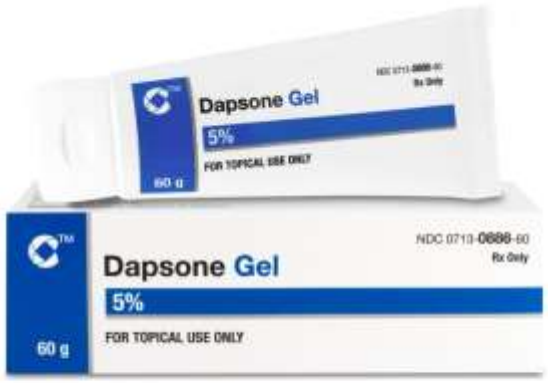

Cream
Azelec
10g
Azelaic acid 20%
For external use only
Azelec
Azelaic acid 20% w/w
For external use only

Topical Agents :

- **Dapsone:** Dapsone gel, a sulfone drug, has antimicrobial and anti-inflammatory properties.
- Dapsone gel may be used as an alternative agent for inflammatory acne as monotherapy or in combination with topical or oral agents.
- Topical dapsone gel has been shown to be more effective in adult females than in males or adolescents.
- Does not have a risk of phototoxicity and Not a preferred agent in pregnancy.
- Dapsone gel that should be applied in a thin layer to the affected areas twice daily.

Topical Agents :

- When administered concomitantly with benzoyl peroxide, topical dapsone may become oxidized, causing orange-brown coloration of the skin which can be brushed or washed off.



Topical Agents :

- **Clascoterone cream:** an androgen receptor inhibitor, decreases sebum production and inflammation that in turn reduces follicular plugging.

- This novel mechanism is the first antiandrogen therapy that can be used in both males and females.

- Clascoterone has demonstrated efficacy and a favorable safety profile in males and nonpregnant females with moderate-severe facial acne.

TOPICAL AGENTS :

- **Keratolytics:** Sulfur, resorcinol, and salicylic acid have limited evidence available to support efficacy but can be used as **second-line therapies** in the treatment of mild-to-moderate acne.

- Although these agents may cause **less skin irritation** than benzoyl peroxide or the topical retinoids, several disadvantages exist.

- **Sulfur** preparations produce an unpleasant odor when applied to the skin, whereas **resorcinol** may cause brown scaling.

- And although rare, the possibility of salicylism exists with continual salicylic acid use.

Oral Agents

- **Antibacterials:** Oral antibiotics are indicated for use in patients with moderate-to-severe acne and forms of inflammatory acne that are resistant to topical therapy.
- When used, oral antibiotics should be **combined** with a topical retinoid and/or benzoyl peroxide.
- The use of oral antibiotics should be limited to short periods of time, ideally 3 to 4 months, or less.
- Assessment of response to oral antibiotics after 6 to 8 weeks of therapy is recommended.

Oral Agents

- After inflammatory lesions have stopped emerging, oral antibiotics should be **discontinued** and **replaced** with topical retinoid or benzoyl peroxide containing maintenance regimens.

- As with topical antibiotics, **oral antibiotics** should **never be used as monotherapy or as long-term maintenance therapy.**

- Additionally, the use of topical antibiotics in combination with oral antibiotics should be avoided due to increased risk of bacterial resistance.

Oral Agents

- **Tetracycline, doxycycline, and minocycline** are the most commonly prescribed oral antibiotics for acne.
- Doxycycline and minocycline are more effective than tetracycline, but neither is superior to each other.
- **Sarecycline**, a recently approved tetracycline, displays a more narrow spectrum of activity designed to target skin bacterium with the potential for fewer gastrointestinal adverse effects.

Oral Agents

- Erythromycin, azithromycin, and trimethoprim (± sulfamethoxazole) are appropriate **second-line agents** for use when patients cannot tolerate or have developed **resistance** to tetracycline or its derivatives.

- Although effectiveness is similar to the tetracyclines, erythromycin use is often limited due to potential adverse outcomes and increased bacterial resistance.

Oral Agents

- **Isotretinoin** works on the four pathogenic factors that contribute to acne development and can produce acne remission rates of up to several years.

- Oral isotretinoin is Food and Drug Administration (FDA) approved for patients with **severe recalcitrant nodular** acne unresponsive to other topical and oral treatment regimens.

- Additional evidence suggests that oral isotretinoin may be useful in **treatment-resistant moderate acne** or acne that is **producing physical scarring or psychosocial distress.**

Oral Agents

- Some expert clinicians suggest that oral isotretinoin therapy may be used as **first-line therapy** in patients with severe nodular acne due to clinical effectiveness, prevention of scarring, and quick improvements in patient quality of life.

- Adverse effects with the use of isotretinoin are frequent and generally dose-related.

Oral Agents

- Isotretinoin is teratogenic and is contraindicated in pregnancy.
- Two negative pregnancy tests prior to initiating therapy and one negative pregnancy test each month thereafter must be obtained .
- These patients must also commit to using **two effective forms of birth control** 1 month prior, during, and at least 1 month after discontinuation of isotretinoin therapy.

Oral Agents

- The dose for treatment of severe acne is titrated as tolerated .
- Treatment with oral isotretinoin should be continued for 4 to 6 months but may be extended for patients with an insufficient response.

Oral Agents

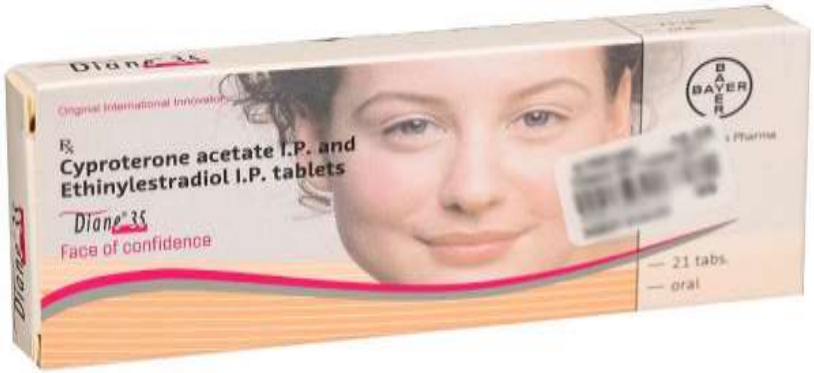
- **Hormonal Agents:** Oral contraceptives and antiandrogens are valuable second-line treatment options for moderate-to-severe inflammatory acne in female patients.

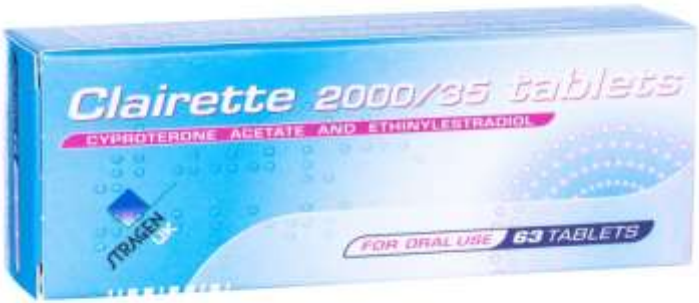
- Hormonal agents primarily work by decreasing androgen production resulting in reduced sebum formation.

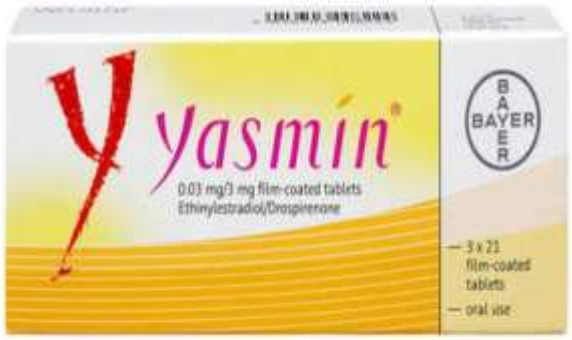
Oral Agents

- Although many contraceptives are effective, agents containing ethinyl estradiol/norgestimate, ethinyl estradiol/norethindrone acetate/ferrous fumarate, and ethinyl estradiol/drospirenone have been FDA approved for the treatment of acne.

- While not FDA approved, spironolactone, at higher doses, is effective for acne through antiandrogenic properties.


Diane 35
Original International Innovation
Cyproterone acetate I.P. and
Ethinylestradiol I.P. tablets
Diane 35
Face of confidence
BAYER
21 tabs.
oral


Clairette 2000/35 tablets
CYPROTERONE ACETATE AND ETHINYLESTRADIOL
FOR ORAL USE
63 TABLETS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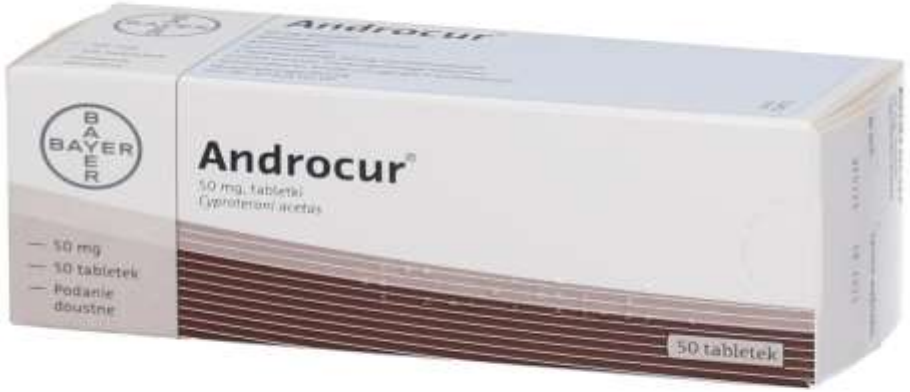
0.03 mg/3 mg film-coated tablets
Ethinylestradiol/Drospirenone
BAYER
3 x 21
film-coated
tablets
oral use


Androcur
BAYER
Androcur
50 mg
50 tabletek
Podanie
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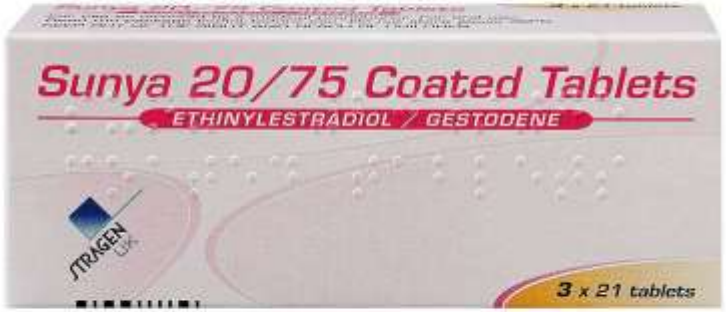
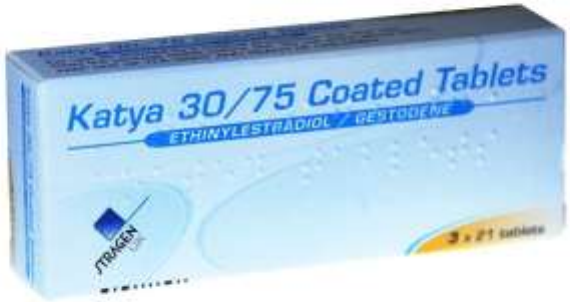
50 tabletek


Sunya 20/75 Coated Tablets
ETHINYLESTRADIOL / GESTODENE
3 x 21 tablets


Katya 30/75 Coated Tablets
ETHINYLESTRADIOL / GESTODENE

Oral Agents

- Other Agents Although use is infrequent, several other agents are available as second- or third-line treatment options for acne when first-line therapies fail :
  - Corticosteroids
  - Chemical peels
  - Surgical extraction
  - Phototherapy/photodynamic therapy
  - Laser treatments

OUTCOME EVALUATION

- Depending on severity, complete resolution of acne lesions may take weeks to months.
- Monitor patients every 4 to 8 weeks during pharmacologic therapy to assess for efficacy.
  - Decreased number of lesions
  - Decreased severity of lesions
  - Relief of pain/irritation
  - Presence of scarring or pigmentation
  - Psychological effects
  - Medication adherence
- If no improvement is reported after 6 weeks of drug therapy or if symptoms have worsened, patients should be reevaluated and a change to an alternative drug regimen may be necessary

Thank you