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Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic Class:
Acne Agents

Overview:
Acne vulgaris is a common condition that affects nearly all adolescents and adults at some time in their lives. Prevalence rates are approximately as high as 75% in teenagers and young adults. Although overall health is not impaired, acne can produce cutaneous and emotional scars. This disease is limited to pilosebaceous follicles of the head and upper trunk because the sebaceous glands in these regions are particularly active. Acne has a complex etiology involving abnormal keratinization, hormonal function, bacterial growth, and immune hypersensitivity.

Several therapeutic options are approved for the treatment of acne vulgaris in the United States. The pathophysiological goal of acne treatment includes the normalization of follicular keratinization and the reductions of interfollicular *Propionibacterium acnes*, inflammation, and sebaceous gland activity. Antibiotics and retinoids are used to treat acne vulgaris both topically and systemically. Topical therapy is recommended for mild-to-moderate non-inflammatory acne. Systemic therapy is reserved for moderate-to-severe acne that does not respond to topical therapy and for acne with high scarring potential.

According to the American Academy of Pediatrics (AAP), topical retinoids are considered an essential part of maintenance therapy and should be the foundation of treatment for most patients with acne. The topical retinoids include adapalene, tazarotene, and tretinoin, and have proven to be highly effective treatments for acne vulgaris. Adapalene and tretinoin are also available in combination products (adapalene/benzoyl peroxide and tretinoin/clindamycin) as topical retinoids have been known to enhance penetration of topical antibiotics and benzoyl peroxide. Adapalene has potent anti-inflammatory and comedolytic properties and may be the best tolerated of the available retinoids. Additionally, tretinoin increases cell turnover in the follicular wall and decreases cohesiveness of cells, leading to extrusion of comedones and inhibition of the formation of new comedones. Tazarotene is indicated for psoriasis as well as acne; however, the exact mechanism of action of tazarotene in the treatment of acne is not defined. Azelaic acid, an alternative topical anti-acne agent, interferes with DNA synthesis in some of the bacteria associated with acne vulgaris. Clinical data suggest some of the aforementioned treatments have similar efficacy and safety profiles; however, some medications have a faster onset of action in the reduction of comedones. With various formulations and concentrations available, therapies may be individualized to specific patient needs while minimizing cutaneous irritation that is often observed with the use of these treatments. Isotretinoin, an oral retinoid, is the treatment of choice for

patients with severe nodular acne that has proven unresponsive to conventional therapy, including systemic antibiotic therapy. Serious side effects, including birth defects, have been associated with isotretinoin; therefore, women taking this medicine must use proper birth control.

Topical antibiotics used in the treatment of acne include benzoyl peroxide, clindamycin, dapsone, erythromycin, and sodium sulfacetamide; however, because antibiotic resistance due to monotherapy is a concern, antibiotic treatment should be discontinued immediately after inflammatory lesions are under good control. The primary mechanism of action of topical antibiotics is the anti-*P. acnes* effect, although they also have some anticomedogenic effect (particularly benzoyl peroxide). Though combination antibiotic therapies with benzoyl peroxide are more effective with less skin irritation, benzoyl peroxide alone is a potent topical antimicrobial and can improve inflammatory acne at low concentrations. Topical antibiotics often used in combination include benzoyl peroxide/clindamycin and benzoyl peroxide/erythromycin. Combining benzoyl peroxide with other antibiotics may minimize antibiotic resistance. Oral antibiotics used include doxycycline and minocycline; these agents should be reserved for patients with moderate-to-severe inflammatory acne.

GENERIC NAME(S)	TRADE NAME	MANUFACTURER	GENERIC
Adapalene	Differin®	Galderma	N
Adapalene/Benzoyl Peroxide	Epiduo™	Galderma	N
Azelaic Acid	Azelex®	Allergan	N
Benzoyl Peroxide/ Clindamycin	Acanya™, BenzaClin®, Duac™	Dermik, Stiefel, Valeant	N
Clindamycin/Tretinoin	Ziana™	Medicis	N
Dapsone	Aczone™	Allergan	N
Isotretinoin (10mg, 20mg, 40 mg)	Amnesteem™, Claravis®, Sotret® (Accutane® discontinued)	Various	Y
Isotretinoin (30 mg)	Claravis®, Sotret®	Barr, Ranbaxy	N
Sodium Sulfacetamide	Klaron®	Dermik	Y
Tretinoin	Retin-A®, Atralin™, Avita®, Altinac®	Various	Y

Notes: Tretinoin 10-mg capsules (Vesanoid®), indicated to treat acute promyelocytic leukemia (APL), are not discussed in this review. Tazarotene (Tazorac®), which is used to treat both acne and psoriasis, is discussed in the Antipsoriatic Therapeutic Class Review.

Summary:

Selection of an acne vulgaris agent for the preferred drug list should be based on the overall efficacy and safety, including the ability of the medication to reduce sebum production, reduce *Propionibacterium acnes*, and normalize the shedding of the skin. In general, acne does not impact overall health, but can produce cutaneous and psychosocial scars. Several alternatives are generically available for the treatment of acne and all should be considered for inclusion on the preferred drug list.