Acne Pharmacotherapy: Relative Effectiveness, Dosing, Adverse Effects, and Evidence

Rank	Drug/Class	Typical Dosing Regimen	Relative Effectiveness	Common Adverse Effects	Key Clinical Evidence
1	Isotretinoin	0.5–1 mg/kg/day orally; cumulative dose 120–150 mg/kg over 5–7 months	**Highest efficacy**; often induces long-term remission	Cheilitis, xerosis, epistaxis, hyperlipidemia, transaminitis, teratogenicity, musculoskeletal symptoms	Multiple RCTs and meta-analyses demonstrate superiority over oral antibiotics and durable remission in severe acne
2	Oral isotretinoin (low-dose regimens)	0.1–0.4 mg/kg/day for longer duration	Very high efficacy with improved tolerability	Same as above, generally less frequent	Increasing evidence supports comparable long-term outcomes with fewer adverse effects in selected patients
3	Combined oral antibiotic + topical retinoid + benzoyl peroxide	Example: Doxycycline 100 mg daily + topical adapalene/BPO	Highly effective for moderate–severe inflammatory acne	GI upset, photosensitivity, candidiasis	Strong guideline-supported evidence; superior to monotherapy
4	Spironolactone (women only)	50–200 mg daily	Comparable to oral antibiotics in many women	Menstrual irregularities, breast tenderness, hyperkalemia (rare in healthy young women)	Recent RCTs (e.g., SAFA trial) demonstrated significant improvement in female acne
5	Combined oral contraceptives (women only)	Standard contraceptive dosing	Moderate-high efficacy for hormonal acne	VTE risk, nausea, breast tenderness	Numerous RCTs show reduction in inflammatory and non-inflammatory lesions
6	Doxycycline	50–100 mg once or twice daily	High efficacy for inflammatory lesions	Photosensitivity, esophagitis, GI upset	Extensive RCT evidence; guideline first-line systemic antibiotic
7	Minocycline	50–100 mg twice daily or ER formulations	Similar efficacy to doxycycline	Vertigo, pigmentation, drug-induced lupus, hepatitis	Comparable efficacy to doxycycline; safety profile often less favorable
8	Sarecycline	1.5 mg/kg once daily	Moderate-high efficacy	GI upset, photosensitivity (less common)	Phase III trials demonstrated significant lesion reduction with narrower antimicrobial spectrum
9	Topical adapalene + benzoyl peroxide	Adapalene 0.1–0.3%/BPO 2.5% once daily	Most effective topical combination	Irritation, erythema, dryness	Large RCTs consistently show superiority to either component alone
10	Tretinoin	0.025–0.1% nightly	Highly effective for comedonal acne	Irritation, peeling, photosensitivity	Decades of evidence supporting comedolytic and preventive effects
11	Adapalene	0.1–0.3% nightly	Similar efficacy to tretinoin, often better tolerated	Dryness, irritation	Strong evidence base; guideline-preferred topical retinoid
12	Trifarotene	50 mcg/g once daily	Effective for facial and truncal acne	Local irritation	Large phase III trials demonstrated efficacy on face and trunk
13	Benzoyl Peroxide	2.5–10% once or twice daily	Moderate efficacy	Irritation, bleaching of fabrics	Strong evidence; reduces antibiotic resistance when combined with antibiotics
14	Topical clindamycin + benzoyl peroxide	Once daily	Moderate efficacy	Irritation, rare diarrhea	Effective but should not be used without BPO due to resistance concerns
15	Clascoterone	1% cream twice daily	Moderate efficacy	Mild local irritation	Phase III studies show significant improvement in inflammatory lesions
16	Azelaic Acid	15–20% once or twice daily	Mild-moderate efficacy	Burning, stinging	Useful in acne with post-inflammatory hyperpigmentation

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17	Dapsone	5% gel BID or 7.5% gel daily	Mild-moderate efficacy	Dryness, erythema	Particularly beneficial in inflammatory acne, especially adult women
18	Oral macrolides (e.g., Azithromycin)	Various pulse regimens	Lower efficacy than tetracyclines	GI upset, QT prolongation	Reserved when tetracyclines are contraindicated
19	Trimethoprim-Sulfamethoxazole	160/800 mg BID	Effective but rarely used	SJS/TEN, marrow suppression	Reserved for refractory cases due to safety concerns

Evidence-Based Hierarchy by Acne Type

Acne Type	Most Effective Treatments
Comedonal acne	Topical retinoids > adapalene/BPO > azelaic acid
Mild inflammatory acne	Adapalene/BPO > BPO + topical antibiotic
Moderate inflammatory acne	Oral doxycycline + topical retinoid/BPO
Female hormonal acne	Spironolactone ± oral contraceptive
Severe nodulocystic acne	Isotretinoin
Truncal acne	Isotretinoin, trifarotene, oral tetracyclines
Acne with PIH	Azelaic acid, retinoids

Current Guideline Pearls

Recommendation	Rationale
Avoid oral antibiotic monotherapy	Resistance prevention
Limit oral antibiotics to ~3–4 months when possible	Stewardship
Combine antibiotics with benzoyl peroxide	Reduces *Cutibacterium acnes* resistance
Retinoids are foundational therapy	Treat existing and prevent new lesions
Isotretinoin is first-line for severe nodulocystic acne	Highest remission rates
Consider spironolactone early in women	Reduces antibiotic exposure
Monitor pregnancy risk with isotretinoin	Highly teratogenic