



DERMATOLOGY EXPRESS REPORT™ FAX

Weight-based Dosing of a Novel Antibiotic for Moderate-to-Severe Acne Vulgaris—Redefining Minocycline

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Expert Commentary

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The recent approval of minocycline extended-release tablets (Solodyn) by the Food and Drug Administration (FDA) offers a significant advancement for treating moderate-to-severe acne vulgaris. Minocycline extended-release tablets were formulated to provide optimal efficacy in treating moderate-to-severe acne vulgaris while potentially minimizing the vestibular adverse effects that have been associated with minocycline administration.¹ Unlike available immediate-release minocycline formulations, minocycline extended-release tablets offer a unique pharmacokinetic delivery that, when dosed on a 1 mg/kg weight-basis,² provides the lowest effective dose of minocycline for treating moderate-to-severe acne vulgaris while minimizing potential adverse events. In addition, minocycline extended-release tablets are administered once daily, thus offering the potential to enhance patient compliance. Minocycline extended-release tablets are indicated for the treatment of inflammatory lesions of non-nodular moderate-to-severe acne vulgaris and represent the first oral systemic antibiotic approved by the FDA as first-line therapy for the treatment of acne.²

Acne affects between 40 and 50 million individuals in the United States.³ Although acne is typically associated with adolescence, affecting 79% to 95% of 16- to 18-year-old adolescents,⁴⁻⁶ acne may also affect children and adults. In 10- to 12-year-old children, acne affects from 28% to 61% of individuals.⁴⁻⁶ In adults older than 25 years, 54% of women and 40% of men exhibit some degree of facial acne, with symptoms persisting into middle age.⁷

As the severity of acne may range from mild to severe, many topical and systemic therapies have been approved by the FDA for treating acne including benzoyl peroxide, topical retinoids (tretinoin, adapalene, tazarotene), topical antibiotic agents (erythromycin, clindamycin), systemic antibiotic agents (tetracycline, doxycycline,

minocycline as adjunctive therapy), systemic retinoids (isotretinoin), and hormonal therapy (oral contraceptives). Systemic antibiotic therapy is typically reserved for the treatment of moderate-to-severe inflammatory acne, or acne considered emotionally burdensome for the patient for psychological or social reasons.⁸

For decades, physicians have used erythromycin, tetracycline, doxycycline, and minocycline to treat acne vulgaris. Compared with doxycycline and tetracycline, minocycline has been associated with the greatest log reduction of *Propionibacterium acnes* (*P. acnes*), most rapid onset of effect, and greatest residual reduction in *P. acnes*.⁹ Moreover, minocycline exhibits the lowest prevalence of *P. acnes* resistance compared with doxycycline, erythromycin, and tetracycline.¹⁰ Increasing resistance of *P. acnes* to oral antibiotics (eg, erythromycin, tetracycline) has been correlated with acne treatment failure.¹¹⁻¹³ Doxycycline may be limited by dose-related phototoxicity in some patients,¹⁴ and minocycline may be associated with vestibular adverse events (eg, vertigo, dizziness, headache) and tissue pigmentation.¹⁵

This *Dermatology Express Report Fax*™ reviews the efficacy data of the newly approved minocycline extended-release tablets. A follow-up *Dermatology Express Report Fax*,™ which will be distributed in the near future, will review the safety and tolerability profiles of minocycline extended-release tablets.

Weight-based Dosing of Minocycline

The efficacy of once-daily minocycline extended-release tablets was evaluated in 2 multicenter, randomized, double-blind, placebo-controlled, 12-week phase 3 studies.² A total of 924 subjects (age ≥12 years) with non-nodular moderate-to-severe acne vulgaris were randomized to 1 mg/kg minocycline extended-release tablets or placebo for 12 weeks. The primary efficacy end points included the mean percent change in inflammatory lesion counts from baseline to 12 weeks and the percentage of subjects with an Evaluator's Global Severity Assessment (EGSA) of "clear" or "almost clear" (dichotomized as "success" or "failure") at 12 weeks. Patients were evaluated at 4, 8, and 12 weeks.

Table 1. Efficacy Results at 12 Weeks for Minocycline Extended-release Tablets and Placebo.

	Minocycline Extended-release (1 mg/kg) (N = 300)	Placebo (N = 151)	P-value	Minocycline Extended-release (1 mg/kg) (N = 315)	Placebo (N = 158)	P-value
Mean % Improvement in Inflammatory Lesions	43.1%	31.7%	.001	45.8%	30.8%	<.001
% of Subjects "Clear" or "Almost Clear" on EGSA	17.3%	7.9%	.006*	15.9%	9.5%	.018*

* P-value determined from Day 84 data only from Cochran-Mantel-Haenszel test. EGSA = Evaluator's Global Severity Assessment.

Table 2. Recommended Dosing of Minocycline Extended-release Tablets.

Patient's Weight (lbs)	Patient's Weight (kg)	Tablet Strength (mg)	Actual Dose (mg/kg)
99 – 131	45 – 59	45	1.00 – 0.76
132 – 199	60 – 90	90	1.50 – 1.00
200 – 300	90 – 136	135	1.48 – 0.99

At the end of 12 weeks, subjects treated with minocycline extended-release tablets demonstrated significantly greater reduction in the number of inflammatory lesion counts from baseline compared with placebo (Table 1). In addition, subjects treated with minocycline extended-release tablets significantly improved in the overall appearance in their acne as judged by the EGSA (Table 1). Although all subjects had an EGSA of moderate or severe at baseline, the majority of subjects treated with minocycline extended-release tablets were graded as "mild," "almost clear," or "clear" (56.8% minocycline vs 42.0% placebo for Study 1; 52.4% minocycline vs 40.2% placebo for Study 2) by the end of the 12-week period.

The results of these studies suggest that the unique pharmacokinetic delivery of minocycline extended-release tablets allows for once-daily administration of minocycline dosed at 1 mg/kg and that minocycline extended-release tablets are clinically effective in reducing the inflammatory lesions associated with moderate-to-severe acne vulgaris.

Moreover, the results of dose-ranging studies revealed no additional therapeutic benefit of dosing minocycline extended-release tablets at 2 mg/kg or 3 mg/kg.² Based on clinical studies, the recommended dosing of minocycline extended-release tablets is illustrated in Table 2.

Conclusion

Minocycline extended-release tablets represent the first oral systemic antibiotic approved by the FDA as first-line therapy for the treatment of inflammatory lesions of non-nodular moderate-to-severe acne vulgaris. In addition, minocycline extended-release tablets may offer advantages over other oral antibiotic agents, potentially fewer vestibular side effects compared with immediate-release minocycline (discussion in next report) and convenient once-daily administration that may enhance patient compliance. Unlike immediate-release minocycline formulations, minocycline extended-release tablets offer a unique pharmacokinetic delivery of minocycline that, when dosed at 1mg/kg, provides the lowest possible effective dose of minocycline for treating moderate-to-severe acne vulgaris while minimizing potential adverse events. Future head-to-head comparative clinical trials of minocycline extended-release tablets are planned to fully assess its potential benefits against other minocycline formulations.

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