

# Oral Isotretinoin for Acne in the US Military: How Accelerated Courses and Teledermatology Can Minimize the Duty-Limiting Impacts of Treatment

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## PRACTICE POINTS

- Acne is a common skin disease with a high prevalence in the active-duty US Military population.
- Oral isotretinoin is a commonly utilized acne medication that can limit the ability for military service members to deploy and is considered disqualifying for some special duty assignments.
- High daily- and cumulative-dose oral isotretinoin therapy as well as teledermatology can minimize the duty-limiting impact of isotretinoin therapy for military service members.

Acne vulgaris is a common dermatologic disease affecting 40 to 50 million individuals in the United States each year. It has a peak incidence in adolescents and young adults; however, for some patients, the disease may persist well into adulthood. These incidence peaks coincide with the age demographic of a large proportion of military service members. Although there are many approaches to treating acne, active-duty service members and military dermatologists must weigh multiple additional challenging factors when selecting a therapy. Untreated acne itself may hinder a military service member's ability to perform, and many of the available therapies also can limit their medical readiness or fitness for full duty. Herein, we review operational restrictions to acne-specific therapeutics and discuss an accelerated course of oral isotretinoin as a safe and effective option for military service members bound by duty restrictions and

operational timelines. In addition, we explore the role of teledermatology for the treatment of acne in military service members.

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Acne vulgaris is an extremely common dermatologic disease affecting 40 to 50 million individuals in the United States each year, with a prevalence of 85% in adolescents and young adults aged 12 to 24 years. For some patients, the disease may persist well into adulthood, affecting 8% of adults aged 25 and 34 years.<sup>1</sup> Acne negatively impacts patients' quality of life and productivity, with an estimated direct and indirect cost of over \$3 billion per year.<sup>2</sup>

Oral isotretinoin, a vitamin A derivative, is approved by the US Food and Drug Administration for the treatment of severe nodulocystic acne. Isotretinoin reduces the size and secretions of sebaceous glands, inhibits growth and resulting inflammation of *Cutibacterium acnes*, and normalizes the differentiation of follicular keratinocytes, resulting in permanent changes in the pathogenesis of acne that may lead to remission.<sup>3</sup> The use of oral isotretinoin in the active-duty US Military population may cause service members to be nondeployable or limit their ability to function in special roles (eg, pilot, submariner).<sup>4</sup> Treatment regimens that minimize the course duration of

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isotretinoin and reduce the risk for relapse that requires a retreat of isotretinoin may, in turn, increase a service member's readiness, deployment availability, and ability to perform unique occupational roles.

Additionally, teledermatology has been increasingly utilized to maintain treatment continuity for patients on isotretinoin during the COVID-19 pandemic.<sup>5</sup> Application of this technology in the military also may be used to facilitate timely isotretinoin treatment regimens in active-duty service members to minimize course duration and increase readiness.

In this article, we discuss an accelerated course of oral isotretinoin as a safe and effective option for military service members bound by duty restrictions and operational timelines and explore the role of teledermatology for the treatment of acne in military service members.

### Isotretinoin for Acne

Isotretinoin typically is initiated at a dosage of 0.5 mg/kg daily, increasing to 1 mg/kg daily with a goal cumulative dose between 120 and 150 mg/kg. Relapse may occur after completing a treatment course and is associated with cumulative dosing less than 120 mg/kg.<sup>6</sup> The average duration of acne treatment with oral isotretinoin is approximately 6 months.<sup>7</sup> At therapeutic doses, nearly all patients experience side effects, most commonly dryness and desquamation of the skin and mucous membranes, as well as possible involvement of the lips, eyes, and nose. Notable extracutaneous side effects include headache, visual disturbances at night, idiopathic intracranial hypertension, and myalgia. Serum cholesterol, triglycerides, and transaminases may be increased in patients taking isotretinoin, which requires routine monitoring using serum lipid profiles and liver function studies. A potential association between isotretinoin and inflammatory bowel disease and changes in mood have been reported, but current data do not suggest an evidence-based link.<sup>6,8</sup> Isotretinoin is a potent teratogen, and in the United States, all patients are required to enroll in iPLEDGE, a US Food and Drug Administration–approved pregnancy prevention program that monitors prescribing and dispensing of the medication. For patients who can become pregnant, iPLEDGE requires use of 2 forms of contraception as well as monthly pregnancy tests prior to dispensing the medication.

### Acne in Military Service Members

Acne is exceedingly common in the active-duty military population. In 2018, more than 40% of soldiers, sailors, airmen, and marines were 25 years or younger, and 75% of all US service members were 35 years or younger, corresponding to acne peak incidences.<sup>1,9</sup> Management of acne in this population requires unique treatment considerations due to distinctive occupational requirements of and hazards faced by military personnel. Use of personal protective equipment, including gas masks, safety restraints, parachute rigging, and flak jackets, may

be limiting in individuals with moderate to severe acne.<sup>10</sup> For example, severe nodulocystic acne on the chin and jawline can interfere with proper wear of the chin strap on a Kevlar helmet. The severity of acne often necessitates the use of oral isotretinoin therapy, which is considered disqualifying for many special military assignments, including submarine duty, nuclear field duty, and diving duty.<sup>11</sup> In military aviation communities, oral isotretinoin requires grounding for the duration of therapy plus 3 months after cessation. Slit-lamp examination, triglycerides, and transaminase levels must be normal prior to returning to unrestricted duty.<sup>12</sup> Furthermore, use of oral isotretinoin may limit overseas assignments or deployment eligibility.<sup>4</sup>

The high prevalence of acne and the operationally limiting consequences of isotretinoin therapy present a unique challenge for dermatologists treating military personnel. The average duration of isotretinoin treatment is approximately 6 months,<sup>7</sup> which represents a considerable amount of time during an average 4-year enlistment contract. Therapeutic treatment strategies that (1) reduce the duration of oral isotretinoin therapy, (2) reduce the risk for relapse, and (3) increase medication compliance can reduce the operational impact of this acne treatment. Such treatment strategies are discussed below.

### High-Dose Isotretinoin

An optimal isotretinoin dosing regimen would achieve swift resolution of acne lesions and reduce the overall relapse rate requiring retreat of isotretinoin, thereby minimizing the operational- and duty-limiting impacts of the medication. Cyrulnik et al<sup>13</sup> studied treatment outcomes of high-dose isotretinoin for acne vulgaris using a mean dosage of 1.6 mg/kg daily with an average cumulative dosage of 290 mg/kg. They demonstrated 100% clearance of lesions over 6 months, with a 12.5% relapse rate at 3 years. Aside from an increased rate of elevated transaminases, incidence of adverse effects and laboratory abnormalities were not significantly increased compared to conventional dosing regimens.<sup>13</sup> The goal cumulative dosing of 120 to 150 mg/kg can be achieved 1 to 2 months earlier using a dosage of 1.6 mg/kg daily vs a conventional dosage of 1 mg/kg daily.

It has been hypothesized that higher cumulative doses of oral isotretinoin reduce the risk for relapse of acne and retreat of oral isotretinoin.<sup>14</sup> Blasiak et al<sup>15</sup> studied relapse and retreat of oral isotretinoin in acne patients who received cumulative dosing higher or lower than 220 mg/kg. A clinically but not statistically significant reduced relapse rate was observed in the cohort that received cumulative dosing higher than 220 mg/kg. No statistically significant difference in rates of adverse events was observed aside from an increase in retinoid dermatitis in the cohort that received cumulative dosing higher than 220 mg/kg. Higher but not statistically significant rates of adverse events were seen in the group that received dosing higher than 220 mg/kg.<sup>15</sup> Cumulative

doses of oral isotretinoin higher than the 120 to 150 mg/kg range may decrease the risk for acne relapse and the need for an additional course of oral isotretinoin, which would reduce a service member's total time away from deployment and full duty.

Relapse requiring a retreat of oral isotretinoin not only increases the operational cost of acne treatment but also considerably increases the monetary cost to the health care system. In a cost-analysis model, cumulative doses of oral isotretinoin higher than 230 mg/kg have a decreased overall cost compared to traditional cumulative dosing of less than 150 mg/kg due to the cost of relapse.<sup>16</sup>

Limitations of high daily and cumulative dosing regimens of oral isotretinoin are chiefly the dose-dependent rate of adverse effects. Low-dose regimens are associated with a reduced risk of isotretinoin-related side effects.<sup>6,17</sup> Acute acne flares may be seen following initial administration of oral isotretinoin and are aggravated by increases in dosage.<sup>18</sup> Isotretinoin-induced acne fulminans is a rare but devastating complication observed with high initial doses of oral isotretinoin in patients with severe acne.<sup>19</sup> The risks and benefits of high daily and cumulatively dosed isotretinoin must be carefully considered in patients with severe acne.

### Teledermatology: A Force for Readiness

The COVID-19 pandemic drastically changed the dermatology practice landscape with recommendations to cancel all elective outpatient visits in favor of teledermatology encounters.<sup>20</sup> This decreased access to care, which resulted in an increase in drug interruption for dermatology patients, including patients on oral isotretinoin.<sup>21</sup> Teledermatology has been increasingly utilized to maintain continuity of care for the management of patients taking isotretinoin.<sup>5</sup> Routine utilization of teledermatology evaluation in military practices could expedite care, decrease patient travel time, and allow for in-clinic visits to be utilized for higher-acuity concerns.<sup>22</sup>

The use of teledermatology for uncomplicated oral isotretinoin management has the potential to increase medication compliance and decrease the amount of travel time for active-duty service members; for example, consider a military dermatology practice based in San Diego, California, that accepts referrals from military bases 3 hours away by car. After an initial consultation for consideration and initiation of oral isotretinoin, teledermatology appointments can save the active-duty service member 3 hours of travel time for each follow-up visit per month. This ultimately increases operational productivity, reduces barriers to accessing care, and improves patient satisfaction.<sup>23</sup>

Although military personnel usually are located at duty stations for 2 to 4 years, training exercises and military vocational schools often temporarily take personnel away from their home station. These temporary-duty assignments have the potential to interrupt medical follow-up appointments and may cause delays in treatment

for individuals who miss monthly isotretinoin visits. When deemed appropriate by the prescribing dermatologist, teledermatology allows for increased continuity of care for active-duty service members and maintenance of a therapeutic isotretinoin course despite temporary geographic displacement.

By facilitating regular follow-up appointments, teledermatology can minimize the amount of time an active-duty service member is on a course of oral isotretinoin, thereby reducing the operational and duty-limiting implications of the medication.

### Final Thoughts

Acne is a common dermatologic concern within the active-duty military population. Oral isotretinoin is indicated for treatment-resistant moderate or severe acne; however, it limits the ability of service members to deploy and is disqualifying for special military assignments. High daily- and cumulative-dose isotretinoin treatment strategies can reduce the duration of therapy and may be associated with a decrease in acne relapse and the need for retreat. Teledermatology can increase access to care and facilitate the completion of oral isotretinoin courses in a timely manner. These treatment strategies may help mitigate the duty-limiting impact of oral isotretinoin therapy in military service members.

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