

# Accutane (isotretinoin) and psychiatric adverse effects

**Reason for posting:** Acne vulgaris is common and can lead to long-lasting physical and emotional scars.<sup>1</sup> Accutane (isotretinoin) is effective for severe forms of the disease.<sup>1,2</sup> Prescriptions of isotretinoin have more than doubled in the last decade,<sup>3</sup> and apart from Accutane's well-publicized teratogenic effects,<sup>4</sup> the drug's potential psychiatric adverse effects<sup>5</sup> have caused concern.

The drug ranks in the top 10 of the US Food and Drug Administration's (FDA's) database of drugs associated with reports of depression and suicide attempts.<sup>5</sup> In Canada, of the 222 cases of adverse events reported to Health Canada since the drug was first marketed in 1983, 56 (25%) involved psychiatric adverse events, including depression and suicidal ideation (Ryan Baker, Health Canada: personal communication, Nov. 22, 2002). A warning of a possible link with depression and suicide was issued in 2001.<sup>6</sup> Recently, the FDA warned that people taking Accutane may also experience aggressive and violent behaviours.<sup>7</sup>

**The drug:** Isotretinoin, a vitamin A derivative, is approved for patients with severe acne not responding to standard therapy, including systemic antibiotic therapy.<sup>8</sup> The drug may act through retinoic acid receptors to cause a variety of effects, including a reversal of androgenic effects on sebaceous glands.<sup>9</sup> Common adverse effects include inflammation of the lips (cheilitis), dry and brittle skin, hair loss and ophthalmologic effects (e.g., dry

eyes, corneal opacifications and night blindness).<sup>8,9</sup> The drug is highly teratogenic, and sexually active women should use at least 2 reliable forms of contraception beginning a month before starting the drug and continuing for a month after stopping it.<sup>8</sup> Myalgias, headache, fatigue and bone changes (hyperostosis) occasionally occur, and cases in which patients experience persistent headaches, nausea, vomiting or blurred vision should be investigated for pseudotumour cerebri.<sup>8</sup> Hypertriglyceridemia is common,<sup>10</sup> and patients also need to be monitored for hepatotoxic effects.

Isotretinoin's link to psychiatric adverse events is controversial. Depressive disorders are common in the population, and up to 5.6% of patients with mild to moderate acne may have pre-existing suicidal ideations.<sup>11</sup> Furthermore, improvement of a person's acne can often reduce symptoms of anxiety and depression,<sup>12</sup> and in one study, involving 20 895 acne patients registered in databases in Saskatchewan and the United Kingdom, isotretinoin users were no more likely than those taking antibiotics for their condition to have depression or commit suicide.<sup>13</sup>

**What to do:** Most acne can be effectively managed with topical agents, oral antibiotic therapy or oral contraceptive therapy.<sup>2</sup> Isotretinoin should be reserved for more severe, recalcitrant, scarring acne. It is not yet clear whether previous psychiatric symptoms increase

a patient's risk of psychiatric adverse events while taking isotretinoin, but the patient's mental state should be regularly monitored before and during treatment.<sup>8</sup> Patients should be warned that, while taking the drug, they may experience symptoms of depression, aggression or suicidal ideation and that they should report these to their physician immediately if they occur.<sup>5</sup> Although discontinuation of the drug may reverse some psychiatric adverse effects, further psychiatric intervention is sometimes required.

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