

**Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide
for Prescribers of Accutane® (isotretinoin)**

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Psychiatric Risk Management—Accutane

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WARNINGS

***Psychiatric Disorders:* Accutane may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts and suicide. Discontinuation of Accutane therapy may be insufficient; further evaluation may be necessary. No mechanism of action has been established for these events (see ADVERSE REACTIONS: *Psychiatric*).**

***Pseudotumor Cerebri:* Accutane use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Concomitant treatment with tetracyclines should therefore be avoided. Early signs and symptoms of pseudotumor cerebri include papilledema, headache, nausea and vomiting, and visual disturbances. Patients with these symptoms should be screened for papilledema and, if present, they should be told**

to discontinue Accutane immediately and be referred to a neurologist for further diagnosis and care (see ADVERSE REACTIONS: *Neurological*)

ADVERSE REACTIONS

Neurological: pseudotumor cerebri (see WARNINGS: *Pseudotumor Cerebri*), dizziness, drowsiness, headache, insomnia, lethargy, malaise, nervousness, paresthesias, seizures, stroke, syncope, weakness

Psychiatric: suicidal ideation, suicide attempts, suicide, depression, psychosis (see WARNINGS: *Psychiatric Disorders*), emotional instability

Of the patients reporting depression, some reported that the depression subsided with discontinuation of therapy and recurred with reinstatement of therapy.

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Reporting Adverse Events

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Specific information about adverse events that occur during Accutane therapy may be reported either to Roche Medical Services at 1-800-526-6367 or to the Food and Drug Administration MedWatch Program at 1-800-FDA-1088.

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Accutane[®] (isotretinoin)

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Accutane is a retinoid related to vitamin A. Patients should be advised against taking vitamin supplements containing vitamin A to avoid additive toxic effects.

Recognizing Psychiatric Disorders in Adolescents and Young Adults

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Introduction

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Mental health problems are underdiagnosed and undertreated.¹ ((Brody 2000))

Dermatologists and other Accutane prescribers often see patients who are otherwise healthy, and they may be among the only professionals who have opportunities to evaluate patients' mental health. Healthcare providers who recognize the signs and symptoms of psychiatric illness and respond appropriately can improve, and perhaps even save, their patients' lives.

Accutane may cause depression, and more rarely other psychiatric disorders. In some cases, the psychiatric illness is severe and there have been suicide attempts and suicides. Although causality has not been established for these reports, awareness of signs and symptoms may save your patient's life. This brochure provides an overview of depression. The goal of this brochure is to help you identify when a psychiatric referral may be appropriate for your patients.

You and your staff may feel uncomfortable evaluating your patients' mental health status. It is often difficult to distinguish clinical depression from other responses. It may also be difficult to decide whether erratic behavior may warrant psychiatric evaluation, especially if

that behavior seems to be age-appropriate in a teenager. However, as with any specialized problem, you may identify patients who seem to need more than dermatologic care, and you may need to refer them to a specialist. Knowing when to make a referral for a patient who may be at psychiatric risk can make a major difference in the patient's life—in extreme cases, it can mean the difference between life and death.

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Depression

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Depression and suicidal tendencies are two important psychiatric conditions that may be observed in dermatology and family practice settings. This brochure provides an overview of depression, because depression is the most commonly reported psychiatric adverse event in patients taking Accutane, and is also a well-established risk factor for suicidal behavior.

Depression is characterized by symptoms including intense, persistent sadness; anxiety; loss of pleasure from usual activities; and loss of energy.² ((NIMH Depression Web site 2001)) These feelings can be normal responses to a negative life event, but clinical depression is either not triggered by such an event or is disproportional to the trigger.³ ((Berkow 2001))

Depression can be episodic. According to the National Comorbidity Survey, 17% of Americans will experience depression at some point during their lives and 5% are depressed in any given month.^{4,5} ((Kessler 1994; Blazer 1994)) Several epidemiological studies

reported that up to 8.3% of adolescents in the United States suffer from depression.⁶ ((NIMH Depression Fact Sheet 9/2000 p.1))

Depression can take several forms; three of the most common are dysthymia, major depression, and bipolar disorder.² ((NIMH Depression Web site 2001)) These three disorders are characterized by various combinations of the symptoms listed in **Table 1**. Not every patient exhibits all depressive symptoms. Some patients, especially adolescents, may display irritability instead of sadness.

((table)) **TABLE 1.** Symptoms of Depression² ((NIMH Depression Web site 2001))

- Persistent sadness, anxiety or feeling of emptiness
- Feelings of guilt, worthlessness or helplessness
- Loss of pleasure from activities that were once enjoyable
- Loss of energy
- Difficulty concentrating or making decisions
- Change in sleep pattern
- Change in appetite
- Physical problems that do not respond to treatment
- Restlessness
- Irritability

Adapted from National Institute of Mental Health. Depression. Available at:

www.nimh.nih.gov/publicat/depression.cfm. Accessed 4/24/01.

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Dysthymia has characteristics similar to those of major depression but is not as disabling.

People with dysthymia often function adequately but not at previous wellness levels, and are at risk for episodes of major depression. In major depression, a combination of symptoms prevents the patient from working, studying and/or engaging in normal activities. In bipolar disorder, the patient alternates between periods of depression and episodes of mania (euphoric feelings).² ((NIMH Depression Web site 2001))

((Sidebar or table))

Symptoms of Mania (NIMH)*

- Excessive elation
- Increased energy and sexual desire
- Decreased need for sleep
- Racing thoughts and impaired judgment
- Increased talking
- Inappropriate behavior

*National Institute of Mental Health

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Suicide

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Suicide accounts for more than 30,000 American deaths each year. It is the third leading cause of death (after accidents and homicide) among people aged 15 to 24, which makes it responsible for more deaths in this age group than any physical illness.^{7,8} ((Zaph 2001; NIMH Suicide Web site 2001)) Healthcare providers often miss the warning signs because patients may hide suicidal intent very successfully. In fact, 60% of people who commit suicide had seen a physician within 1 month of their deaths.⁹ ((Jacobs 1998)) Suicidal tendencies rarely arise spontaneously; 93% of people who commit suicide suffer from depression, schizophrenia and/or substance abuse.¹⁰ ((Goodwin 1992))

Up to 60% of adolescents and young adults think about suicide at some point,⁷ ((Zaph 2001)) but fortunately these thoughts usually pass. Few people who have suicidal thoughts make the attempt, and most attempts at suicide are unsuccessful.⁸ ((NIMH Suicide Web site 2001))

An analysis of completed suicides showed the following common characteristics¹¹ ((National Depression Screening Day)):

- Ideation (thoughts of death or suicide)
- Suicidal intent
- Plan (specific time, place and method)

- Means (eg, a firearm in the house or a supply of drugs)

Women are twice as likely as men to attempt suicide, but men are four times more likely to be successful. Women usually use means from which they may be rescued, such as a drug overdose,¹² ((Screening for suicide risk Web site 2001)) whereas men tend to use firearms or automobiles. Firearms are used in 58% of all completed suicides.⁸ ((NIMH Suicide Web site 2001))

Despite a patient's attempt to hide suicidal thoughts, he or she may send deliberate warning signals, some of which can be explicit.² ((NIMH Depression Web site 2001)) **Every mention or discussion of "killing myself" should be treated with utmost seriousness.**

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Causes of Depression

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The causes of depression are often multi-factorial and may include:

- Genetic predisposition² ((NIMH Depression Web site 2001))
- Stress at home, work or school² ((NIMH Depression Web site 2001))
- Loss of a parent or loved one¹³ ((Wells 1985))
- Alcohol or substance abuse⁹ ((Jacobs 1998))
- Breakup of a romantic relationship¹⁴ ((Monroe 1999))

- Medications (American Psychiatric Association [DIAGNOSTIC AND STATISTICAL MANUAL - TEXT REVISION \(DSM-IV-TR™, 2000\)](#)¹⁵)

Evaluating and Referring Patients for Psychiatric Disturbance

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Although only 5% of the population is depressed at any given time, the incidence has been found to be closer to 15% to 20% in primary care settings.¹¹ ((National Depression Screening Day)) Given that 1 in 5 patients who come to your office may have some degree of depression, a few questions can identify patients who may be at risk.

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Asking the Right Questions

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While taking a history, the prescriber should suspect the likelihood of depression if the patient has symptoms such as ⁶ (NIMH Depression Fact Sheet):

- Persistent sad or irritable mood
- Loss of interest in activities once enjoyed

- Significant change in appetite or body weight
- Difficulty sleeping or oversleeping
- Psychomotor agitation or retardation
- Loss of energy
- Feelings of worthlessness or inappropriate guilt
- Difficulty concentrating
- Recurrent thoughts of death or suicide

In children and young adolescents, other signs to look for include:

- Frequent vague, non-specific physical complaints such as headaches, muscle aches, stomachaches or tiredness
- Frequent absences from school or poor performance in school
- Talk of or efforts to run away from home
- Outbursts of shouting, complaining, unexplained irritability, or crying
- Being bored
- Lack of interest in playing with friends
- Alcohol or substance abuse
- Social isolation, poor communication
- Fear of death
- Extreme sensitivity to rejection or failure
- Increased irritability, anger, or hostility

- Reckless behavior
- Difficulty with relationships

The prescriber should also discuss with the patient:

- Alcohol or substance abuse
- Chronic pain
- Real or perceived disfigurement

Studies indicate that acne is associated with symptoms such as social embarrassment, low self esteem, and anxiety, but an association of acne with frank depressive disorders has not been established nor has treatment of acne by itself been shown to ameliorate frank depressive disorders.¹⁶⁻¹⁸ ((Niemeier 1998; Kellet 1999; Rubinow 1987))

((Sidebar or table))

Talking About Depression

Although it can be awkward to explain to a patient that he or she may have signs of depression (or any mental illness), the awkwardness can be minimized by reminding the patient that:

- Depression is very common
- It matches some of the symptoms the patient described
- It is treatable

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Suicide Screening

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Psychiatric specialists have identified several factors for suicide risk. These include¹²

((Screening for suicide risk Web site 2001)):

- Presence or history of depression, bipolar disorder or other psychiatric disorder
- Access to firearms in the home
- Family history of suicide or violence, including abuse
- Poor physical health, chronic illness or chronic pain
- Alcohol or substance abuse
- Previous suicide attempt

It is important to note that depression itself is a major risk factor for suicidal behavior. Thus, special attention is needed when prescribing drugs that may cause depression. An association with Accutane should be considered in patients with signs and symptoms of depression, even in the presence of other life stressors. Discontinuation of Accutane may be insufficient intervention and formal psychiatric evaluation should be conducted. It is also important to note that signs and symptoms of depression are not included in all reported cases of suicidal behavior. It is not known if this means the signs were masked by the patient, unrecognized by observers, or if the suicidal tendency arose impulsively. It is

important that patients taking Accutane be made aware of this so that they might recognize any such signs and symptoms. Patients (and parents, if the patient is a minor) should be instructed to stop Accutane and seek immediate medical help.

Talking with patients about suicide does not encourage or remind them that suicide is an option.¹¹ ((National Depression Screening Day))

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Knowing When to Refer

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You should refer the patient to a psychiatric specialist for further evaluation if any of the following apply:

- Risk factor(s) for suicide is (are) present
- The patient has, or may have, clinical depression or bipolar disorder, or if the prescriber believes that there may be a problem but cannot classify it
- The patient has expressed interest in, or spontaneously mentioned, suicide
- There is any question about the patient's safety

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Summary

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Prescribers who are alert to the warning signs of psychiatric disorders can guide patients to receive the help they need. Observing patients for signs of depression and suicidal ideation, and referring appropriate patients to a psychiatric specialist, need not be complicated. The benefits to patients can be immense, even life-saving.

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