Recognizing Psychiatric Disorders in Adolescents And Young Adults

A guide to recognizing psychiatric disorders in adolescents and young adults for prescribers of isotretinoin
Isotretinoin must not be used by patients who are or may become pregnant. There is an extremely high risk that life-threatening birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.
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A Guide For Prescribers of Isotretinoin

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>5</td>
</tr>
<tr>
<td>Depression</td>
<td>5</td>
</tr>
<tr>
<td>Suicide</td>
<td>7</td>
</tr>
<tr>
<td>Evaluating and referring patients for psychiatric disorders</td>
<td>8</td>
</tr>
<tr>
<td>Knowing when to refer</td>
<td>10</td>
</tr>
</tbody>
</table>
CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by patients who are or may become pregnant. There is an extremely high risk that life-threatening birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a patient who is taking isotretinoin, isotretinoin must be discontinued immediately, and the patient should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

SPECIAL PRESCRIBING REQUIREMENTS

Because of isotretinoin’s teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This REMS is called iPLEDGE®. Isotretinoin must only be prescribed by prescribers enrolled and activated in the iPLEDGE REMS. Isotretinoin must only be dispensed by pharmacies enrolled and activated in the iPLEDGE REMS, and must only be dispensed to patients enrolled and meet all the requirements of the iPLEDGE REMS (see PRECAUTIONS).
WARNINGS
Psychiatric Disorders: Isotretinoin may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. No mechanism of action has been established for these events (see ADVERSE REACTIONS: Psychiatric). Prescribers should read the brochure, Recognizing Psychiatric Disorders In Adolescents And Young Adults: A Guide For Prescribers Of Isotretinoin. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin therapy, patients and family members should be asked about any history of psychiatric disorder, and at each visit during therapy patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary. Signs and symptoms of depression, as described in the brochure Recognizing Psychiatric Disorders In Adolescents And Young Adults, include sad mood, hopelessness, feelings of guilt, worthlessness or helplessness, loss of pleasure or interest in activities, fatigue, difficulty concentrating, change in sleep pattern, change in weight or appetite, suicidal thoughts or attempts, restlessness, irritability, acting on dangerous impulses, and persistent physical symptoms unresponsive to treatment. Patients should stop isotretinoin and the patient or a family member should promptly contact their prescriber if the patient develops depression, mood disturbance, psychosis, or aggression, without waiting until the next visit. Discontinuation of isotretinoin therapy may be insufficient; further evaluation may be necessary. While such monitoring may be helpful, it may not detect all patients at risk. Patients may report mental health problems or family history of psychiatric disorders. These reports should be discussed with the patient and/or the patient’s family. A referral to a mental health professional may be necessary. The physician should consider whether isotretinoin therapy is appropriate in this setting; for some patients the risks may outweigh the benefits of isotretinoin therapy.

Pseudotumor Cerebri: Isotretinoin 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 isotretinoin 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, paresthesia, seizure, stroke, syncope, weakness
Psychiatric: suicidal ideation, suicide attempts, suicide, depression, psychosis, aggression, violent behaviors (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.

REPORTING ADVERSE EVENTS
Specific information about adverse events that may occur during isotretinoin therapy may be reported to the individual makers of isotretinoin and/or to the Food and Drug Administration MedWatch Program at 1-800-FDA-1088 or via www.fda.gov/medwatch/report.htm. The contact information for specific brands of isotretinoin can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

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

Mental health problems are underdiagnosed and undertreated. Dermatologists and other isotretinoin 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.

Isotretinoin may cause depression, psychosis, and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. 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 consult is advisable.

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.

Depression

Depression and suicidal tendencies are 2 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 isotretinoin and is also a well-established risk factor for suicidal behavior.

Depression is characterized by symptoms that include intense, persistent sadness; anxiety; loss of pleasure from usual activities; and loss of energy. These feelings can be normal responses to a negative life event, but clinical depression is either not triggered by such an event or is disproportionate to the trigger.

Depression can be episodic. According to the National Comorbidity Survey, 16.2% (between 32.6 and 35.1 million) of Americans will experience depression at some point during their lives, and 6.6% (between 13.1 and 14.2 million) are depressed in any given month. Several epidemiological studies reported that up to 8.3% of adolescents in the United States suffer from depression. Older adolescents experience more depressive symptoms than adults and comparable symptom persistence, suggesting that these adolescents may be at the highest risk for depression.
Depression (Cont.)

Depression can take several forms: 3 of the most common are dysthymia, major depression, and bipolar disorder. These 3 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 1. Symptoms of Depression**

- Persistent sad, anxious, or “empty” mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being “slowed down”
- Difficulty concentrating, remembering, making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight loss or overeating and weight gain
- Thoughts of death or suicide; suicide attempts
- Restlessness, irritability
- Persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real


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 (severe lows) and episodes of mania (severe highs).²

### Symptoms of Mania²

- Abnormal or excessive elation
- Unusual irritability
- Decreased need for sleep
- Grandiose notions
- Increased talking
- Racing thoughts
- Increased sexual desire
- Markedly increased energy
- Poor judgment
- Inappropriate social behavior

### Cause of Depression

The causes of depression are often multifactorial and may include:

- Genetic predisposition²
- Stress at home, work, or school²
- Loss of a parent or loved one⁸
- Alcohol or substance abuse⁹
- Breakup of a romantic relationship¹⁰
- Medications¹¹

### Suicide

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.¹²-¹⁴ Of the total number of suicides among people ages 15 to 24 in 2001, 86% were male and 14% were female.¹⁵,¹⁶ 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 Suicidal tendencies rarely arise spontaneously; 93% of people who commit suicide suffer from depression, schizophrenia, and/or substance abuse.¹⁷
Suicide (Cont.)
Up to 60% of adolescents and young adults think about suicide at some point, but fortunately these thoughts usually pass. Few people who have suicidal thoughts make the attempt, and most attempts at suicide are unsuccessful. The following are some elements of a suicide risk assessment that can be used to determine the individual’s risk level for suicide:

- Ideation (thoughts of death or suicide)
- Suicidal intent
- Plan (specific time, place, and method)
- Means (e.g., a firearm in the house or a supply of drugs)

Women are twice as likely as men to attempt suicide, but men are 4 times more likely to be successful. Women usually use means from which they may be rescued, such as a drug overdose, whereas men tend to use firearms or automobiles. Firearms are used in 55% of all completed suicides.

Despite a patient’s attempt to hide suicidal thoughts, he or she may send deliberate warning signals, some of which can be explicit. Every mention or discussion of “killing myself” should be treated with utmost seriousness.

Evaluating and Referring Patients for Psychiatric Disorders
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. 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.

It is important to find out whether a patient is under care or has ever been under care for an emotional problem or psychiatric disorder, particularly depression. Knowing a patient’s current medications, for example, if he or she is taking antidepressants, can further identify those patients who may be at even greater risk than the general population.

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
Assessments: Depression

While taking a history, the prescriber should suspect the likelihood of depression if the patient has symptoms such as:

- 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, stomach aches, 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.
Evaluating and Referring Patients for Psychiatric Disorders (Cont.)

Assessments: Suicide

Psychiatric specialists have identified several factors for suicide risk. These include:

- 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 isotretinoin should be considered in patients with signs and symptoms of depression, even in the presence of other life stressors. Discontinuation of isotretinoin may be insufficient intervention and a 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 isotretinoin 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 isotretinoin and seek immediate medical help.

Talking with patients about suicide does not encourage or remind them that suicide is an option.

Knowing When to Refer

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

Summary

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.
References

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