Naltrexone

Generic name	Naltrexone
Available brands	ReVia, Vivitrol
Available strengths and formulations	50-mg tablet (ReVia) 380-mg/vial intramuscular injection (Vivitrol)
Available in generic	Tablet only

General Information

Naltrexone was approved by the U.S. Food and Drug Administration in 1984 for treatment of opioid dependence and then in 1994 for treatment of alcohol dependence. Naltrexone is available in a 50-mg tablet (**ReVia**) and a long-acting intramuscular injection (**Vivitrol**); the tablet is also available in generic, but the injection is not.

Naltrexone is an **opiate antagonist**. It blocks the effects of opioids in the central nervous system and prevents their euphoric effects in the opioid-dependent person. Although naltrexone's chemical structure is similar to a morphine derivative, it does not behave like one—that is, it is not associated with euphoria, tolerance, or dependence. Naltrexone can precipitate **withdrawal symptoms** when administered to a person physically dependent on opioids.

It is not clearly understood how an opiate antagonist like naltrexone works in alcohol dependence. One explanation postulates that opiate neural pathways in the brain interact with dopamine neurons and enhance dopamine neurotransmission, especially in the area of the brain that plays an important role in the motivation, pleasure, and reward associated with reinforcement of behavior. Opioid receptors are stimulated by endogenous opioids, such as enkephalins and endorphins (morphine-like substances originating within the central nervous system). Alcohol either acts directly on opioid receptors or causes release of these endogenous opioids, but the net result is enhanced dopamine neurotransmission. By blocking opioid receptors with antagonists such as naltrexone, this action inhibits opiate neural pathways and, in turn, blunts dopamine neurotransmission and reduces the pleasure and craving associated with alcohol.

In retrospective studies, it was found that naltrexone alone is seldom successful in treatment of opioid or alcohol dependence. Other factors are associated with achieving successful abstinence: the type, intensity, and duration of treatment programs; the management of other problems (e.g., depression); the use of community-based support groups (e.g., Alcoholics Anonymous and Narcotics Anonymous); and the use of compliance-enhancing methods to ensure medication adherence, such as administration of naltrexone injection by a practitioner. Abstinence rates were higher when these components of treatment were incorporated with naltrexone than when medication alone was the treatment. And, of course, it takes a motivated individual to achieve sustained abstinence.

Dosing Information

For treatment of alcohol dependence, the recommended dosage of naltrexone is a 50-mg tablet taken once a day, which is also the maintenance dosage. The patient should not have taken any narcotics for the previous 7–10 days.

To prevent the risk of withdrawal symptoms in patients with opioid dependence, the patient should be opioid-free for no fewer than 7–10 days. The recommended initial dosage is 25 mg, and if no withdrawal symptoms are observed, the patient may take 50 mg once a day thereafter.

Naltrexone can also be given by intramuscular injection for treatment of alcohol or opioid dependence. It is recommended that the patient be given a trial of oral naltrexone before administration of Vivitrol injection, although pretreatment with oral naltrexone is not a requirement. Vivitrol is administered by a health care practitioner. A single vial containing the 380-mg powder is reconstituted and administered intramuscularly every 4 weeks.

Common Side Effects

The side effects most commonly associated with naltrexone include nausea, headaches, fatigue, insomnia, vomiting, abdominal pain, anxiety, and dizziness. With Vivitrol, pain and tenderness at injection sites are also commonly reported. Moreover, it is not always easy to discern if some of these reported side effects are low-intensity withdrawal symptoms resulting from abstinence from the opioid or alcohol or effects from the naltrexone. These side effects generally subside with continued therapy.

Adverse Reactions and Precautions

Patients should be cautioned that after naltrexone is discontinued, their tolerance to opioids may have been lowered. If the patient uses previously tolerated doses of an opioid, there is a risk of opioid intoxication and respiratory distress. Cases of fatal opioid overdose have been reported in patients relapsing after discontinuing naltrexone. Moreover, patients should be warned of the danger of using narcotics while taking naltrexone. Because it negates the euphoric effects of opioid drugs, an individual may be tempted to administer larger amounts of a narcotic in an attempt to attain the desired effects, and in doing so, a fatal overdose may result. Naltrexone should not be combined with narcotic medications unless they are prescribed under the close supervision of a practitioner.

In clinical trials, naltrexone was associated with asymptomatic elevation of liver enzymes, suggesting liver cell injury. However, patients who have a substance use disorder may have preexisting liver disease or hepatitis B and/or C, which may also cause elevation of liver enzymes. Patients should stop their medication and inform their practitioner if they have signs and symptoms of liver problems, such as fatigue, flu-like symptoms, yellowing of the eyes or skin (**jaundice**), or dark urine.

Depression is often associated with alcohol- and opioid-dependent patients. Family members and caregivers are alerted to observe patients being treated with naltrexone, especially during the early phase of abstinence, for development of depression and suicidal thinking or behavior and to report their findings to the patient's practitioner.

In emergency situations, patients taking long-acting Vivitrol may need pain management with narcotic analgesics.

If opioid therapy is needed for anesthesia or analgesia, higher doses of narcotic are generally needed to reverse the opioid blockade of naltrexone. Opioids must be administered by trained personnel in a setting staffed and equipped for cardiopulmonary resuscitation. Therefore, patients should carry an emergency card or some documentation to alert emergency personnel they are taking naltrexone.

Risk During Pregnancy and Breast-Feeding

Studies have not been conducted in pregnant women to determine the safety of naltrexone during pregnancy. The effects of naltrexone on the developing human fetus are unknown. In animal studies, there was no evidence of naltrexone causing **teratogenicity** (developmental malformations). Data are also lacking as to whether naltrexone may affect labor or delivery. Because of this paucity of data, the risk of naltrexone in human pregnancy cannot be adequately assessed. Naltrexone should not be used during pregnancy unless the potential benefits outweigh the potential risk to the fetus. Women of childbearing age should be cautioned of the potential hazards to the fetus if they become pregnant while taking this drug.

Nursing mothers should not take naltrexone because small amounts may pass into breast milk and may be ingested by the baby. If stopping the drug is not an alternative, breast-feeding should not be started or should be discontinued.

Potential Drug Interactions

There are no significant drug interactions with naltrexone that are known. Naltrexone is extensively metabolized, and then the metabolites are excreted by the kidneys. Naltrexone does not interact with antianxiety medications (e.g., benzodiazepines such as Valium) or any sleep medications. Naltrexone, however, can decrease or negate the benefits of narcotic medications, such as cough preparations containing codeine, antidiarrheal preparations, and opioid analgesics. Caution is advised regarding the use of narcotic medications with naltrexone because higher doses may be needed to achieve analgesia or cough suppression, which may depress respiration.

Overdose

Clinical experience with naltrexone overdose is limited. In one study, subjects who received 800 mg/day for 1 week showed no signs of toxicity. However, it should not be assumed that an overdose of naltrexone is benign. High doses of naltrexone may cause liver injury. The severity of toxicity depends on the amount ingested, the age and weight of the person, idiosyncratic reactions, if other medications were ingested, and whether the person has liver disease. The effect of naltrexone in overdose in children is unknown.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department for observation and treatment. The prescription bottle of medication (and any other medication suspected in the overdose) should be brought along as well because the information on the prescription label can be helpful to the treating practitioner in determining the number of pills ingested.

The American Association of Poison Control Centers (www.aapcc.org) can also be contacted via their helpline at 1-800-222-1222, and they can provide the location of the local poison center.

Treatment Summary

- **Warning:** Always let your practitioner or a family member know if you have suicidal thoughts. Notify your practitioner whenever your depressive symptoms worsen or whenever you feel unable to control suicidal urges or thoughts.
- Naltrexone is taken once a day or as directed by your practitioner. If you miss a dose, take it as soon as possible. If it is late in the day, skip the missed dose and continue on your regular dosing schedule. Do not take double doses.
- Vivitrol is administered intramuscularly every 4 weeks by your practitioner.

- If relapse occurs, do not get discouraged; discuss your drinking or opioid use with your practitioner, counselor, or therapist. Continue taking ReVia or receiving Vivitrol injections as directed, and consult your practitioner as soon as possible.
- Carry some documentation to alert emergency personnel that you take naltrexone in the event of an emergency.
- Store naltrexone in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of your medication, and the medication may lose its therapeutic effects.
- Keep your medication out of the reach of children.
- The following Web sites can provide you and your family with additional information:
  - Alcoholics Anonymous: www.aa.org
  - National Institute on Alcohol Abuse and Alcoholism: www.niaaa.nih.gov
  - National Organization on Fetal Alcohol Syndrome: www.nofas.org
  - Narcotics Anonymous: www.na.org
  - National Council on Alcoholism and Drug Dependence (NCADD): https://ncadd.org
    List of NCADD Affiliates: https://ncadd.org/about-ncadd/our-affiliates
  - Substance Abuse and Mental Health Services Administration (SAMHSA): www.samhsa.gov

If you have any questions about your medication, consult your medical practitioner or pharmacist.

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