

SLEEP MEDICATION SIDE EFFECTS

DIPHENHYDRAMINE (BENADRYL) ANTIHISTAMINE EFFECTS / SIDE EFFECTS

- A first-generation antihistamine
- Can cause strong sedation, due to H1 receptor antagonism
- As such, has also been used as an anxiolytic because of this side effect
- A potent anticholinergic agent, leading to these side effects:
 - Dry mouth and throat
 - Increased heart rate
 - Pupil dilation
 - Urinary retention
 - Constipation
 - At high doses: hallucinations or delirium
- Further side effects include:
 - Motor impairment (ataxia)
 - Flushed skin
 - Blurred vision at nearpoint owing to lack of accommodation (cycloplegia)
 - Abnormal sensitivity to bright light (photophobia)
 - Difficulty concentrating
 - Short-term memory loss
 - Visual disturbances
 - Irregular breathing
 - Dizziness
 - Irritability
- Also:
 - Itchy skin
 - Confusion
 - Decreased body temperature (generally in the hands and/or feet)
 - Erectile dysfunction
 - Excitability
- Some side effects such as twitching may be delayed until the drowsiness begins to cease and the person is in more of an awakening mode.

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HOW ANTIHISTAMINES DISRUPT SLEEP / CREATE ANXIETY

- Second-generation H1 antagonists are also called non-sedating antihistamines
- Different side effects from first-generation antihistamines (Diphenhydramine / Benadryl) which cause severe drowsiness

5-HT ANTIDEPRESSANTS SIDE-EFFECTS

- Dizziness and lightheadedness
- Headache
- Oversedation
 - Prolonged drowsiness
- Dry mouth
- Nausea
- Irregular heartbeat
- Weight gain
- Daytime memory and performance problems
- Constipation

5-HTP (L-5-Hydroxy-Tryptophan)

- Serotonin precursor
- Caution: Very high doses of 5-HTP can be metabolized peripherally and can trigger excess serotonin formation
- 5-HTP is not recommended for pregnant or lactating women and should be avoided by those with any form of cardiovascular disease
- 5-HTP should not be used by those taking selective serotonin receptor agonists
 - e.g., migraine medications:
 - Imetrex / sumatriptan
 - Zomig /zolmitriptan
 - Amerge / naratriptan

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BENZODIAZEPINES SIDE EFFECTS

Long-term use is controversial

- Concerns about adverse psychological & physical effects
- Increased questioning of effectiveness
- Prone to cause tolerance, physical dependence & upon cessation, a withdrawal syndrome

Due to adverse effects associated with the long-term use of benzodiazepines, withdrawal from benzodiazepines in general leads to improved physical and mental health

NOTE: Benzodiazepines make it difficult for Stage 3 & 4 sleep and stimulate GABA A receptors. Valerian stimulates GABA B receptors

Other concerns about the long-term effects of benzodiazepines include

- Dose escalation
- Benzodiazepine abuse
- Tolerance
- Benzodiazepine dependence
- Benzodiazepine withdrawal problems
- The elderly are at an increased risk of suffering from both short- and long-term adverse effects.
- There is controversy concerning the safety of benzodiazepines in pregnancy.
- Known to cause withdrawal symptoms in the newborn
- Benzodiazepines can be taken in overdoses and can cause dangerous deep unconsciousness.
- When combined with other central nervous system depressants such as alcohol and opiates, the potential for toxicity increases.[12]

Benzodiazepines are commonly misused and taken in combination with other drugs of abuse.

- While benzodiazepines are highly effective in the short term, adverse effects associated with long-term use including impaired cognitive abilities, memory problems, mood swings, overdoses when combined with other drugs may make the risk-benefit ratio unfavorable
- Additionally benzodiazepines have reinforcing properties in some individuals and thus are considered to be **addictive drugs**
 - Physical dependence can develop after a few weeks or months of use
- Many of these adverse effects of long-term use of benzodiazepines begin to show improvements three to six months after **withdrawal of benzodiazepines**.
- The **long-term effects of benzodiazepines** include drug dependence as well as the possibility of adverse effects on cognitive function, physical health, and mental health
- There are significant risks associated with the long-term use of benzodiazepines. However, not all people experience problems associated with the long-term use of benzodiazepines

- There is evidence that reduction or **withdrawal from benzodiazepines** can lead to a reduction in anxiety symptoms
- There are a number of side effects associated with addiction to benzodiazepines such as **depression** and flu like symptoms
- Due to these increasing physical and mental symptoms from long-term use of benzodiazepines **withdrawal from benzodiazepines** is recommended for many long-term users

BENZODIAZEPINES – Most Frequent Withdrawal Symptoms

- Insomnia
- Gastric problems
- Tremors
- Agitation
- Fearfulness
- Muscle spasms

BENZODIAZEPINES – Less Frequent Withdrawal Symptoms

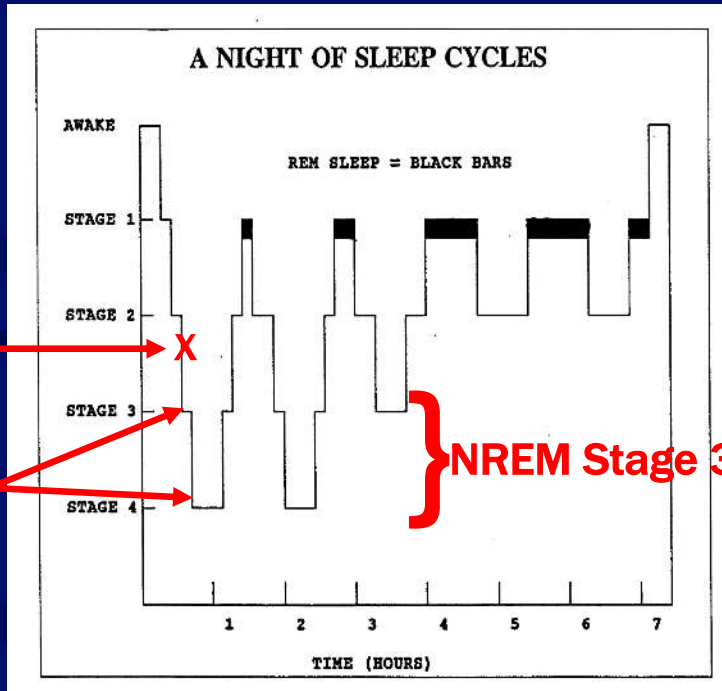
- Severe symptoms usually occur as a result of abrupt or over-rapid withdrawal. Abrupt withdrawal can be dangerous, therefore a gradual reduction regime is recommended
- Irritability
- Sweating
- Depersonalization
- Derealization
- hypersensitivity to stimuli
- Depression
- suicidal behavior
- Psychosis
- Seizures
- Delirium Tremens

BENZODIAZEPINES – Symptoms which may occur as a result of long-term use

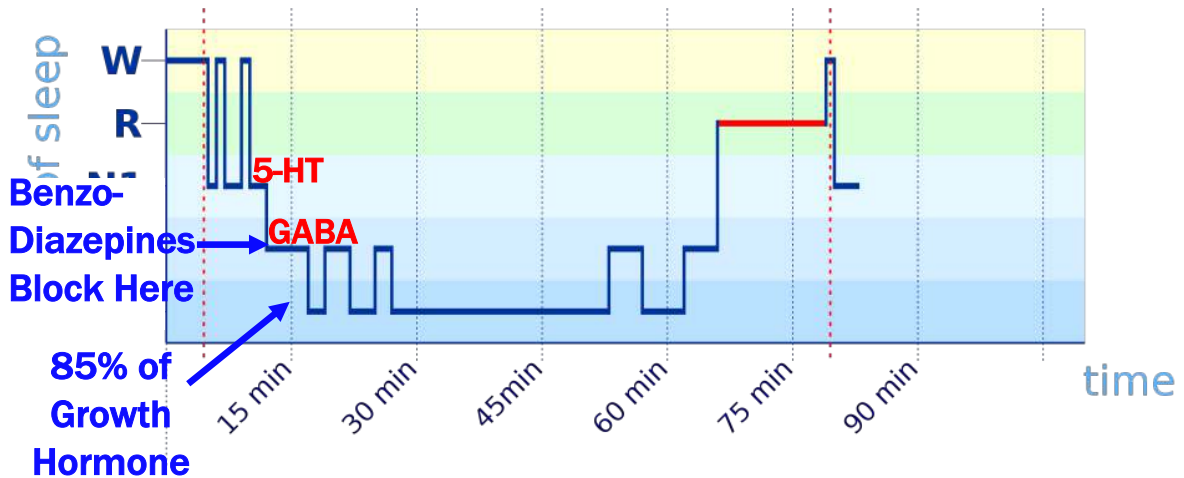
- Emotional clouding
- Nausea
- **Headaches**
- Dizziness
- Irritability
- **Lethargy**
- **Sleep problems**
- Memory impairment, personality changes, aggression, **depression**, agoraphobia, anxiety and **panic attacks**, social deterioration as well as employment difficulties
- Symptoms may also occur during a gradual dosage reduction, but are typically less severe and may persist as part of a protracted withdrawal syndrome for months after cessation of benzodiazepines.
- Approximately 10% of patients will experience a notable protracted withdrawal syndrome, which can persist for many months or in some cases a year or longer.
- Protracted symptoms tend to resemble those seen during the first couple of months of withdrawal but usually are of a sub acute level of severity
- Such symptoms do gradually lessen over time, eventually disappearing altogether

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SLEEP CYCLES



Hypnogram one sleep cycle



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“Z” DRUGS SIDE EFFECTS

- Next-day hangover effect of residual somnolence/drowsiness, dizziness, and ataxia
- Parasomnias and vivid dreams
- The FDA has also warned that eszopiclone and zolpidem can impair next-day operation of machinery and driving

AMBIEN® (ZOLPIDEM) SIDE EFFECTS

- May impair thinking or reactions
- May still feel sleepy the morning after taking them
- Until you know how this medication will affect you during waking hours, be careful if you drive, operate machinery, pilot an airplane, or do anything that requires you to be awake & alert
- Avoid Ambien during travel, such as sleeping on an airplane. You may be awakened before the medication effects have worn off
 - Amnesia (forgetfulness) is more common if you do not get a full 7 to 8 hours of sleep after taking Ambien.
- Do not drink alcohol while you are taking Ambien
 - Increases some side effects, including drowsiness
- Nausea
- Vomiting
- Anterograde amnesia
- Hallucinations, through all physical senses, of varying intensity
- Delusions
- Altered thought patterns
- Ataxia or poor motor coordination, difficulty maintaining balance
- Euphoria and/or dysphoria
- Increased appetite
- Increased Libido or decreased libido / destrudo
- Amnesia
- Impaired judgment and reasoning
- Uninhibited extroversion in social or interpersonal settings
- Increased impulsivity
- When stopped, rebound insomnia may occur
- Headaches in some people
- Short term memory loss

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LUNESTA® (ESZOPICLONE) SIDE EFFECTS

- Lunesta may cause a severe allergic (anaphylactic) reaction that requires immediate medical attention:
 - Hives
 - Difficulty breathing
 - Swelling of the face, lips, tongue, or throat
- Serious side effects
 - Aggression, agitation, changes in behavior
 - Thoughts of hurting yourself
 - Hallucinations
- Less serious side effects may include:
 - Day-time drowsiness, dizziness, "hangover" feeling;
 - Problems with memory or concentration;

- Anxiety, depression, nervous feeling;
- Headache;
- Nausea, stomach pain, loss of appetite, constipation;
- Dry mouth;
- Unusual or unpleasant taste in your mouth; or
- Mild skin rash.

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SONATA® (ZALEPON) SIDE EFFECTS

- Hallucinations
- Abnormal behavior
- Severe confusion
- Day-time drowsiness
- Dizziness / lightheadedness
- Unsteadiness and/or falls
- Double vision / other vision problems
- Agitation
- Headache
- Nausea, vomiting, diarrhea or abdominal pain
- Depression
- Muscle weakness
- Tremor
- Vivid or abnormal dreams
- Memory difficulties or amnesia.
- General
 - General side effects including headache (28% to 38%), asthenia (5% to 8%), fever (2%), malaise (<1% to 2%), and photosensitivity (<1% to 1%) have been reported.
- Nervous system
 - Nervous system side effects including dizziness (7% to 8%), somnolence (5%), amnesia (2% to 4%), anxiety (less than 1% to 3%), paresthesia (3%), depersonalization (less than 1% to 2%), tremor (2%), hypesthesia (less than 1% to 2%), hallucinations (less than 1% to 1%), and vertigo (less than 1% to 1%) have been reported.
- Gastrointestinal
 - Gastrointestinal side effects including nausea (7% to 8%), dyspepsia (4% to 7%), abdominal pain (5% to 6%), anorexia (<1% to 2%), and colitis (1%) have been reported.
- Musculoskeletal
 - Musculoskeletal side effects including myalgia (5% to 7%)
- Ocular
 - Ocular side effects including eye pain (4%) and abnormal vision (<1 to 2%) have been reported.
- Genitourinary
 - Genitourinary side effects including dysmenorrhea (2% to 4%) have been reported.
- Other
 - Other side effects including hyperacusis (2%), parosmia (<1% to 2%), and ear pain (<1% to 1%) have been reported.
- Respiratory
 - Respiratory side effects including epistaxis (<1% to 1%) have been reported.
- Metabolic
 - Metabolic side effects including peripheral edema (<1% to 1%) have been reported

- Zaleplon is habit-forming
- Addiction or drug dependence may occur
- Stopping suddenly after prolonged or frequent use may cause withdrawal effects such as:
 - Mood changes
 - Anxiety
 - Restlessness
 - Rebound insomnia

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OREXIN RECEPTOR AGONIST SIDE EFFECTS www.belsomra.com

- Not thinking clearly
- Acting strangely, confused, or upset
- “Sleep-walking” or doing other activities when you are asleep like eating, talking, having sex, or driving a car
 - Parasomnias
- Next-day drowsiness (most common)
- Diarrhea
- Dry mouth
- Upper respiratory tract infection
- Headache
- Dizziness
- Abnormal dreams
- Cough

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