Neuropharmacology revision

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BENZODIAZEPINES & BARBITURATES

SEDATIVES & ANXIOLYTICS

PANIC DISORDER

ANXIETY DISORDERS ✓

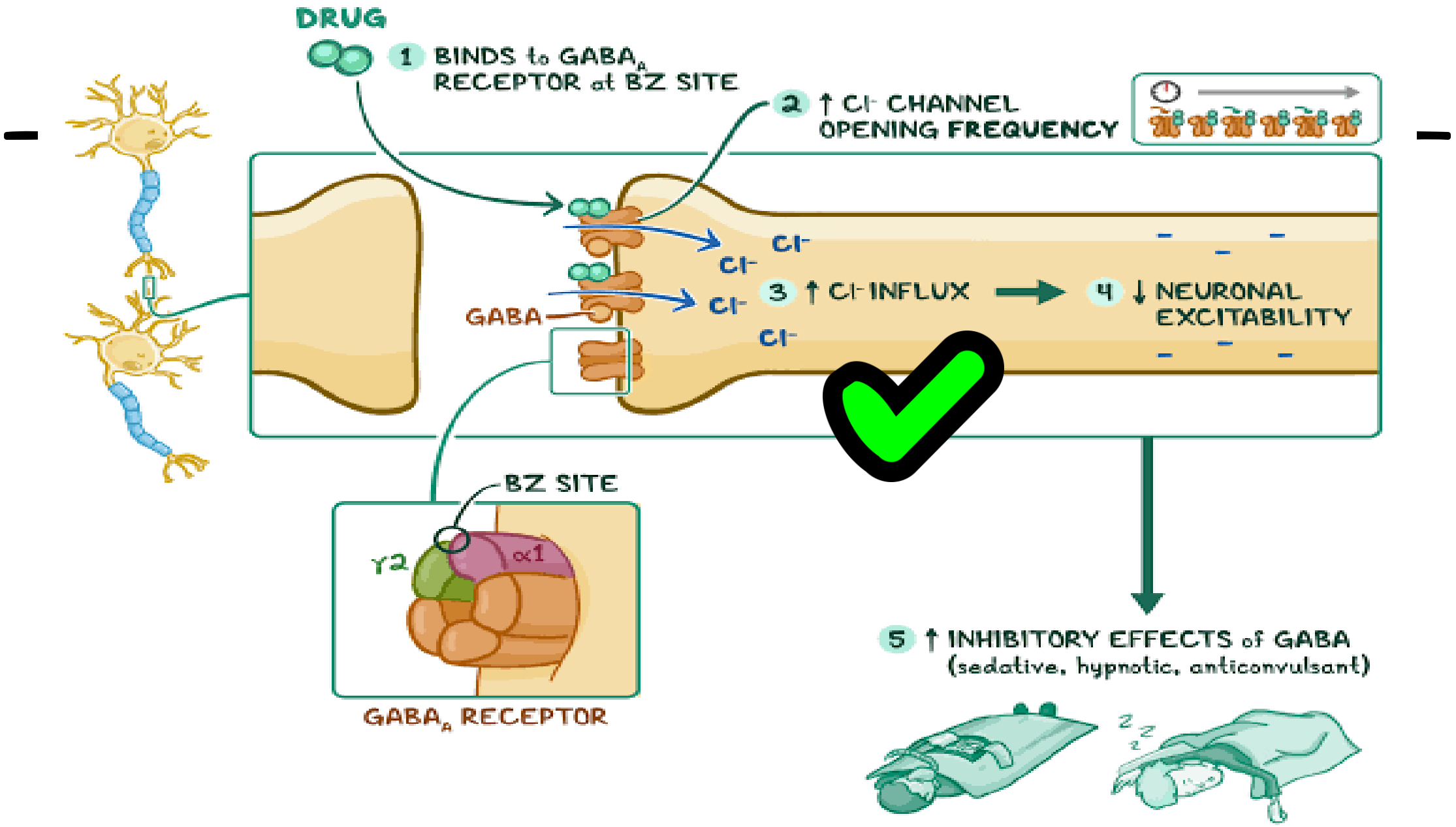
INSOMNIA ✓

* BIND to GAMMA-AMINOBUTYRIC ACID (GABA) RECEPTORS ✓

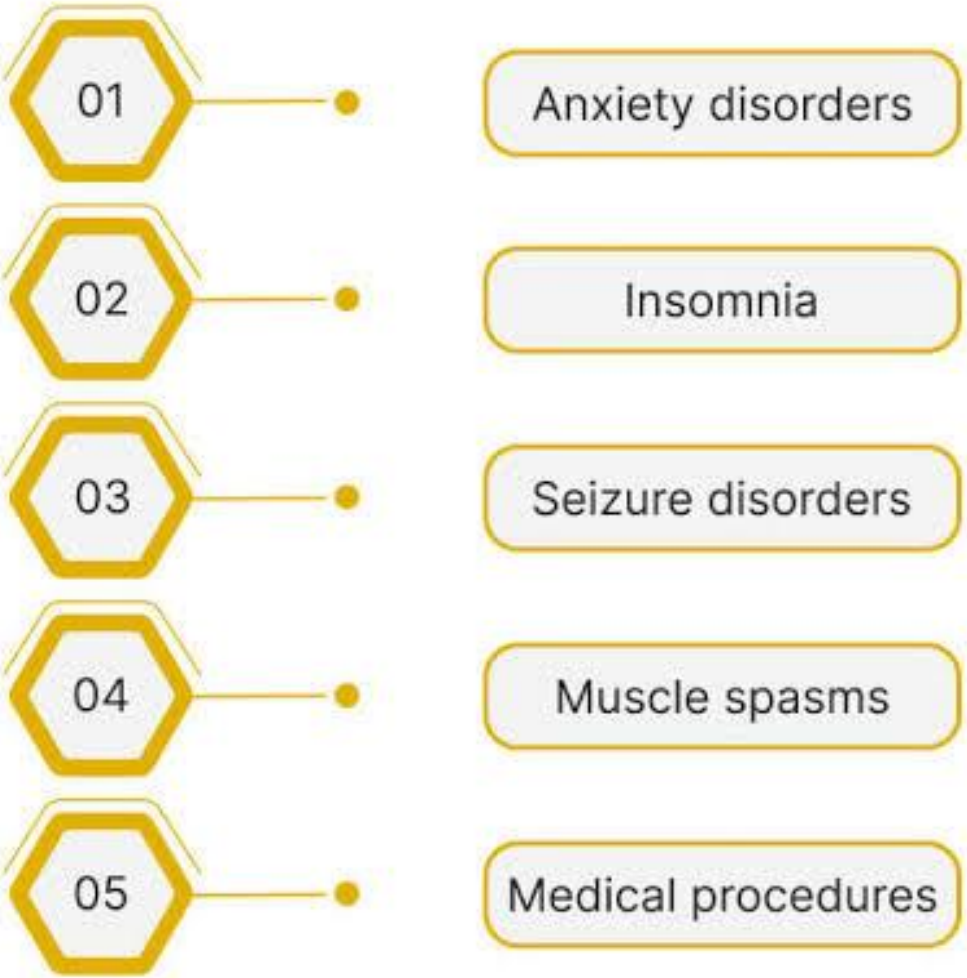
↳ ↑ AFFINITY of RECEPTOR to BIND to GABA

↳ 1° INHIBITORY NEUROTRANSMITTER

BENZODIAZEPINES



COMMON USES OF BENZODIAZEPINES



MED vidi

EZCare Clinic • Mango Clinic

Consult a healthcare provider to get an accurate diagnosis and proper personalized treatment.

Question

A 42-year-old man recently diagnosed with generalized anxiety disorder had started a treatment with sertraline, but the drug caused some sexual dysfunction, and the psychiatrist decided to switch to a short course of alprazolam. Which of the following molecular actions on neuronal membranes most likely mediated the therapeutic effect of alprazolam in the patient's disorder?

A. Decreased outward Na^+ current

B. Increased inward Cl^- current

C. Decreased outward K^+ current

D. Increased inward Ca^{2+} current

E. Increased inward H current

Question

A 58-year-old man was admitted to the hospital for a laparoscopic surgery. Anesthesia was induced by IV diazepam, and the patient lost consciousness in about 1 minute. He regained consciousness about 35 minutes later. Knowing that the half-life of diazepam is about 40 hours, which of the following items best explains the short action of the drug?

A. Rapid metabolism of the drug within the central nervous system

B. Rapid excretion of the drug by the kidneys

C. Redistribution of the drug from central nervous system to other tissues

D. Biotransformation of the drug into inactive metabolites

E. Development of a rapid tolerance to drug effects

Question

A 26-year-old woman, suffering from cerebral palsy secondary to head injury, was seen in a clinic for a scheduled visit. She was spastic and unable to walk. Which of the following drugs would be appropriate to improve her muscle spasms?

A. Buspirone

B. Lithium

C. Fluoxetine

D. Haloperidol

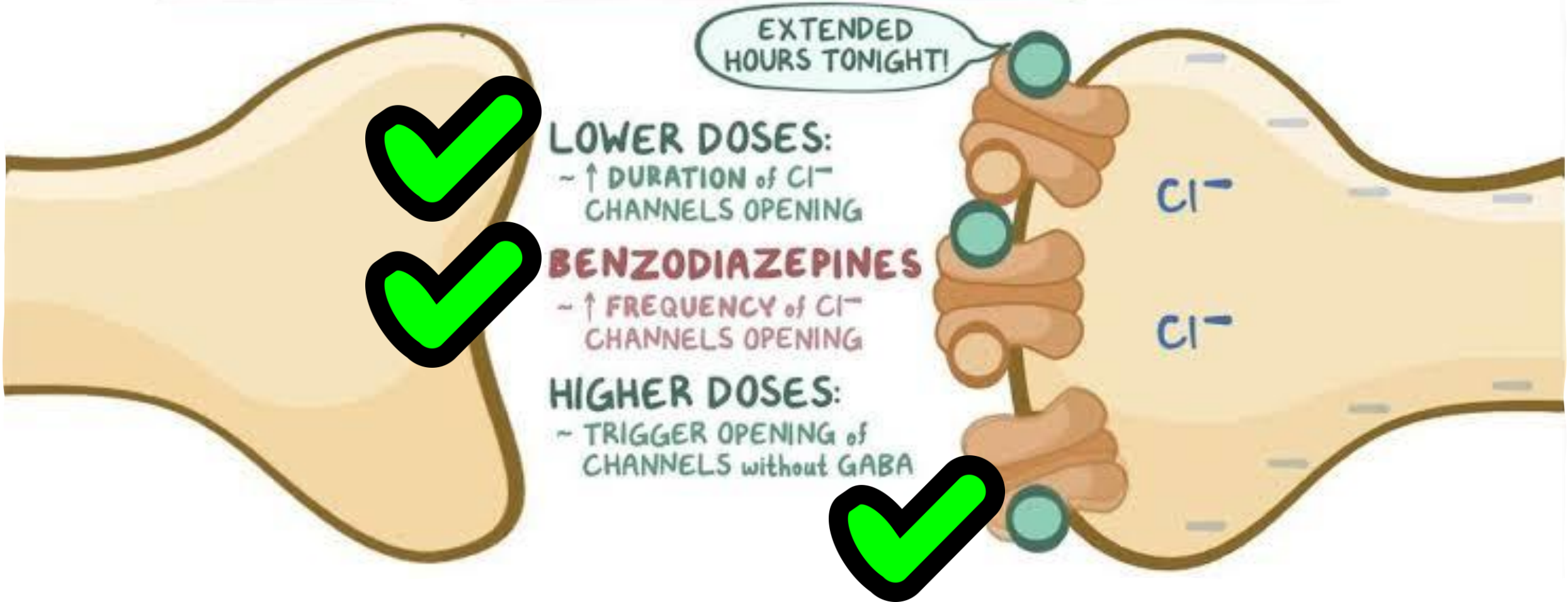
E. Diazepam

BARBITURATES

~ DECREASE EXCITATORY SIGNALS

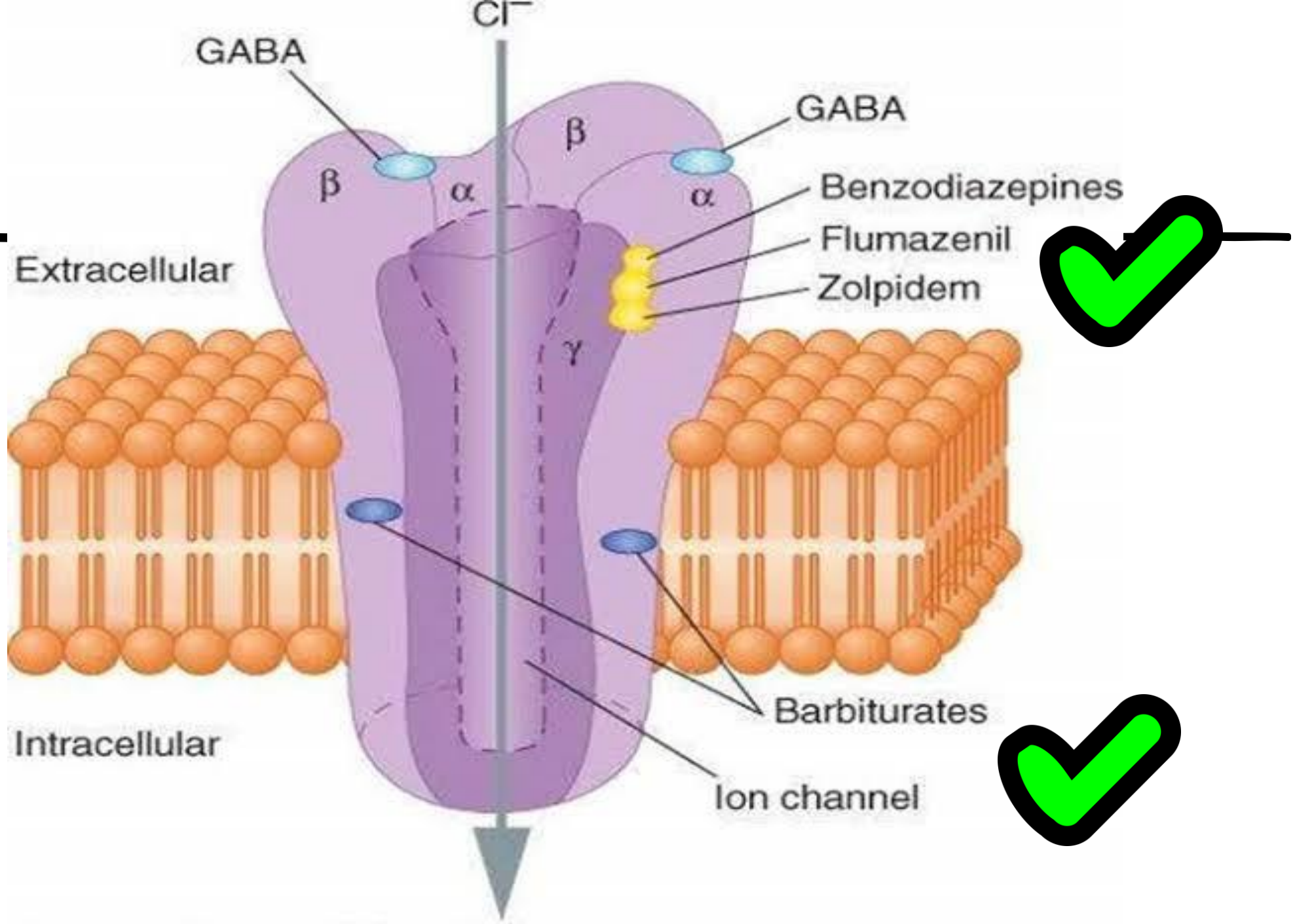
AMOBARBITAL | BUTABARBITAL | METHOHEXITAL | PENTobarbital

PRIMIDONE | PHENobarbital | THIOPENTAL



Approved Medication for Insomnia Treatment

Categories of Medication:	Receptors:
Benzodiazepines	GABA-A
Non-benzodiazepine hypnotics	GABA-A alpha-1 subunit
DORAs	Orexin-1 and orexin-2
Melatonin agonists	Melatonin-1 and melatonin-2
H1 antagonists	H1


Cl⁻
GABA
GABA
β
β
α
α
Benzodiazepines
Flumazenil
Zolpidem
γ
Extracellular
Intracellular
Barbiturates
Ion channel

Question

A	Q
A. Alprazolam B. Buspirone C. Clonazepam D. Flumazenil E. Lorazepam F. Midazolam G. Phenobarbital H. Thiopental I. Zolpidem	1. A partial agonist at 5-HT1A receptors buspirone 2. A competitive antagonist at benzodiazepine receptors flumazenil 3. A hypnotic drug with negligible effects on sleep architecture and stages Zolpidem 4. The barbiturate most frequently used to induce general anesthesia 5. A benzodiazepine with a very short half-life (about 2 hours) midazolam 6. An anxiolytic drug with negligible abuse liability buspirone

Question

A 63-year-old woman complained to her physician of difficulty in falling asleep. She denied nocturnal insomnia or early awaking. The doctor prescribed ramelteon, one tablet at bedtime. Which of the following molecular actions most likely mediated the therapeutic effect of the drug?

A. Activation of GABAB receptors

B. Blockade of α 1 receptors

C. Activation of melatonin receptors

D. Blockade of glutamate receptors

E. Activation of serotonin 5-HT3 receptors

Question

A 36-year-old man was referred to a psychiatrist because of irritability, worrying thoughts, palpitations, dry mouth, and insomnia of 1-month duration. The man had a history of alcohol abuse, but he was able to quit 1 year ago after psychological counseling and drug therapy. Recently, he suffered from erectile dysfunction, treated with sildenafil. A provisional diagnosis of generalized anxiety disorder was made, and cognitive behavioral therapy with a drug treatment was prescribed. Which of the following drugs would be most appropriate for this patient?

A. Diazepam

B. Fluoxetine

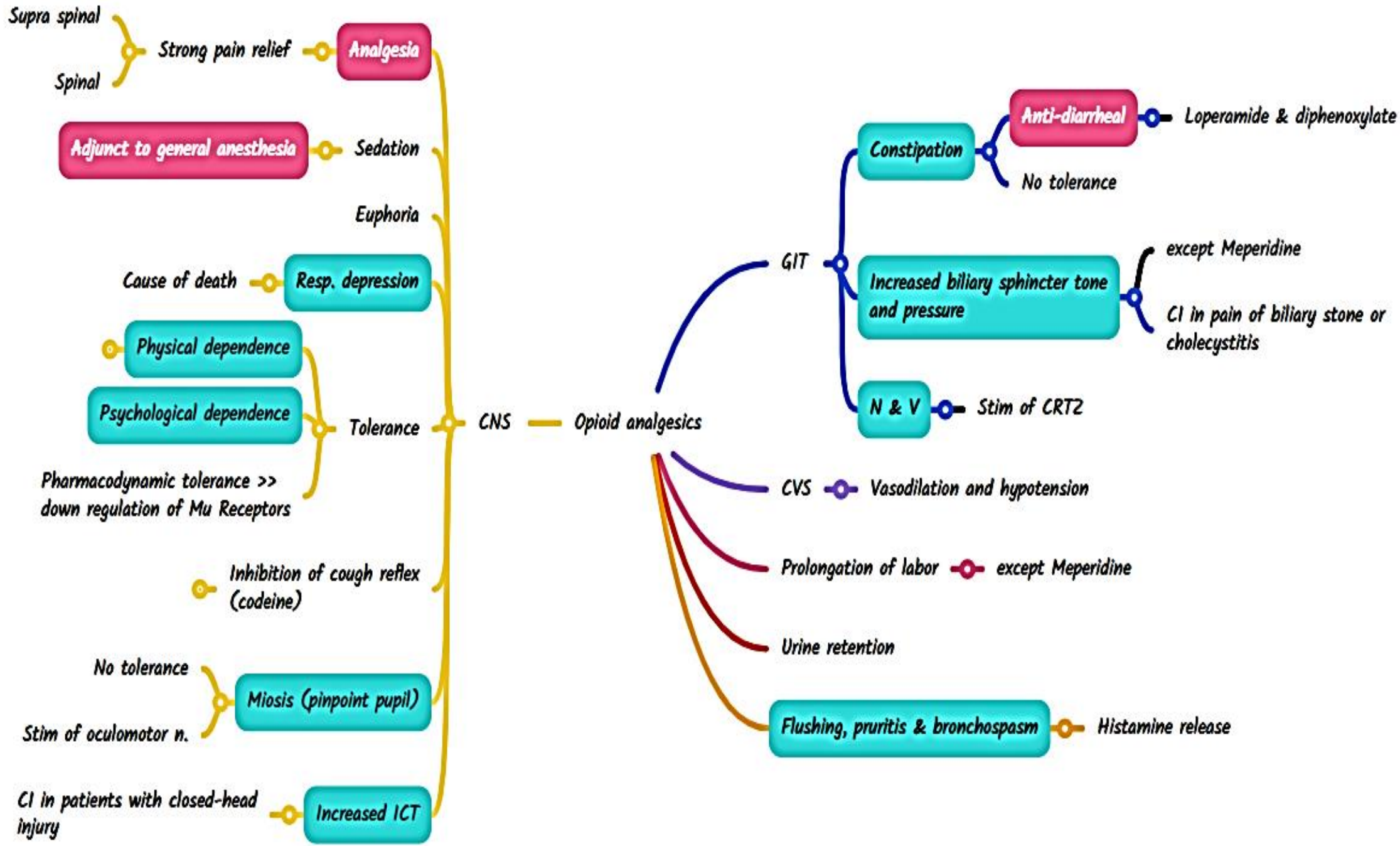
C. Lorazepam

D. Haloperidol

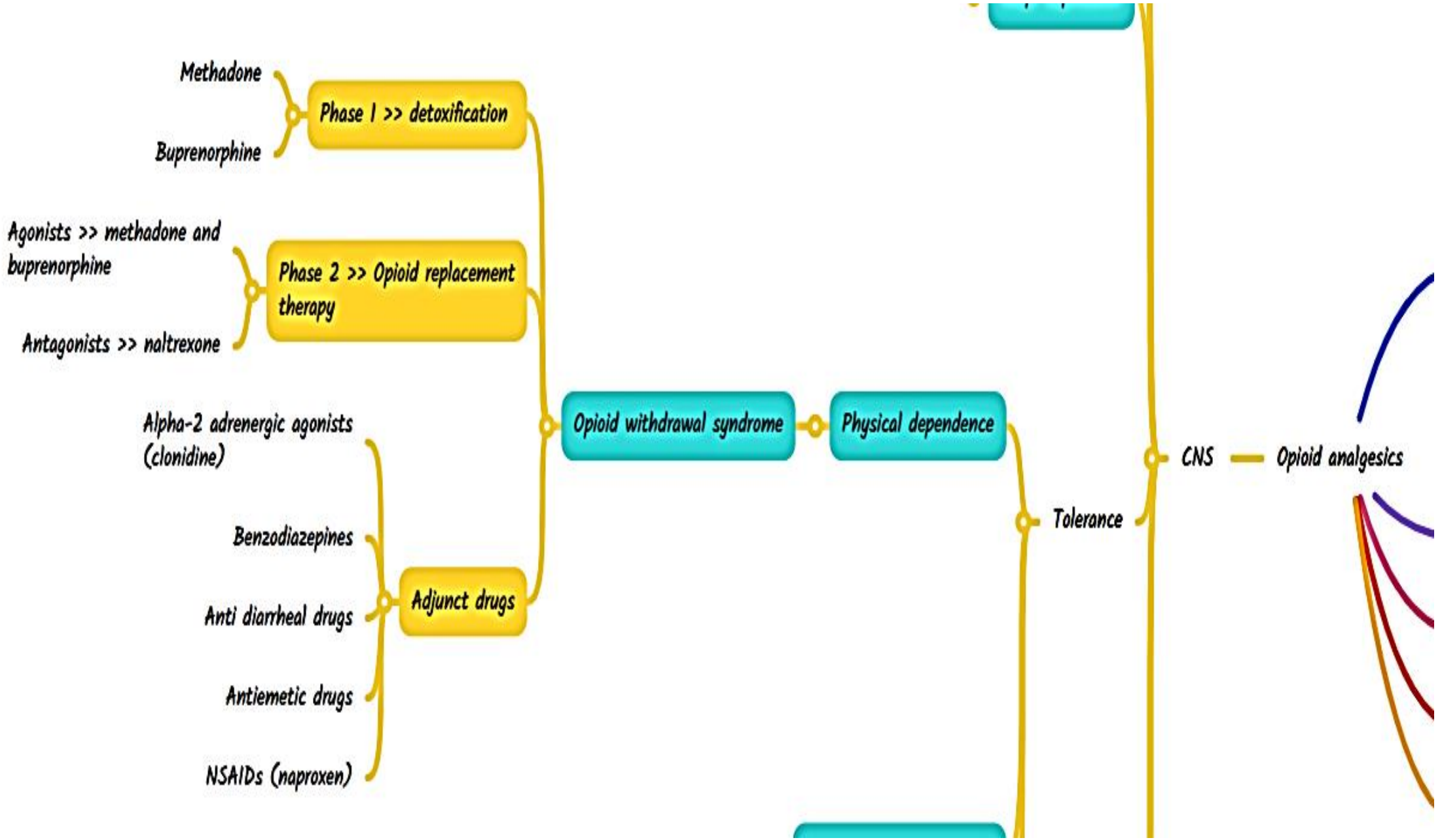
E. Lithium

F. Buspirone

Opioid analgesics



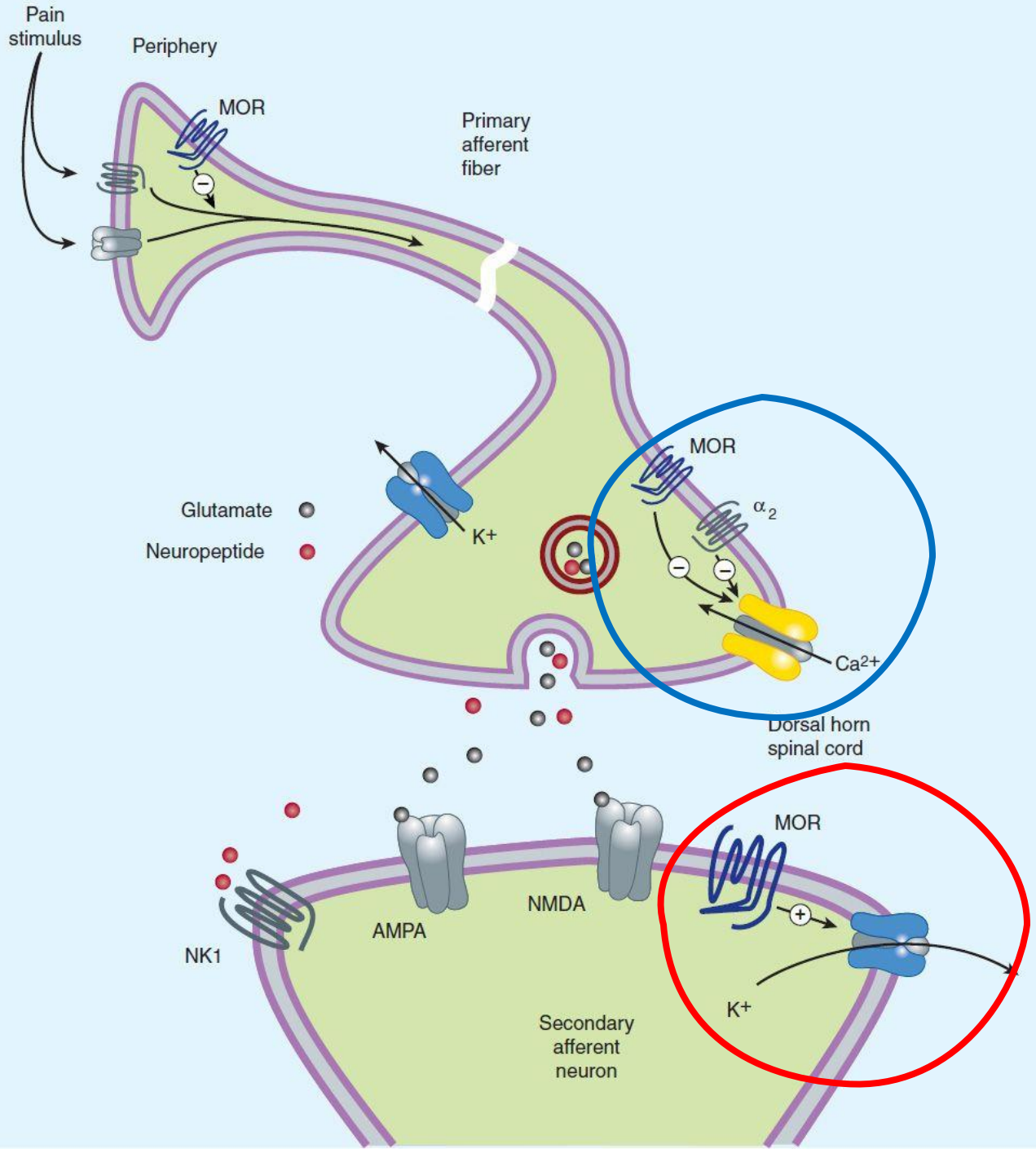
Opioid analgesics



Opioid receptors

- Opioid receptors localized at presynaptic neurons ↓ release of pain neurotransmitters (substance P & glutamate) mainly through ↓ in Ca^{++} influx
- Opioid receptors localized at postsynaptic neurons decrease firing through increase in K^+ efflux → hyperpolarization

The net effect of μ receptor activation is to inhibit neuronal activity → so pain transmission is either blocked or diminished



Pharmacological effects of Morphine

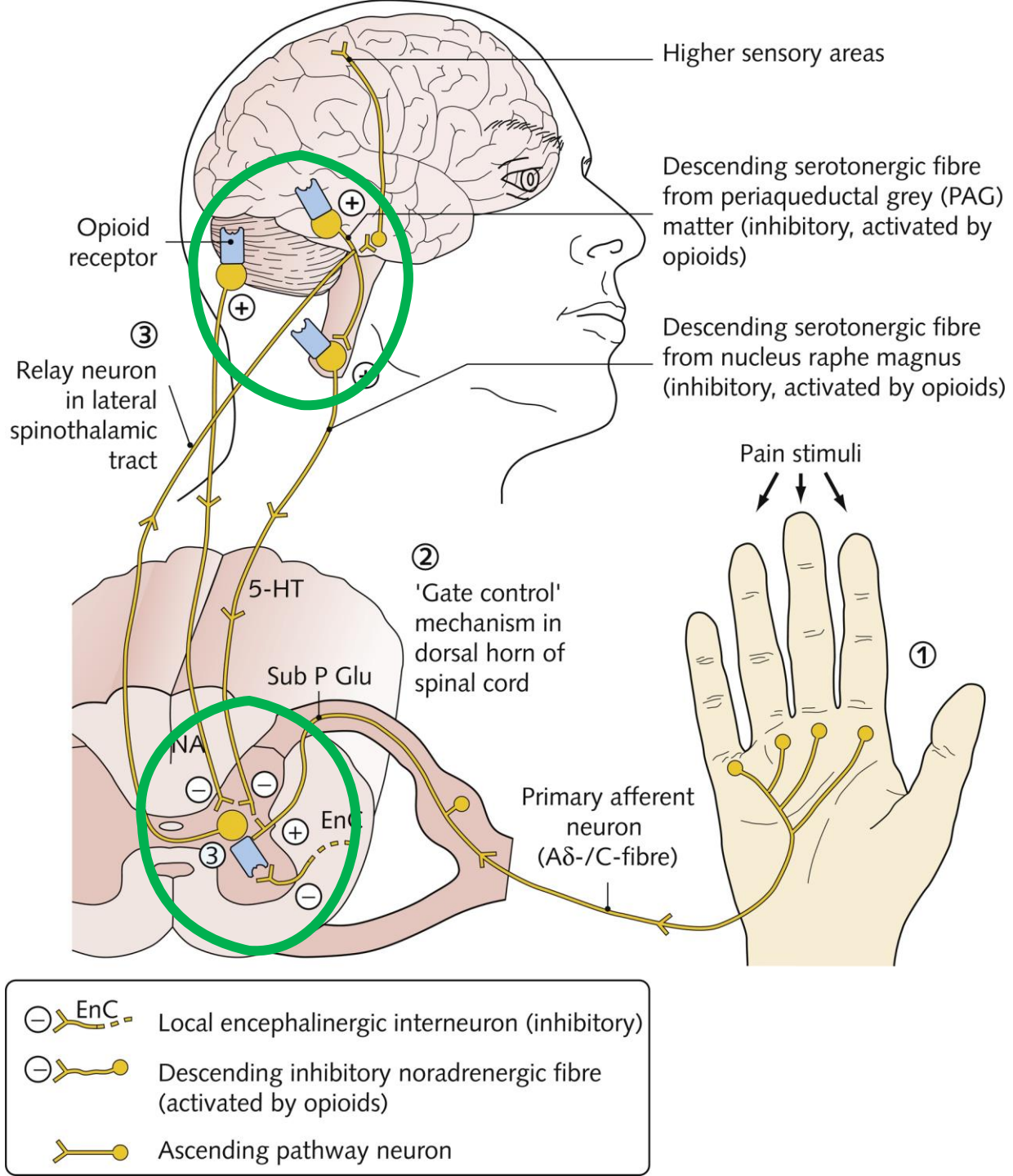
Analgesia

Supra spinal

- Activation of the descending inhibitory tracts

Spinal

- Decrease substance P & glutamate release from presynaptic neuron
- Hyperpolarization of the post synaptic neuron



Question

A 34-year-old woman was admitted to the emergency department because of multiple fractures sustained in a car accident. The patient complained of severe pain, and an intramuscular injection of morphine was given. Which of the following molecular actions most likely mediated the analgesic effect of the drug in this patient?

A. Opening of Ca2+ channels on presynaptic nerve terminals

B. Closing of chloride channels on postsynaptic neurons

C. Stimulation of substance P release from nociceptive nerve terminals

D. Opening of K+ channels on postsynaptic neurons

E. Closing of Na+ channels on presynaptic nerve terminals

F. Stimulation of glutamate release from nociceptive nerve terminals

Question

A 61-year-old woman complained of severe pain a few hours after surgery for renal cancer. An intramuscular inject ion of morphine was given. Which of the following actions most likely contributed to the analgesic effect of morphine?

A. Activation of brain stem neurons that modulate pain transmission

B. Stimulation of substance P release from nerve terminals in the spinal cord

C. Induction of dissociative feeling and dysphoria

D. Inhibition of adrenergic pathways from the locus ceruleus

E. Inhibition of serotonergic pathways from the raphe nuclei

Question

A	Q
A. Buprenorphine B. Codeine C. Fentanyl D. Heroin E. Loperamide F. Methadone G. Morphine H. Naloxone I. Pentazocine J. Propoxyphene K. Tramadol	1. A partial agonist at μ (mu) opioid receptors and antagonist at κ (kappa) opioid receptors Buprenorphine 2. A full opioid agonist with the highest oral bioavailability methadone 3. A drug with very weak opioid activity used in the treatment of diarrhea loperamide 4. A partial agonist at μ (mu) opioid receptors and full agonist at κ (kappa) opioid receptors pentazosine 5. A drug with high affinity but no intrinsic activity at opioid receptors naloxone

Classification of opioid analgesics

- Opioid analgesics can be classified as full μ agonists, partial μ agonists/mixed agonist-antagonists.
- Based on their analgesic potency, full μ agonists can be further subdivided into strong or moderate agonists.

N.B. Pure opioid antagonists have no analgesic effects. They are used to counteract the adverse effects of opioid analgesics taken in overdose and for the treatment of opioid dependence.

Strong μ agonists	Weak/moderate μ agonists	Partial μ agonists	Mixed agonist-antagonists
▪ Morphine → μ agonist ▪ Meperidine → μ agonist ▪ Methadone → μ agonist ▪ Fentanyl → μ agonist	▪ Codeine → μ agonist ▪ Oxycodone → μ agonist ▪ Hydrocodone → μ agonist	▪ Pentazocine → partial μ agonist & κ agonist ▪ Buprenorphine → partial μ agonist & κ antagonist	▪ Pentazocine → partial μ agonist & κ agonist ▪ Buprenorphine → partial μ agonist & κ antagonist

Question

Morphine, all are true EXCEPT:

A. Acts as an agonist at opioid receptors (especially μ) in the brain and spinal cord

B. Causes pupillary constriction by stimulation of the Edinger-Westphal nucleus in the mid-brain

C. Acts as an antihistamine

D. Is subject to presystemic metabolism

E. Stimulates the chemoreceptor trigger zone

Question

A 36-year-old man complain ed of severe abdominal pain after surgery to remove a kidney stone. An analgesic drug was administered intramuscularly. Shortly after the administration, an itchy weal developed at the injection site, along with generalized pruritus. Which of the following drugs was most likely given to the patient?

A. Morphine
B. Acetaminophen
C. Indomethacin
D. Clonidine
E. Ibuprofen

Question

A 34-year-old woman complained to her physician of annoying constipation. One week earlier, she had developed a sore throat and a dry, nonproductive cough and was diagnosed with acute bronchitis. A drug treatment was started, and the cough gradually disappeared. Which of the following drugs most likely caused the constipation reported by the patient?

A. Buprenorphine
B. Fentanyl
C. Albuterol
D. Codeine
E. Theophylline
F. Morphine

Question

A young man is brought to the emergency department in an anxious and agitated state. He informs the attending physician that he uses "street drugs" and that he gave himself an intravenous "fix" approximately 12 h ago. He now has chills and muscle aches and has also been vomiting. The attending physician notes that his pupil size is larger than normal. What is the most likely cause of these signs and symptoms?

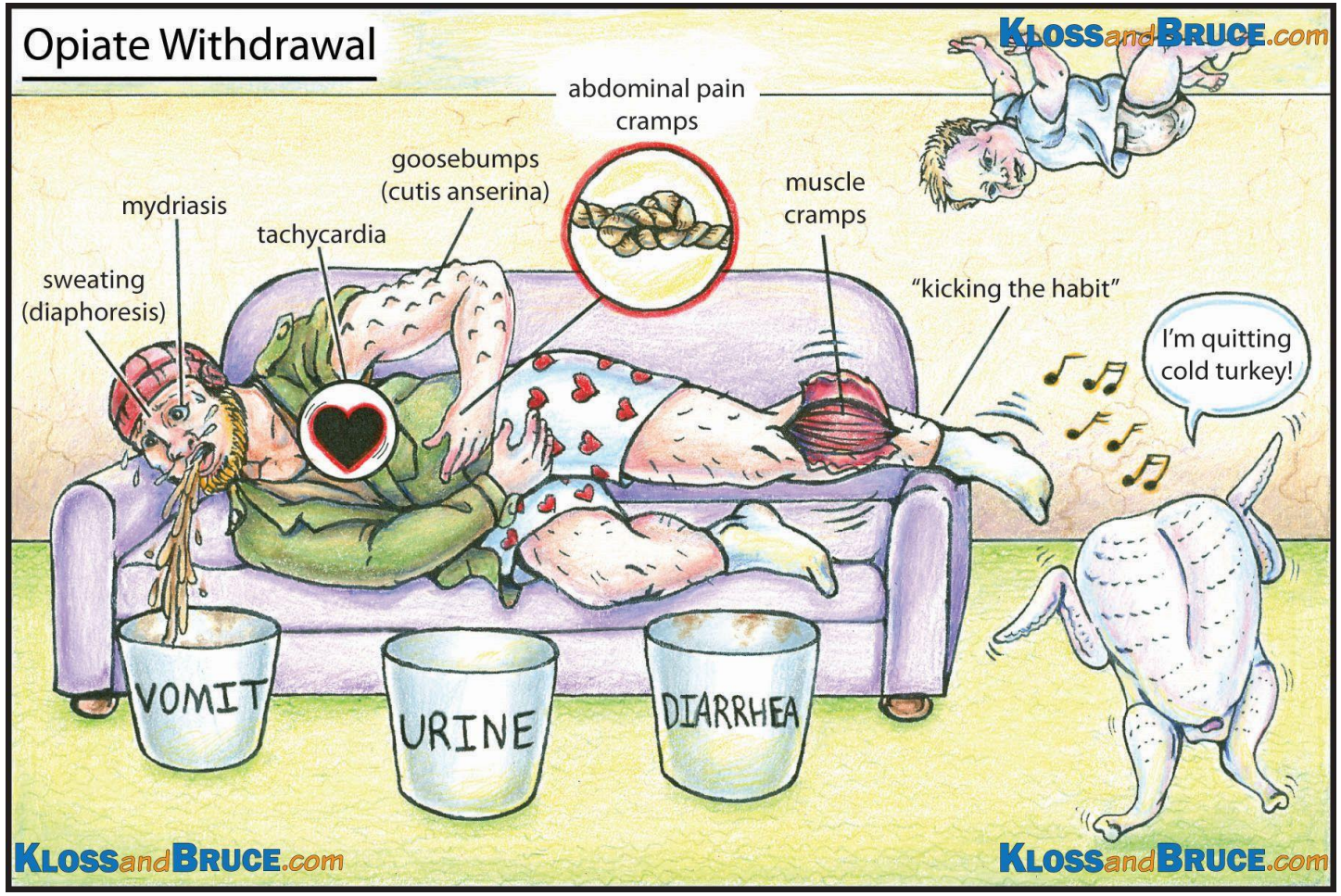
(A) The patient had injected amphetamine
(B) The patient has hepatitis B
(C) The patient has overdosed with an opioid
(D) The signs and symptoms are those of the opioid withdrawal syndrome
(E) These are early signs of toxicity due to contaminants in "street heroin"

Opioid withdrawal syndrome

A state of **irritable** and sometimes aggressive behavior, plus:

- Fever and sweating
- Tachycardia.
- **Nausea and vomiting**.
- **Pupillary dilation** is an important sign of opioid withdrawal (X opioid intoxication causes pinpoint pupils).
- Piloerection.
- Abdominal cramps and **diarrhea.**

Opioid withdrawal is not life-threatening.



Question

Which drug will be most effective in alleviating the symptoms experienced by the patient in the previous case?

(A) Naloxone

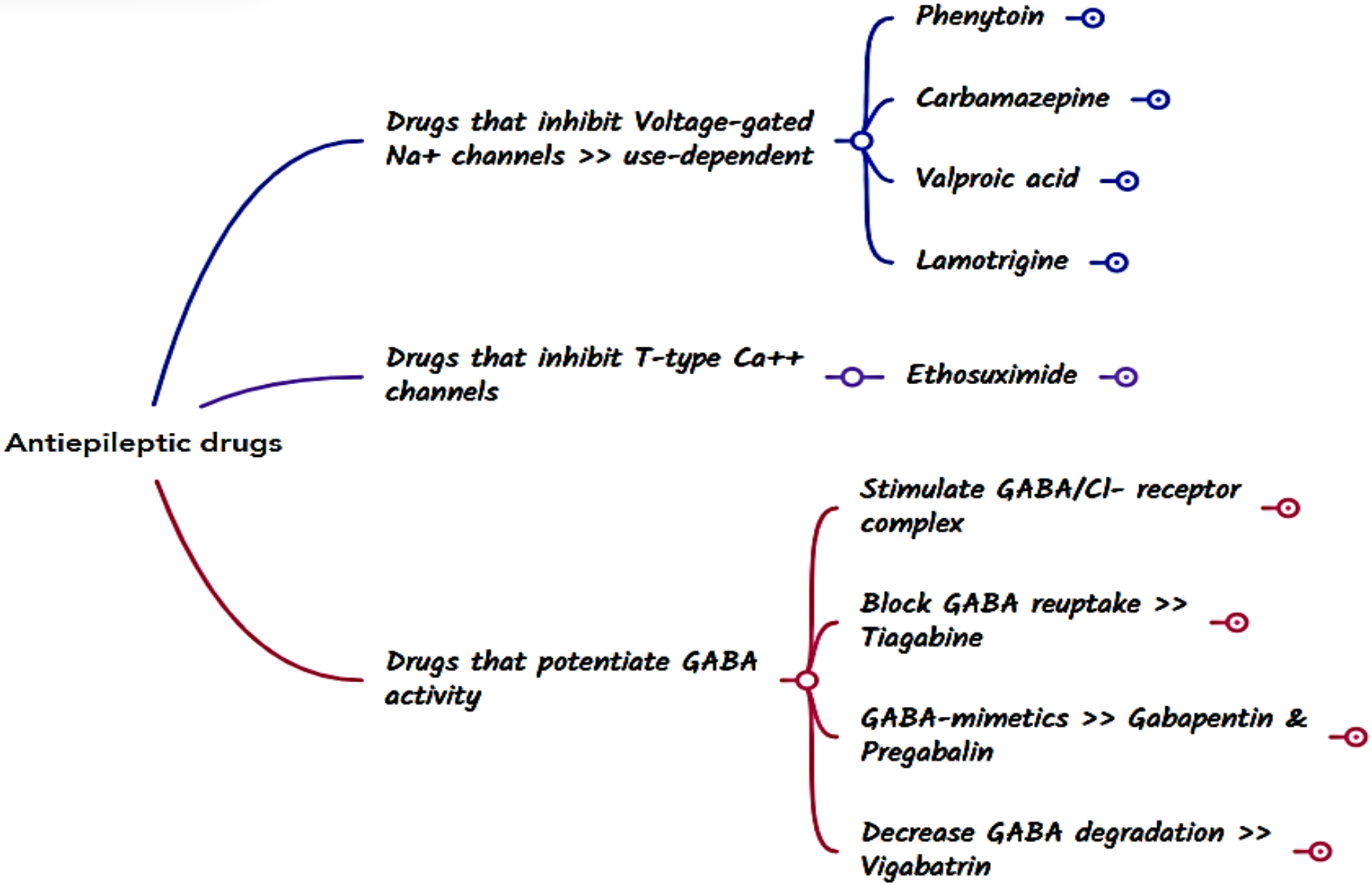
(B) Codeine

(C) Methadone

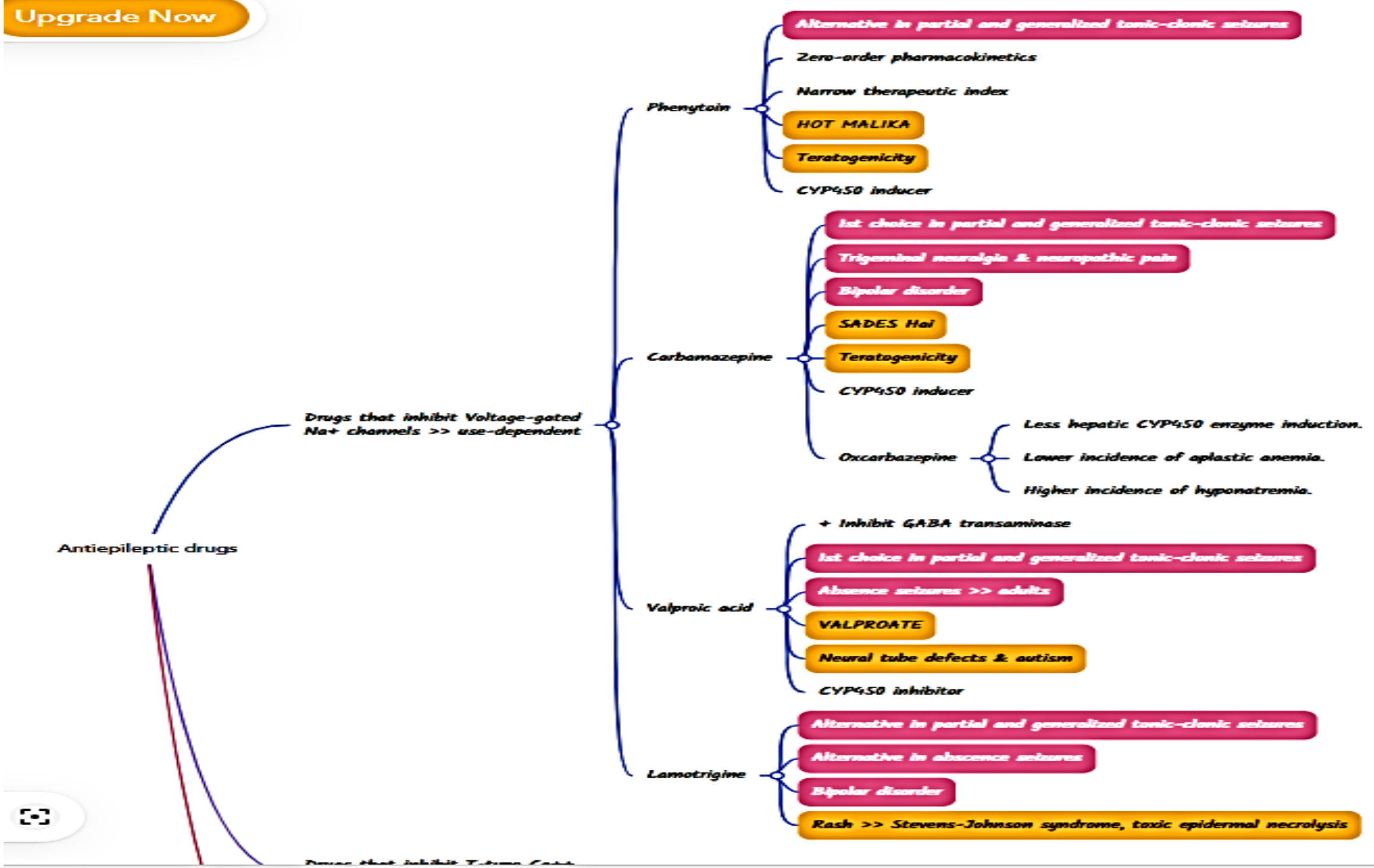
(D) Naltrexone

(E) Tramadol

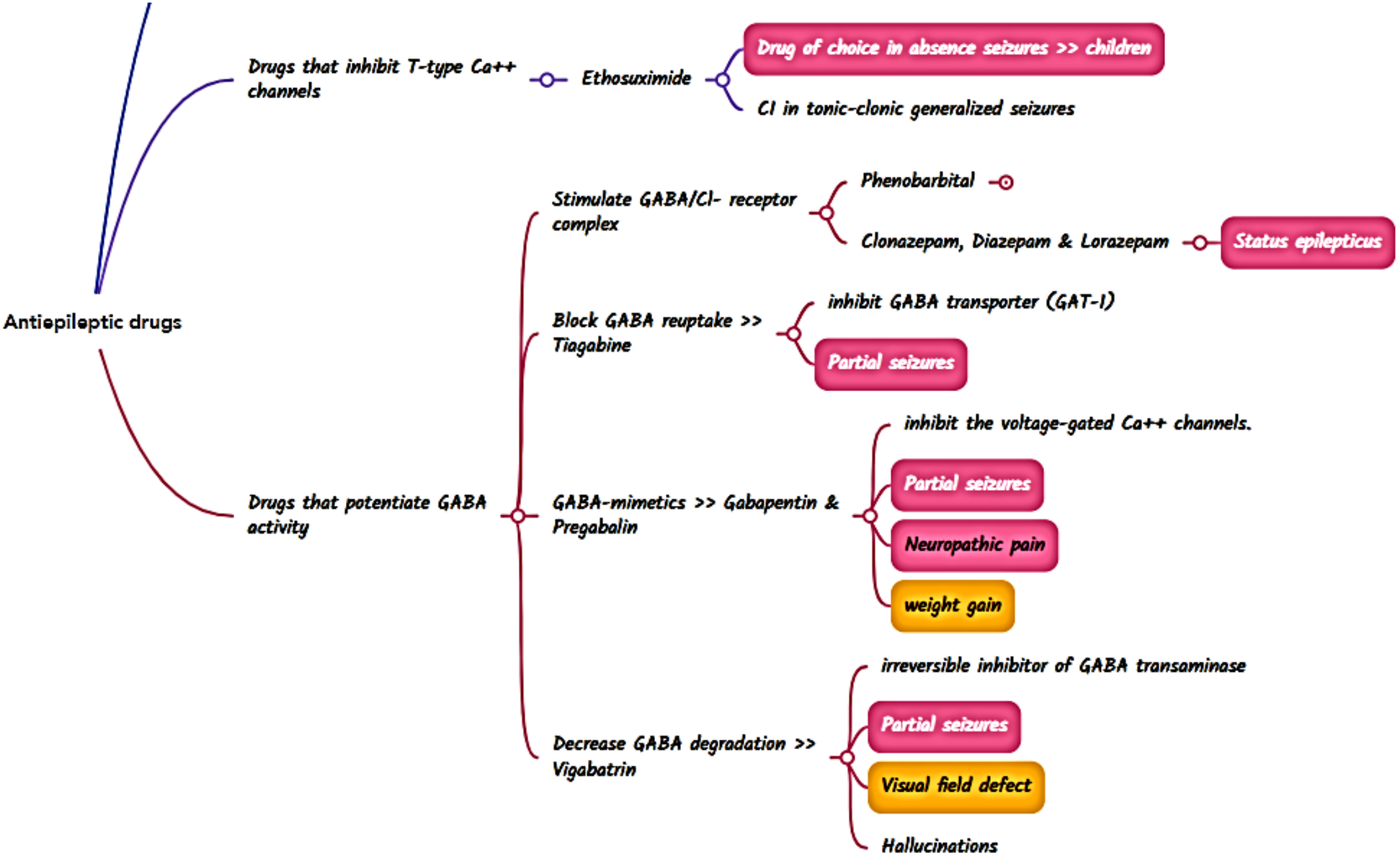
Antiepileptic drugs



Antiepileptic drugs



Antiepileptic drugs



Adverse Effect Of Phenytoin

mnemonic : HOT MALIKA

- Hirsutism
  - Hypertrophy of gums
- Osteomalacia
- Teratogenicity
- Megaloblastic anemia
- Ataxia and nystagmus
- Lymphadenopathy
- Inhibits insulin release (hyperglycemia)

Carbamazepine side effects

SADES Hai

S ✓ Steven · Jonsen syndrome / Rashes

A ✓ Aplastic · Anemia (Agranulocytosis)

D ✓ Diplopia . Ataxia (Neurotoxic)

E Eosinophilia

S ✓ SIADA (Dilutional hyponatremia)

Hai Hepatotoxic

MNEMONIC

Valproate Side Effects (VALPROATE)

V omiting
A lopecia
L iver toxicity
P ancreatitis/pantcytopenia
R etention of fat (weight gain)
O edema (edema)
A ppetite increase
T remor/thrombocytopenia
E nzyme inhibitor (liver)

Question

A 37-year-old woman was at a routine neurology clinic visit. The woman had a long history of refractory grand mal epilepsy. She was being treated with several drugs, but with poor results. The neurologist decided to prescribe phenytoin. Blockade of which of the following types of ion channels is most likely to mediate the therapeutic efficacy of the drug in the patient's disease?

A. Na+ channels in the resting state
B. Na+ channels that open and close at high frequency
C. Na+ channels that open and close at low frequency
D. K+ channels in a resting state
E. K+ channels that open and close at high frequency
F. K+ channels that open and close at low frequency

Question

The mechanism of antiseizure activity of carbamazepine is:

(A) Block of sodium ion channels

(B) Block of calcium ion channels

(C) Facilitation of GABA actions on chloride ion channels

(D) Glutamate receptor antagonism

(E) Inhibition of GABA transaminase

Question

Which statement concerning the proposed mechanisms of action of anticonvulsant drugs is most accurate?

(A) Benzodiazepines facilitate glutamate-mediated inhibitory actions

(B) Ethosuximide selectively blocks potassium ion (K+) channels in thalamic neurons

(C) Phenobarbital produces a selective blockade of calcium ion (Ca2+) channels

(D) Phenytoin prolongs the inactivated state of the Na+ channel

(E) Zonisamide blocks voltage-gated K+ channels

Question

A 37-year-old man recently diagnosed with generalized seizures started treatment with valproic acid, but 1 month later the frequency of seizures was not signficantly reduced. His neurologist decided to add a second-generation antiepileptic drug that blocks voltage-gated Na+ channels and may inhibit the synaptic release of glutamate. Which of the following drugs was most likely prescribed?

A. Gabapentin
B. Lamotrigine
C. Phenobarbital
D. Diazepam
E. Ethosuximide
F. Felbamate

Question

Which statement about phenytoin is accurate?

(A) Displaces sulfonamides from plasma proteins

(B) Drug of choice in myoclonic seizures

(C) Half-life is increased if used with phenobarbital

(D) Isoniazid (INH) decreases steady-state blood levels of phenytoin

(E) Toxic effects may occur with only small increments in the dose

Question

A 32-year-old woman complained to her physician that two breakthrough seizures occurred last week. One month earlier the woman was diagnosed with simple partial seizure and started treatment with an antiepileptic drug. The physician increased the dose of the drug, thinking that the decreased effect was most likely because the drug is a potent enzyme inducer and can induce its own metabolism. Which of the following drugs did the patient most likely take?

A. Valproic acid

B. Carbamazepine

C. Lamotrigine

D. Ethosuximide

E. Clonazepam

Question

A 26-year-old woman discovered she was unexpectedly pregnant. She had been regularly taking an oral contraceptive medication for several years. Two months earlier, she was diagnosed with complex partial seizures and started the prescribed therapy. Which of the following drugs was she most likely taking?

A. Lamotrigine
B. Valproic acid
C. Clonazepam
D. Gabapentin
E. Levetiracetam
F. Carbamazepine

Question

A 50-year-old man complained of occasional episodes of excruciating unilateral facial pain that arose near the mouth, diffused toward the nostrils and eyes, and seemed to be triggered by eating or talking. The pain lasted about 1 minute. He was referred to a neurologist, who made a presumptive diagnosis and ordered an appropriate treatment . Which of the following drugs would be appropriate for this patient?

A. Phenobarbital

B. Clonazepam

C. Codeine

D. Diclofenac

E. Carbamazepine

Question

A 36-year-old woman recently diagnosed with simple partial seizures started a therapy with lamotrigine. Which of the following adverse effects is most likely to occur during the therapy?

A. Macrocytic anemia

B. Hallucinations

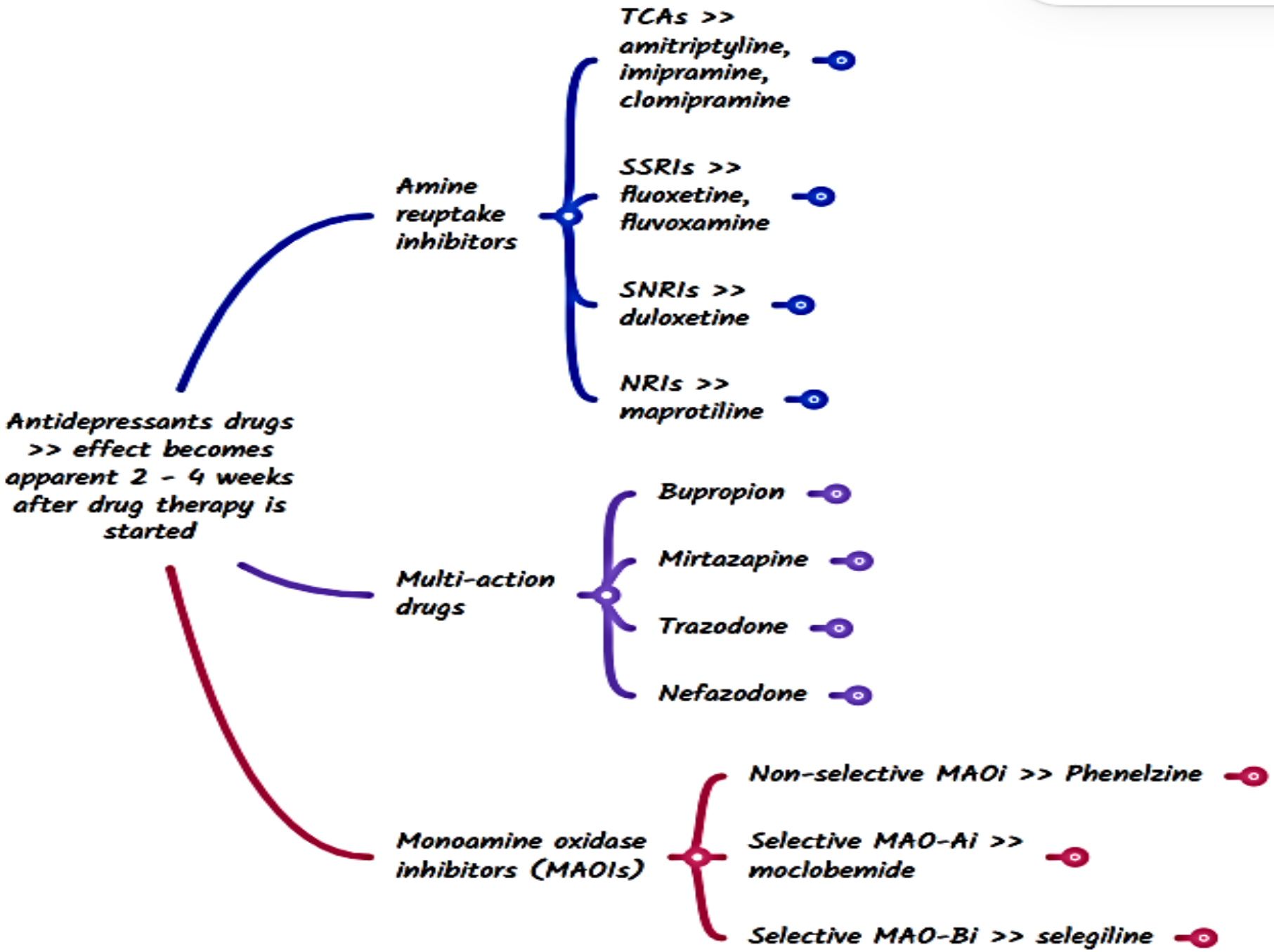
C. Liver cirrhosis

D. Pancreatitis

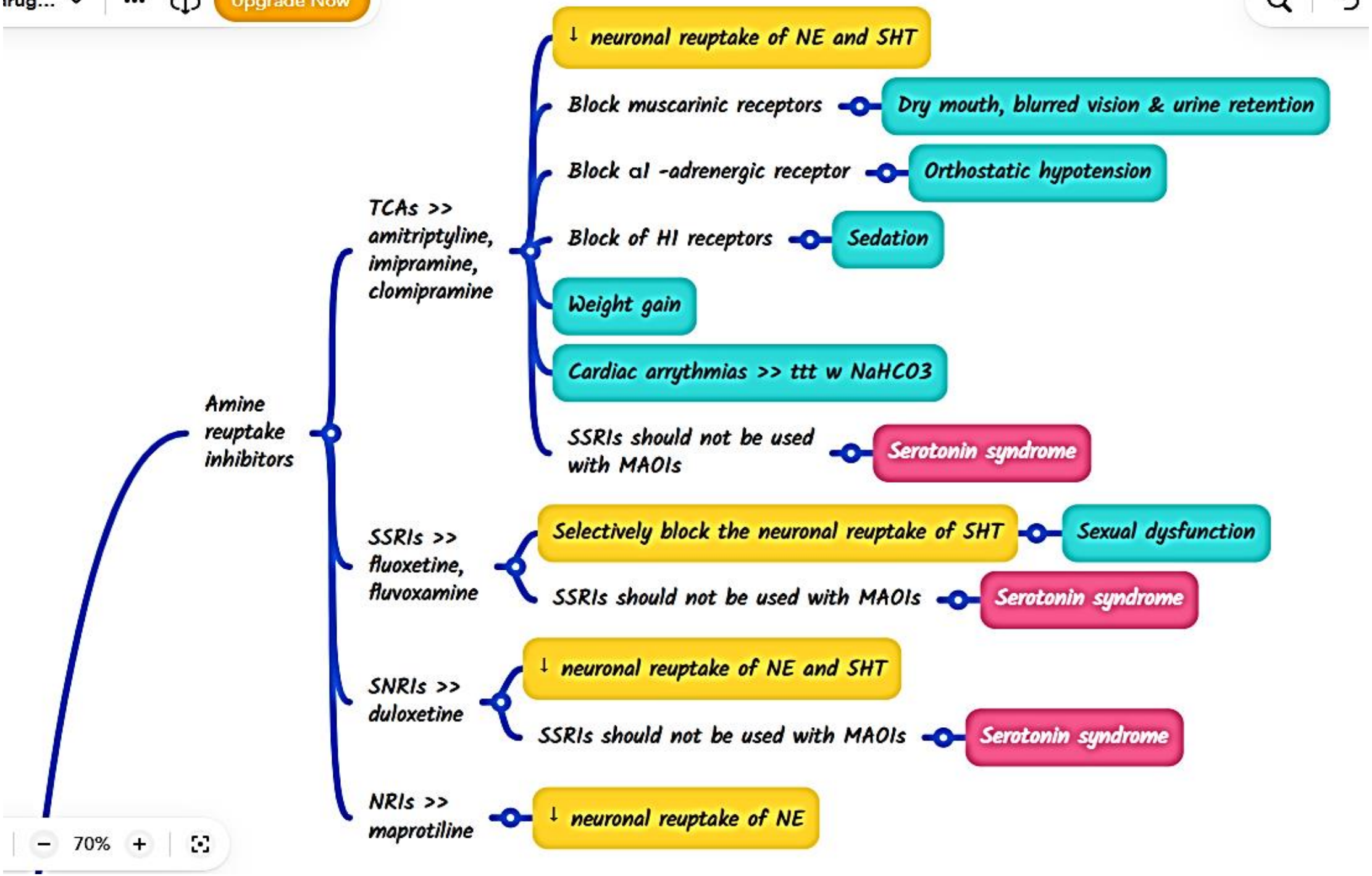
E. Lupoid syndrome

F. Erythematous skin rash

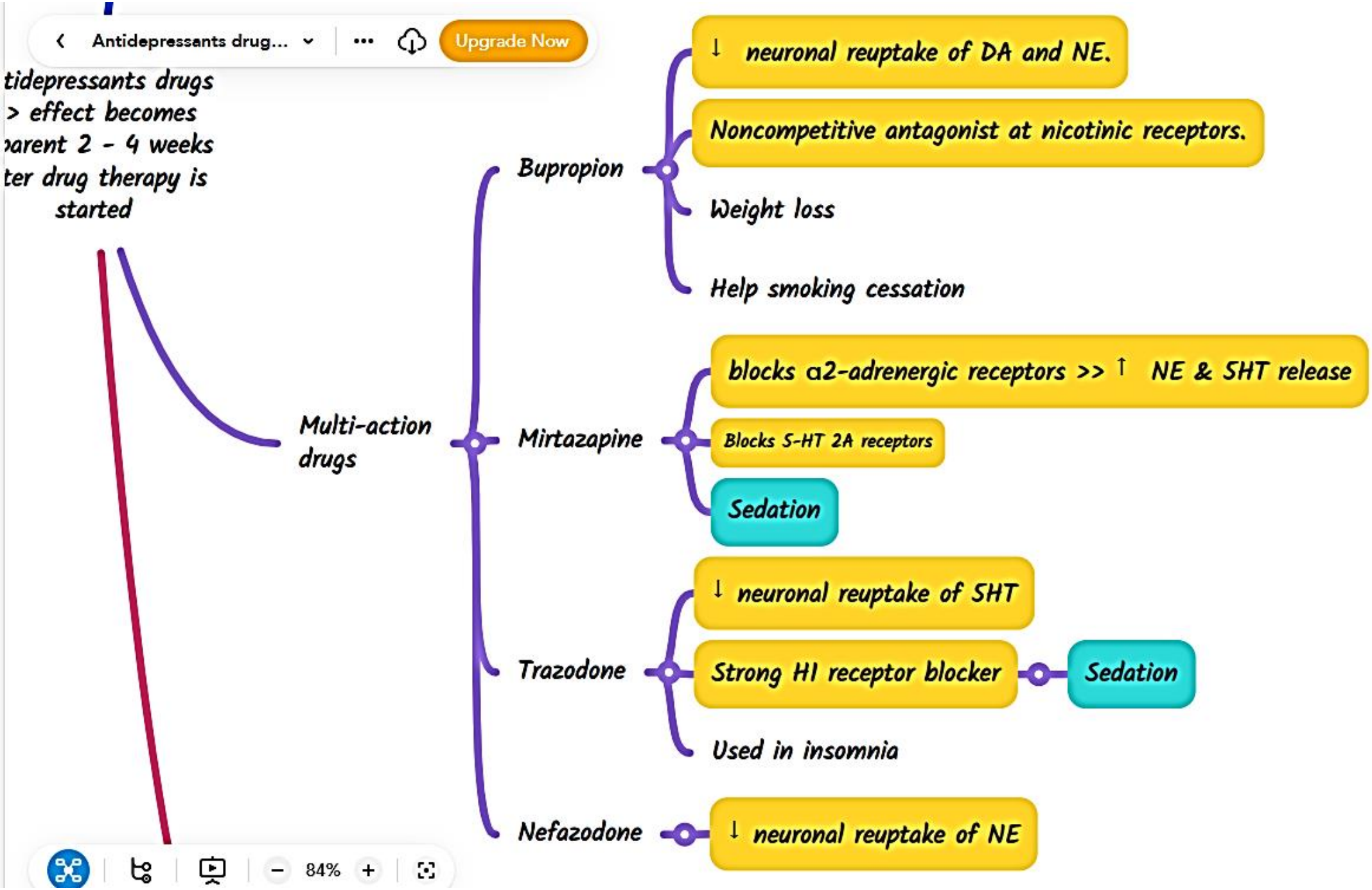
Antidepressants



Antidepressants



Antidepressants



Antidepressants

Monoamine oxidase inhibitors (MAOIs)

- Non-selective MAOi >> Phenelzine — Irreversible
- Selective MAO-Ai >> moclobemide — Reversible — metabolizes SHT
- Selective MAO-Bi >> selegiline — metabolizes DA >> Used in Parkinson disease
- interact with SSRIs & TCAs — Serotonin syndrome
- Cheese reaction

Question

A patient under treatment for a major depression is brought to the emergency department after ingesting 30 tablets of imipramine. Which of the following would be LEAST useful?

(A) Administer bicarbonate to correct acidosis.
(B) Administer lidocaine to control cardiac arrhythmias.
(C) Initiate hemodialysis to hasten drug elimination.
(D) Maintain heart rhythm by electrical pacing
(E) Use intravenous diazepam to control seizures

Question

A 36-year-old woman presents with symptoms of major depression. Drug treatment is to be initiated with sertraline. In your information to the patient, you would tell her that:

(A) Sertraline may take 2 wk or more to become effective
(B) It is preferable that she take the drug in the morning
(C) Insomnia is likely to decrease with continued use
(D) She should notify you if she anticipates using other prescription drugs
(E) All of the above

Question

Which drug is an antagonist at 5-HT2 receptors and can be used for the management of insomnia?

(A) Estazolam

(B) Flurazepam

(C) Trazodone

(D) Triazolam

(E) Zolpidem

Question

17-year-old girl was admitted to an eating disorder clinic with a 3-month history of binge eating and vomiting and purging episodes occurring from twice per week to four times a day. After physical examination and lab tests, psychotherapy and a drug treatment were prescribed. Which of the following drugs would be appropriate for this patient?

A. Fluoxetine
B. Diazepam
C. Phenobarbital
D. Haloperidol
E. Clozapine
F. Lithium

Question

A 38-year-old man complained to his physician that the drug he was taking was effective in relieving his anxiety but caused a disturbing adverse effect. The patient had been recently diagnosed with a social anxiety disorder and started treatment with venlafaxine 2 weeks ago. Which of the following adverse effects did the patient most likely experience?

A. Obstinate constipation

B. Negligible orgasm during intercourse

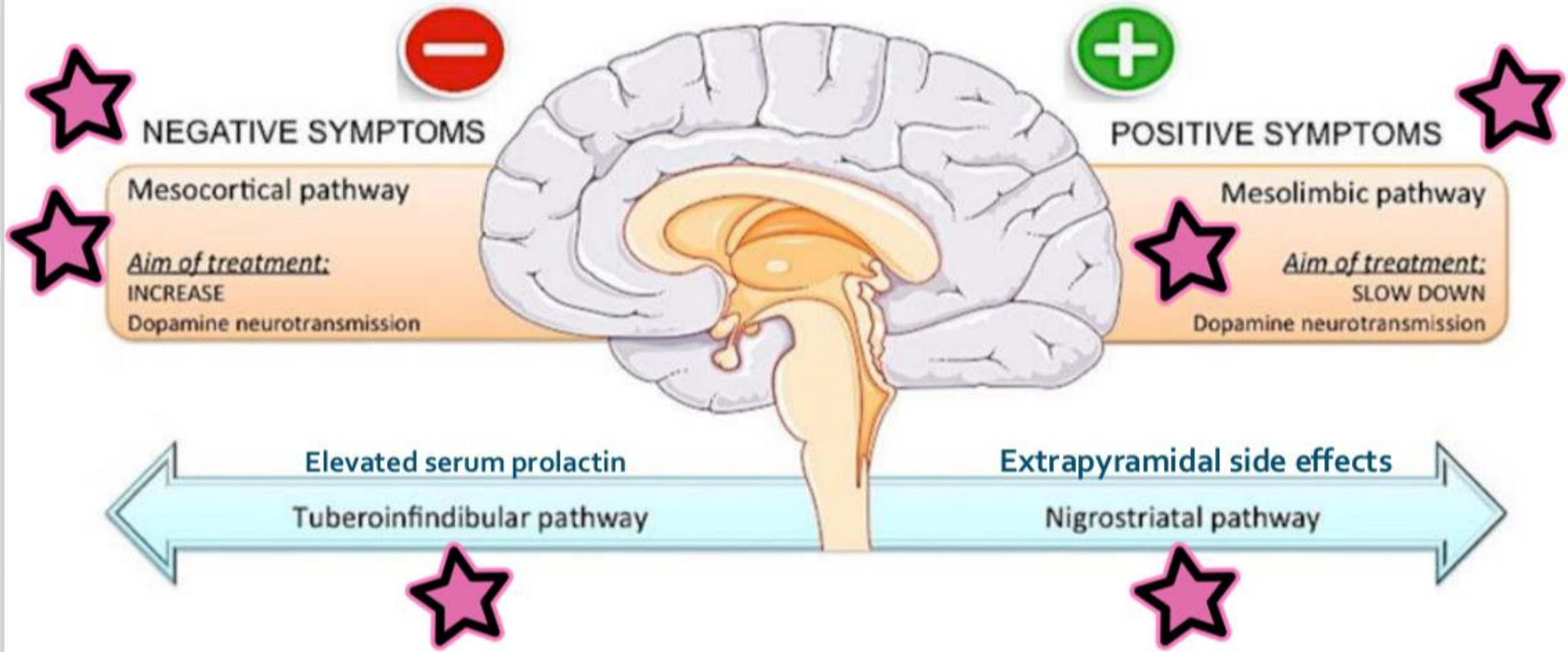
C. Urge urinary incontinence

D. Dizziness and vertigo upon standing

E. Dry mouth, most of the day

F. Difficulty in near vision

Dopamine hypothesis

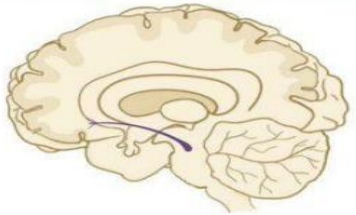


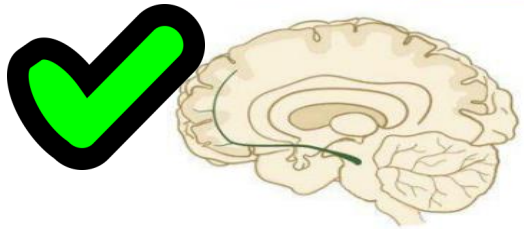
TYPICAL ANTIPSYCHOTICS

HIGH POTENCY
- ~ HALOPERIDOL
- ~ TRIFLUOPERAZINE
- ~ FLUPHENAZINE

LOW POTENCY
- ~ THIORIDAZINE
- ~ CHLORPROMAZINE
- ~ THIOTHIXENE

* BLOCK DOPAMINE D2 RECEPTORS in MESOLIMBIC
  ↳ ALLEVIATE POSITIVE SYMPTOMS

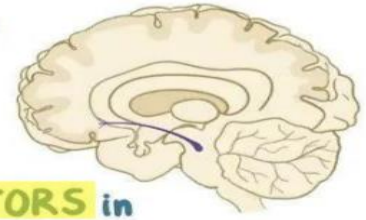


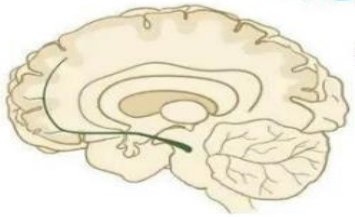


* BLOCK DOPAMINE RECEPTORS in MESOCORTICAL

ATYPICAL ANTIPSYCHOTICS

* BLOCK DOPAMINE D_2 RECEPTORS in MESOLIMBIC
  ↳ ALLEVIATE POSITIVE SYMPTOMS

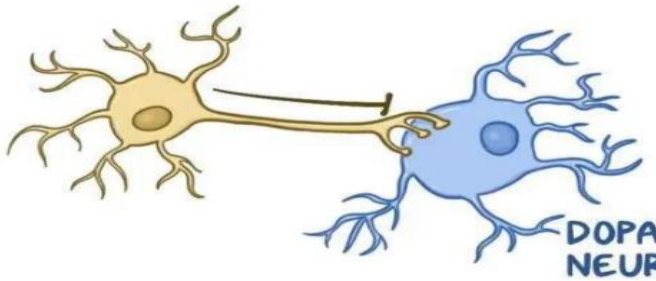




* BLOCK SEROTONIN 5-HT_{2A} RECEPTORS in MESOCORTICAL

ALLEVIATE NEGATIVE SYMPTONS

INHIBITORY NEURON



DOPAMINERGIC NEURON

Differentiate among the classes of antipsychotics drugs

	High-Potency Typical Agents	Low-Potency Typical Agents	Atypical Agents *
Prototype drug	Haloperidol	Chlorpromazine	Cariprazine, risperidone, olanzapine, aripiprazole, paliperidone, quetiapine, ziprasidone clozapine
EPS side effects	High incidence	Low incidence	Low incidence
ANS side effects †	Low incidence	High incidence	Medium incidence
Positive symptoms	Works well	Works well	Works well
Negative symptoms	Works poorly	Works poorly	Works fairly well

Individual differences ➔ Atypical antipsychotics

1. **Clozapine**

Its therapeutic effects result from ➔ blockade of 5-HT2 Rs and D4 Rs ➔ Greater activity against the negative symptoms + significantly fewer EPS

- Block H1, muscarinic, and α1 R ➔ significant sedation and autonomic side effects.
- Associated with a potentially fatal agranulocytosis ➔ mostly during the first-year after initiation ➔ FDA requires weekly monitoring of leukocyte counts during the first 6 months of therapy ➔ then biweekly

2. **Olanzapine** ➔ like clozapine, but

- Causes fewer autonomic side effects
- Has not been reported to cause agranulocytosis.

Individual differences ➔ Atypical antipsychotics

3. **Risperidone** ➔ like olanzapine, but

- Cause a higher incidence of EPS.
- Elevates levels of serum prolactin.
- lengthens the QT interval ➔ predispose patients to cardiac dysrhythmias, including torsade de pointes

4. **Aripiprazole** ➔ a partial agonist at D2R and 5-HT1 R but a 5-HT2 R antagonist

Question

A 34-year-old woman recently diagnosed with schizophrenia started treatment with haloperidol. Which of the patient's presenting symptoms was most likely best controlled after 1 week of therapy?

A. Social withdrawal
B. Lack of emotion
C. Low energy
D. Persecutory delusions
E. Affective flattening

Question

A 17-year-old boy presented with brief episodes of protruding tongue, grimacing, and spasmodic torticollis on day 2 after admission to the psychiatric emergency department. The patient was brought there by the police because of assaultive behavior toward his mother. A drug treatment was started to control his assaultive behavior, and he received three intramuscular injections over 24 hours. Which of the following drugs most likely caused the adverse effects reported by the patient?

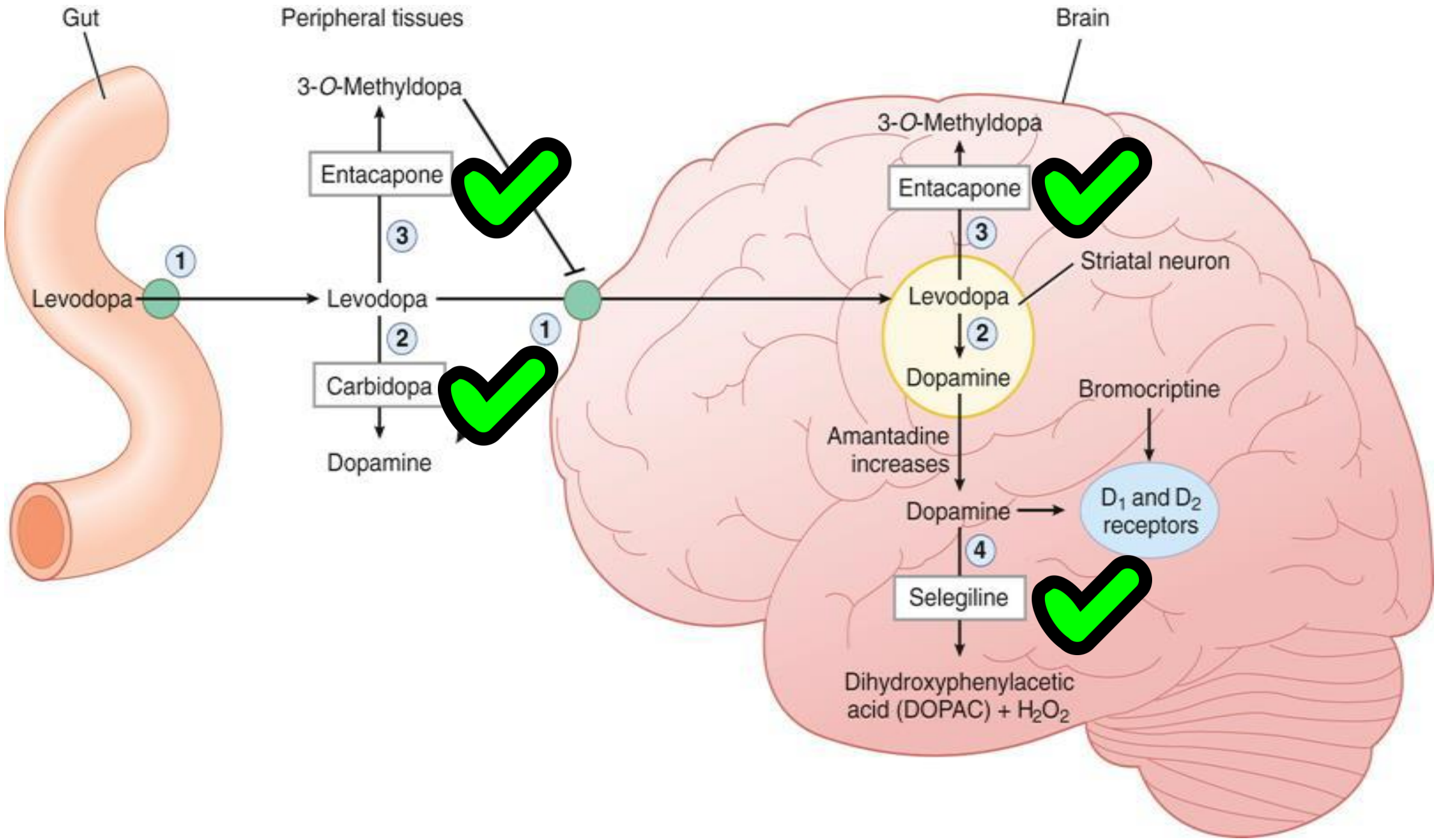
A. Haloperidol

B. Lorazepam

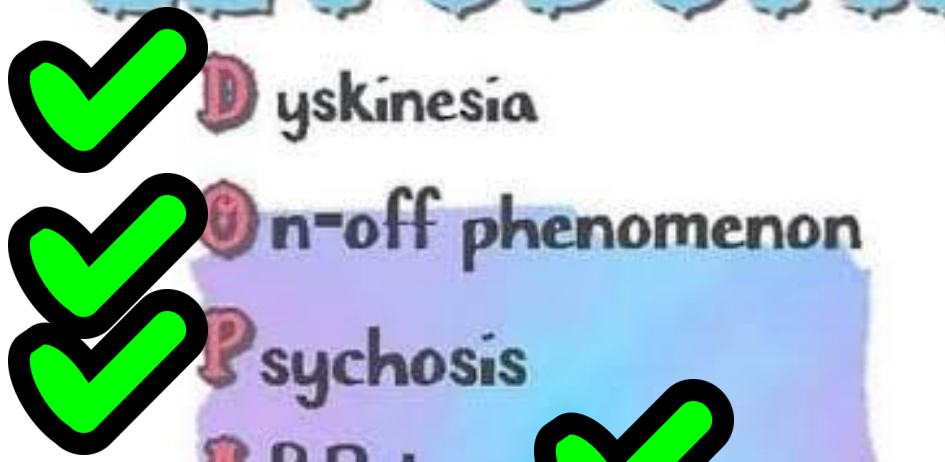
C. Buspirone

D. The large dose of ethanol

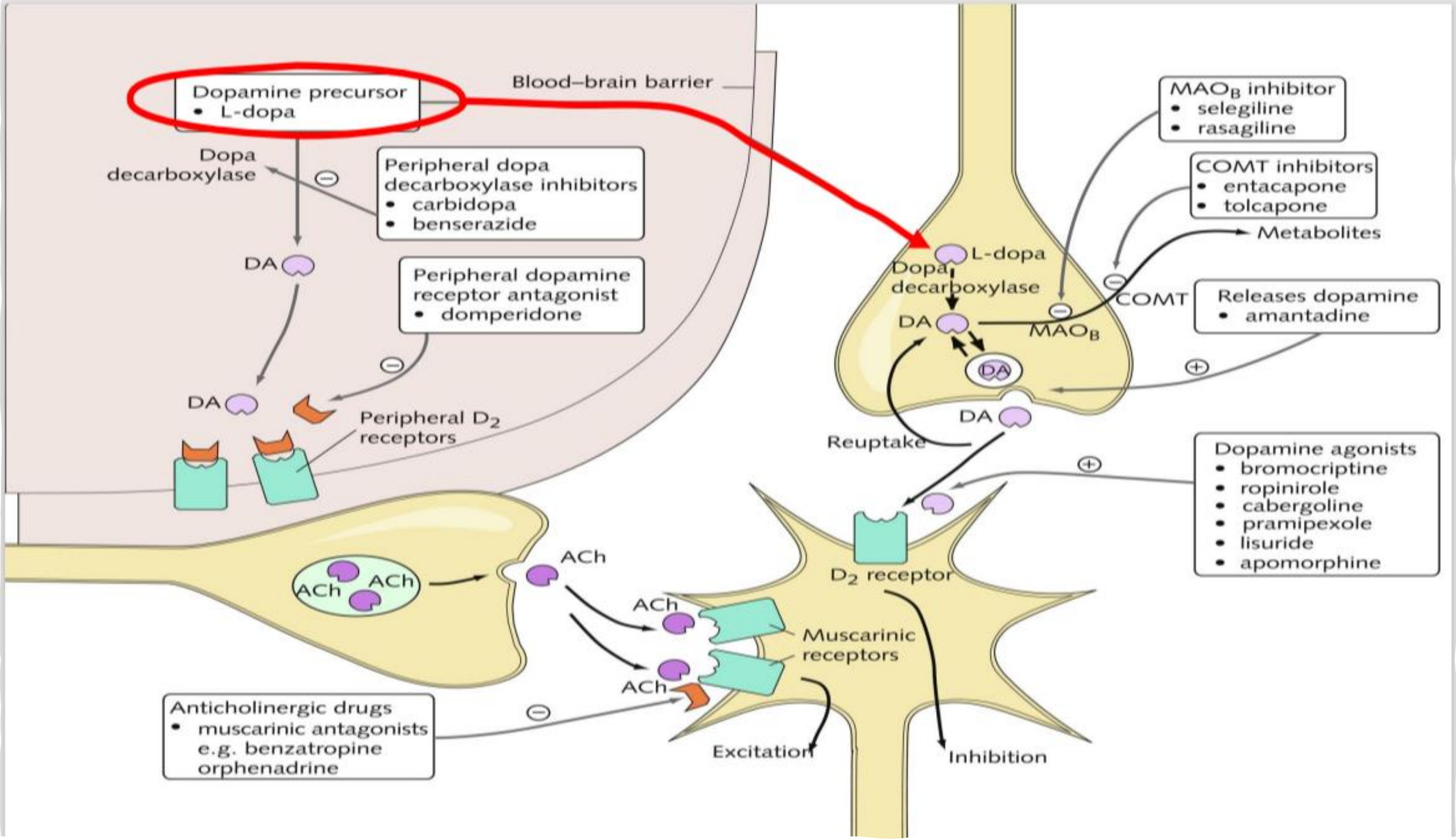
E. Clozapine


Gut
Peripheral tissues
Brain
3-O-Methyldopa
Entacapone
3
1
Levodopa
Levodopa
2
Carbidopa
Dopamine
1
3-O-Methyldopa
Entacapone
3
Striatal neuron
Levodopa
2
Dopamine
Bromocriptine
Amantadine increases
Dopamine
D1 and D2 receptors
4
Selegiline
Dihydroxyphenylacetic acid (DOPAC) + H2O2

SIDE EFFECTS OF LEVODOPA



- **D**yskinesia
- **O**n-off phenomenon
- **P**sychosis
- **A**BP drop
- **M**outh dryness
- **I**nsomnia
- **N**ausea/vomiting
- **E**xcessive daytime sleepiness


Dopamine precursor
• L-dopa
Blood–brain barrier
Dopa decarboxylase
Peripheral dopa decarboxylase inhibitors
• carbidopa
• benserazide
DA
Peripheral dopamine receptor antagonist
• domperidone
DA
Peripheral D_2 receptors
ACh
ACh
ACh
ACh
ACh
Anticholinergic drugs
• muscarinic antagonists e.g. benzatropine orphenadrine
Muscarinic receptors
Excitation
Inhibition
D_2 receptor
Dopamine agonists
• bromocriptine
• ropinirole
• cabergoline
• pramipexole
• lisuride
• apomorphine
Reuptake
DA
DA
DA
L-dopa
Dopa decarboxylase
DA
MAO_B
COMT
Metabolites
MAO_B inhibitor
• selegiline
• rasagiline
COMT inhibitors
• entacapone
• tolcapone
Releases dopamine
• amantadine

Question

A 62-year-old man complained to his physician of facial grimacing, lip smacking, and rocking of the trunk that occurred 1 to 2 hours after taking his prescribed medication. The man, who suffered from Parkinson disease, had been receiving an antiparkinsonian drug for 3 years. Which of the following drugs most likely caused the adverse effects reported by the patient?

A. Selegiline

B. Levodopa

C. Entacapone

D. Amantadine

E. Benztropine

Question

Tolcapone may be of value in patients being treated with levodopa-carbidopa because it

(A) Activates COMT

(B) Decreases the formation of 3-O-methyldopa

(C) Inhibits monoamine oxidase type A

(D) Inhibits neuronal reuptake of dopamine

(E) Releases dopamine from nerve endings

Question

With respect to pramipexole, which of the following is most accurate?

(A) Activates brain dopamine D2 receptors

(B) Effective as monotherapy in mild parkinsonism

(C) May cause postural hypotension

(D) Not an ergot derivative

(E) All of the above

Thank you