SECTION A

ANESTHETIC DRUGS

1

Local Anesthetics

Local anesthetics (LA) are drugs which upon local injection or topical application, cause a reversible loss of sensory perception, especially of pain, in a demarcated area of the body. These drugs prevent the generation and conduction of nerve impulses.

Classification of Local Anesthetics

A. INJECTABLE ANESTHETIC

1. ***Low potency & short duration:*** Chloroprocaine, Procaine
2. ***Intermediate potency and intermediate duration:*** Lidocaine (Lignocaine), Prilocain
3. ***High potency, long duration***: Bupivacaine, Dibucaine (Cinchocaine), Ropivacaine, Tetracaine (Amethocaine)

B. SURFACE ANESTHETIC

1. ***Soluble:*** Benoxinate, Cocaine, Lidocaine, Tetracaine
2. ***Insoluble:*** Benzocaine, Butylaminobenzoate (Butamben), Oxethazaine

A. INJECTABLE ANESTHETIC

LIGNOCAINE (LIDOCAINE)

Lignocaine is the most commonly used LA. It can be used as surface application as well as injection.

Brand Names

Lidocaine 2% & 4%: • Biocaine • Caligno • Gesicain • Lidfast • Lignocad • Lignocaine • Lox • Lox Heavy • Loxicard • Nummit • Oculan • Themicaine • Xylocaine • Xylocaine Adrenaline • Xynova • Xylocard

Lidocaine 5%: • Xylocaine

Lidocaine + Calcium Dobesilate + Hydrocortisone + Zinc: • Caldob • Dobesoft • Doboless • Eversmooth • Logisil-H • Pileplus • Pilo-Smooth • Pilowis • Retiver

Lidocaine + Adrenaline: • Anthacaine A • Biocaine ADR • Dentonum • Elscain • Lignomax AD • Lignopar Plus • Lignox • Themicaine AD • Xicaine

Lidocaine + Betamethasone + Chloramphenicol: • Otina

Lidocaine + Beclometasone + Clotrimazole + Chloramphenicol: • Candibiotic • Clozotic • Earwel • Glybiotic • Mycotic • Orecure Plus • Otek-AC Plus • Otidrop • Otocin • Perfocyn Plus

Contd...

Indications	Dosage
As jelly or ointment	(For local application): urethral catheterization, rectal, vaginal and ontological examination.
Topical spray	For bronchoscopy, (ENT) surgeries, obstetric and dental procedures.
Topical eye drops	In eye surgeries.
Surface application	2% jelly, 2% viscous, 5% solution.
Topical application	4% solution.
Local infiltration	0.5–1%: Without adrenaline up to 4.5 mg/kg can be given. With adrenaline, maximum dose can be increased (up to ~7 mg/kg).
Spinal anesthesia	1.5–5% solution, 1–2 mL given every 60–90 minutes. Total dose 25–100 mg.
Epidural anesthesia	2% solution is most frequently used; 2–3 mL administered for each dermatome which needs to be anesthetized.

Drug Interactions

Lignocaine should be cautiously used in patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) as the toxic effects are additive and potentially synergistic.

Adverse Effects: Drowsiness ♦ Dizziness ♦ Tinnitus ♦ Dysgeusia ♦ Twitching ♦ Seizures ♦ Respiratory depression and coma ♦ Cardiovascular depression ♦ Arrhythmias ♦ Bradycardia ♦ Cardiac arrest ♦ Allergic and anaphylactic reactions

Contraindication: Hypersensitivity to lignocaine or to any other amide type local anesthetic.

Considerations in

Pregnancy	• Can be used	**Elderly**	• Can be used
Lactation	• Use with caution	**Children**	• Use with caution

Nursing Considerations

- Assess fluid and electrolyte level (sodium, potassium and chloride); assess respiratory system for rate, rhythm, crackle sound, lung field; assess CNS (confusion, psychosis, giddiness, paresthesias, convulsions).
  - Monitor continuously for PR or QRS interval, if increased interval is observed, decrease or stop the administration of drug.
  - Monitor for ventricular ectopic beats and blood pressure.
  - Observe patient for malignant hyperthermia (increased body temperature, unstable BP, tachycardia, tachypnea).

Contd...

- Therapeutic blood level is 1.5–5 µg/mL.
- **Management of overdose:** Oxygen (O_2) supply, cardiac monitoring, mechanical ventilator, dopamine (to treat circulatory depression), thiopental or diazepam (to treat seizure).

LIGNOCAINE AND PRILOCAINE

Lignocaine and prilocaine are a unique combination (ratio of 1:1), which can anesthetize intact skin after surface application. This combination is an example of eutectic mixture, which refers to lowering of melting point of two solids when they are mixed together.

Eutectic mixture is formed by mixing lignocaine and prilocaine in equal amounts at 25°C and forming a cream.

Brand Names

• Asthesia • Delay Plus • Dolocaine • Emla • Epilido • Lidonair • Lovelong • Numbex • Prilox • Primla • RE Nopain • Toplap • Xyloplus • Xynova P • Xylap

Mechanism of Action: Similar to lignocaine/lidocaine

Available Forms: Cream/Ointment

Pharmacokinetics: Similar to those mentioned for lignocaine.

Indications and Dosage: *Local analgesia* (for normal intact skin), *minor surgical procedure over a genital mucous membrane as preanesthetic* (removal of condylomata acuminata).

Drug Interactions

Similar to those mentioned for Lignocaine.

Adverse Effects: Localized reactions ♦ Drowsiness ♦ Bradycardia ♦ Hypotension and cardiovascular arrest.

Contraindication and Considerations in (Pregnancy, Lactation, Elderly and Children) Similar to those mentioned for Lignocaine.

Nursing Considerations

- Assess skin for intactness.
- This drug should not be used if any wound or lesion is present.
- It is used for minor procedures such as IV cannulation, venepuncture, lumbar puncture, etc.
- Instruct patient not to rub or expose to heat or cold temperature and avoid any injury until regain of complete sensation.
- ***Instruction for patient/family member*** *regarding its application:* It is applied under occlusive dressing for 1 hour prior to IV cannulation; anesthetic lasts for about 2 hours up to a depth of 5 mm of skin. It is employed as an alternative to lignocaine infiltration.

Adverse Effects: Drowsiness ♦ Respiratory depression ♦ CNS depression ♦ Difficulty in breathing ♦ Shallow or weak breathing ♦ Cardiotoxic ♦ Brady/tachycardia ♦ Neurological deficit and allergic reaction.

Contraindications

- Hypersensitivity to bupivacaine or to any other amide type local anesthetic.
- IV regional anesthesia (Bier's block)
- Obstetrical paracervical block

Considerations in

Pregnancy	• Can be used; 0.75% concentration is contraindicated for obstetrical anesthesia, as there have been few reports of cardiac arrest with difficult resuscitation and death.
Lactation	• Use with caution
Elderly	• Can be used
Children	• Not recommended

Nursing Considerations

- Assess vital signs (temperature, pulse, respiration and BP); CNS status (dizziness, paresthesias, twitching, level of consciousness, irritability); GI system (bowel sound, metallic taste, gastritis); cardiovascular system (rate, rhythm, peripheral pulses, BP, dysrhythmias).
- W **Monitor for cardiotoxicity:** Myocardial depression, ventricular tachycardia, ventricular arrhythmia and cardiac arrest. Bupivacaine-induced cardiotoxicity can be difficult to treat and may be exacerbated by coexisting hypoxemia, acidosis and hypercarbia.
- Assess motor and sensory system before, during and after administration of the drug.
- **Instruct patient** to notify if signs and symptoms of toxicity occur (tingling sensation, numbness, ringing sensation in ears, blurred vision, decreased speech, tremors, irritability, seizure and cardiac dysrhythmias) occur.
- Assist patient during ambulation as patient may have orthostatic hypotension.

B. SURFACE ANAESTHETIC

BENZOCAINE

Benzocaine is an ester local anesthetic, prevents transmission of impulses through nerve fibers and at nerve endings.

It is a paraaminobenzoic acid (PABA) derivative; hence, it can antagonize sulfonamides at local site.

Brand Names

• Benzonac • Buz • Clear Wax • Mucopain • Mamdew Baby

Contd...

2 General Anesthetics and Preanesthetic Medication

General anesthetics (GA) are drugs which cause a reversible depression of all sensations as well as consciousness. The key features of general anesthesia include loss of all sensations, unconsciousness and amnesia, immobility and loss of somatic and autonomic reflexes.

The classification of general anesthetics is given below:

INHALATIONAL	INTRAVENOUS
• **Gas:** Nitrous oxide • **Liquids:** Desflurane, Ether, Enflurane, Halothane, Isoflurane, Sevoflurane.	• **Inducing drugs:** Etomidate, Methohexitone, Propofol, Thiopentone sodium. • **Slower-acting drugs:** ▪ *Benzodiazepines*—Diazepam ▪ *Dissociative anesthetics*—Ketamine ▪ *Opioid analgesics*—Fentanyl, Pethidine

INHALATIONAL ANESTHETICS

HALOTHANE

Halothane is a volatile liquid at room temperature and has a sweet odor. It is less commonly used for induction and maintenance of general anesthesia in children and for maintenance of anesthesia in adults.

Brand Names

• Fluothane • Halothane • Hypnothane

Mechanism of Action: Halothane acts *via* multiple ion channels, which ultimately depresses nerve conduction, breathing, and cardiac contractility. It binds potassium channels in cholinergic neurons resulting in an immobilizing effect. Hyperpolarization of NMDA and calcium channels also occur with halothane administration.

Available Form: Inhalational vapor-liquid

Pharmacokinetics: Halothane is marketed in amber-colored bottles with thymol added as a preservative. Approximately 60–80% of halothane is eliminated unchanged by the lungs; the remaining that enters the blood is metabolized in the liver. Halothane has a relatively high blood: Gas partition coefficient; the induction is therefore, relatively slow. As halothane is soluble in fat and other tissues, it

Mechanism of Action: Thiopentone binds with chloride (Cl) ionopore at GABAA receptors and prolongs the post-synaptic inhibitory effect of GABA, thereby resulting in anesthetic effects.

Available Form: **Injection:** 500 mg, 1000 mg, per vial

Pharmacokinetics: Following IV administration, unconsciousness occurs within 30 seconds and mostly lasts for 20–30 minutes after a single dose. Repeated IV doses lead to prolonged anesthesia because fatty tissues act as reservoir; they accumulate thiopental in concentrations 6–12 times higher than the plasma concentration and then slowly release the drug to cause prolonged anesthesia.

Thiopentone is mainly metabolized in the liver and the metabolites are excreted in the urine. The half-life of the distribution phase after a single intravenous dose is 2–4 hours and the half-life of the elimination phase is 9–11 hours.

Indications and Dosage

Indications	Dosage
• **Induction of general anesthesia prior to administration of other anesthetics.** • **As the sole anesthetic agent for brief (15-minute) procedures.** • **As an adjunct to provide hypnosis during balanced anesthesia with other anesthetics.** • **For the rapid control of convulsions (during or following anesthesia or other causes), status epilepticus.** • **For historical/rare use in psychiatric disorders.**	*Test dose:* 25–75 mg (1–3 mL of a 2.5% solution) IV. • *Induction dose:* For moderately slow induction—50–75 mg by slow IV injection at 20–40 seconds intervals. Once anesthesia is established, additional injections of 25–50 mg can be given whenever the patient moves. • *As a sole anesthetic:* Small repeated doses, as needed or by a continuous IV drip in a 0.2–0.4% concentration. • *For convulsive states:* 75–125 mg (3–5 mL of a 2.5% solution) should be given as soon as possible after the convulsion starts. Initially, 3–7 mg/kg, then 1 mg/kg, as required.

Drug Interactions

- *Steroids (including oral contraceptives), Warfarin, tolbutamide, Griseofulvin, theophylline:* Thiopentone induces liver enzymes; hence, may increase the elimination and decrease the plasma concentration of these drugs.

Contd...

- Monitor patient for allergic response (hypotension, bronchospasm, hives and facial edema).
- Monitor for thrombophlebitis.
- Assist patient during ambulation if drowsiness and dizziness occur.
- W **Instruct patient**, not to involve in hazardous activities, such as driving and other activities which require alertness; avoid sudden change in position (to prevent postural hypotension).
- Instruct patient not to use any OTC drug without physician's order (e.g., antihistamines); do not take this drug with alcohol or other CNS depressant.

PROPOFOL

Propofol is an oily liquid formulated for IV administration (as a 1% emulsion in soyabean oil, glycerol and egg phosphatide).

Brand Names

• Celofol • Diprivan • Fresofol • Hypro • Mct Rof • Neorof • Proanes • Profol • Profol Spiva • Rofol • Propofol • Propovan • Troypofol • Troypofol-Mct • Zyfol

Mechanism of Action: Propofol is thought to produce sedative/anesthetic effects by the positive modulation of the inhibitory function of the neurotransmitter GABA through ligand-gated $GABA_A$ receptors.

Available Form: **Injection:** 10 mg/mL, 20 mg/mL

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
IV	<40 seconds	Not known	Distribution—2–4 minutes, Elimination—30–60 minutes	~10 minutes

Indications and Dosage

Indications	Dosage
Induction and maintenance of general anesthesia:	**<55 years classified as ASA-PS I or II:** 2–2.5 mg/kg IV. Give in 40 mg boluses every 10 seconds until desired effect is achieved. **3–16 years classified as ASA-PS I or II:** 2.5–3.5 mg/kg IV. **Debilitated or ASA-PS III or IV patients:** 1–1.5 mg/kg IV. Give in 20 mg boluses every 10 seconds until desired effect is achieved.
Maintenance of general anesthesia	**<55 years:** 0.1–0.2 mg/kg/minute (4–12 mg/kg/hr) IV or 25–50 mg intermittent boluses.

Contd...

Nursing Considerations

- Assess history of allergies with drugs, drug interactions and previous use of drugs.
- Assess for hypersensitivity.
- Assess medical history of respiratory, cardiac and seizure disorders.
- Assess for increased intracranial pressure, pregnancy/lactation and any neurological condition (movements, tremor, dizziness, loss of consciousness).
- Monitor vital signs (especially pulse, respiration and BP) before, during and after the therapy.
- Advise patient that this drug may cause shivering and trembling, nausea/vomiting, headache and sleepiness.
- Monitor patient for allergic response (hypotension, bronchospasm and hives).
- Monitor for thrombophlebitis.
- Assist patient during ambulation if drowsiness and dizziness occur.
- Instruct patient, not to involve in hazardous activities, such as driving and other activities which require alertness; avoid sudden change in position (to prevent postural hypotension).
- Instruct not to use any OTC drug without physician's order (e.g., antihistamines); do not take this drug with alcohol or other CNS depressant.

SLOWER-ACTING DRUGS

BENZODIAZEPINES

DIAZEPAM

For details, Refer to Section B: Central Nervous System; Chapter 4: Sedatives and Hypnotics; page no. 55.

DISSOCIATIVE ANESTHETICS

KETAMINE

Ketamine is a congener of hallucinogen phencyclidine. It induces a state called *Dissociative anesthesia* characterized by profound analgesia, amnesia, immobility, patient appears conscious but is dissociated from surroundings, and a feeling of dissociation from own body and surroundings.

Brand Names

• Aneket • GB-Ket • Ketafast • Ketajet • Ketamax
• Ketamine Hydrochloride • Ketalar • Ketam • Ketmin • Ketanik
• Kmin • Kmine • Oblar

Mechanism of Action: Ketamine, is a nonselective, noncompetitive antagonist of the N-methyl-d-aspartate (NMDA) receptor, an ionotropic glutamate receptor.

Available Form: **Injection:** 50 mg/mL

Pharmacokinetics: Following IV administration, ketamine concentration has an initial slope (alpha phase) lasting around 45 minutes with a half-life of 10–15 minutes. This first phase corresponds clinically to the anesthetic effect of the drug. The elimination half-life of ketamine (beta phase) is 2–3 hours. Ketamine is mainly metabolized in the liver.

Indications and Dosage

Indications	Dosage
• **Induction of anesthesia prior to administration of General Anesthetics, Surgical Procedures that do not require Skeletal Muscle Relaxation.** • **Short procedures such as painful dressings, dilatation and curettage, dental extractions, etc.**	• ***Intravenous:*** 1–4.5 mg/kg by slow injection. The average amount required to produce 5–10 minutes of surgical anesthesia is 2 mg/kg. • ***Intramuscular:*** 6.5–13 mg/kg. The amount required to produce 12–25 minutes of surgical anesthesia is 10 mg/kg. A low initial IM dose of 4 mg/kg has been used in diagnostic procedures not involving intensely painful stimuli. • ***Maintenance:*** The maintenance dose should be adjusted according to the patient's anesthetic needs and whether an additional anesthetic agent is used.

Drug Interactions

- *Barbiturates, Narcotics:* Concomitant use with ketamine may prolong the recovery time from anesthesia.
- *CNS depressants:* Concomitant use can potentiate CNS depression and may increase the risk of respiratory depression. Use cautiously.

Adverse Effects: Increased blood pressure ♦ Tachycardia ♦ Bradycardia ♦ Arrhythmia ♦ Hypertonia ♦ Tonic and clonic movements ♦ Respiratory depression ♦ Anorexia ♦ Nausea and vomiting ♦ Emergence delirium (hallucinations, vivid dreams).

Contraindications

- Hypersensitivity to ketamine.
- Patients with hypertension, severe coronary or myocardial disease, cerebrovascular accident or cerebral trauma.

3 Skeletal Muscle Relaxants

Skeletal muscle relaxants are drugs that act either **Peripherally** (at muscle fiber/neuromuscular junction or directly acting skeletal muscle relaxants, e.g., Dantrolene) or **Centrally** (at cerebrospinal axis, e.g., Baclofen) to decrease muscle tone and/or result in paralysis. Other muscle relaxants are also mentioned.

PERIPHERALLY ACTING MUSCLE RELAXANTS

The classification of peripheral neuromuscular blockers is as follows:

A. Neuromuscular Blocking Drugs:

A.1. Nondepolarizing (competitive) blockers

a. *Long-acting:* Pancuronium, Pipecuronium, d-tubocurarine (d-TC), Doxacurium

b. *Intermediate-acting:* Vecuronium, Atracurium, Rocuronium, Cisatracurium.

c. *Short-acting:* Mivacurium.

A.2. Depolarizing blockers: Succinylcholine (suxamethonium), Decamethonium

B. Directly acting skeletal muscle relaxants—e.g., Dantrolene

NEUROMUSCULAR BLOCKING DRUGS

A.1. NONDEPOLARIZING (COMPETITIVE) BLOCKERS

The competitive blockers have affinity (but no intrinsic activity) for the nicotinic (NM) cholinergic receptors at the muscle end plate.

They block the action of ACh; hence, the muscle is not able to contract in response to nerve impulse.

The neuromuscular blockers are quaternary compounds; hence, they are not absorbed orally and do not cross the cell membranes or blood-brain barrier. They are mostly administered intravenously.

PANCURONIUM

Pancuronium has vagolytic effects and may increase HR and BP.

It is ~5 times more potent than d-TC and has a lower histamine releasing potential. It has a longer duration of action and is mainly eliminated by renal excretion.

Brand Names

• Neocuron • Panconium • Pancuronium Bromide • Panuron • Pavulon

Adverse Effects: Hyperkalemia ♦ Cardiac arrest ♦ Flushing ♦ Postoperative muscle pain ♦ Prolonged respiratory depression ♦ Bronchospasm ♦ Anaphylactic reactions ♦ Malignant hyperthermia ♦ Increased salivation.

Contraindications

- Hypersensitivity to succinylcholine.
- Stroke with paralysis (>72 hours).
- Personal or family history of malignant hyperthermia.
- Skeletal muscle myopathies.
- Chronic renal failure with hyperkalemia.
- Acute phase of injury following major burns, multiple trauma, upper motor neuron injury or skeletal muscle denervation.
- Neuromuscular diseases (GBS, MS).

Considerations in

Pregnancy	• Use only if clearly indicated and if the potential benefits outweigh the potential risks
Labor and delivery	• Succinylcholine is commonly used to provide muscle relaxation during cesarean section. • While small amount of succinylcholine is known to cross the placental barrier; under normal conditions, the amount of drug that enters fetal circulation (after a single dose of 1 mg/kg to the mother) should not endanger the fetus.
Lactation	• It is not known if the drug appears in breast milk. Use cautiously
Elderly	• Use with caution
Children	• Use with caution

Nursing Considerations

- **Assess vital signs:** Respiratory system—Rate, rhythm, airway, oxygen saturation, respiratory distress, and wheezing sound; pulse rate and BP.
- **Monitor electrolyte imbalance:** Magnesium and potassium; Cardiovascular system: rate, rhythm, ECG, tachycardia and BP continuously.
- **I&O ratio:** Frequency, retention of urine, hesitancy.
- **GI system:** Assess bowel sound and constipation.
- Assess respiratory system until patient completely recovers; this can be assessed by checking muscle strength (ask patient to cough and lift head and hand grip).
- Assess communication difficulty if any, during recovery from effect of drug. Postoperative stiffness is common which subsides soon after the therapy.
- W Monitor for allergic reaction such as rash, pruritus, and urticaria. If occurs stop administration of drug and inform the physician.
- W Keep emergency tray ready with drugs (atropine, neostigmine) and mechanical ventilator.

Nursing Considerations

- **Assess vital signs:** Respiratory system: Rate, rhythm, airway, oxygen saturation, respiratory distress, and wheezing sound; pulse rate and BP.
- **Monitor electrolyte imbalance:** Magnesium and potassium; Cardiovascular system: Rate, rhythm, ECG, tachycardia, and blood pressure continuously.
- **I&O ratio:** Frequency, retention of urine, hesitancy.
- **GI system:** Assess bowel sound and constipation.
- IM injection should not be given more than 5 mL into each gluteal muscle.
- Tell patient about dark brown/black/green color urine is normal during therapy.
- Assist patient during ambulation if drowsiness and dizziness occur.

W Instruct patient, not to get involved in hazardous activities, such as driving and other activities which require alertness; avoid sudden change in position (to prevent postural hypotension).

- Instruct patient not to use any OTC drug without physician's order (e.g., antihistamines); do not take this drug with alcohol or other CNS depressant.
- **Advise patient** to take medicine with meal/food (to avoid GI upset); prefer small frequent meals.
- **Teach patient** to take drug therapy as per physician's order, and do not double the dose.

A Advise patient to report if he/she experiences any of the following: Rash, nausea, fever, nasal congestion.

W Do not use in pregnancy. If used, weigh risk and benefits to mother and fetus.

B. BENZODIAZEPINE

DIAZEPAM AND OTHERS

Diazepam is the prototype drug in this group. It increases GABAergic transmission by acting on specific receptors in the brain. The muscle tone is decreased by supraspinal action. It is well-tolerated and does not cause gastric irritation, although a high incidence of sedation limits its use as a muscle relaxant. It is particularly useful in spinal injuries and tetanus. It is also commonly used for rheumatic disorders associated with muscle spasm.

Long-term use → dependence and withdrawal

For details, Refer to Section B: Central Nervous System, Chapter 4: Sedatives and Hypnotics; page no. 55.

C. CENTRAL α-2 AGONIST

TIZANIDINE

Tizanidine is an α_2 adrenergic agonist.

Contd...

- **Teach patient** to take drug therapy as per physician's order, and do not double the dose.

A Advise patient to report if he/she experiences any of the following: Change in stools or urine, difficulty in vision and swallowing.

D. GABA DERIVATIVE

BACLOFEN

Baclofen is a GABA-ergic agonist. Baclofen decreases spasticity in many neurological disorders such as multiple sclerosis, amyotrophic lateral sclerosis, spinal cord injuries, etc.

Brand Names

• Baclent • Baclesta • Baclodon • Baclof • Bacloren • Baclosure • Baclotop • Bizlo • Liofen • Lioresal • Lobaset • Riclofen • Spinobak

Mechanism of Action: Baclofen is an analogue of the inhibitory transmitter GABA and may exert its effects by stimulation of the $GABA_B$ receptor subtype. The main site of action is considered to be in the spinal cord. Baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by decreasing excitatory neurotransmitter release from afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect.

Available Form: **Tablets:** 10 mg, 20 mg, 25 mg, 30 mg

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	2–3 hours	2.5–4 hours	Not known

Indications and Dosage

Indications	Dosage
Spasticity in multiple sclerosis; spinal cord injury.	**>12 years:** Initially, 5 mg orally three times a day for 3 days; then 10 mg three times a day for 3 days; then 15 mg three times a day for 3 days; then 20 mg three times a day for 3 days. The daily dose may be further increased, based on the response, upto a maximum of 80 mg daily (20 mg four times a day).

Drug Interactions

CNS depressants—May have additive CNS depressant effects, avoid using together.

Adverse Effects: Drowsiness ♦ Dizziness ♦ Hypotension ♦ Nausea ♦ Constipation ♦ Dry mouth ♦ Respiratory depression.

Contraindication: Hypersensitivity to Baclofen.

Considerations in

Pregnancy	• Use only if the potential benefits outweigh the potential risks
Lactation	• Drug appears in breast milk • Use with caution
Elderly	• Use with caution in lower doses
Children	• Not recommended in children <12 years of age

Nursing Considerations

- **Assess in multiple sclerosis condition:** Muscle spasm, muscle spasticity and ataxia.
- **Assess vital signs**: Respiration, pulse rate and BP.
- **I&O ratio:** Frequency, retention of urine, hesitancy.

W Monitor for allergic reaction such as rash, pruritus, fever, and respiratory distress.

- Monitor for tolerance (pain does not relieved/increase dose).

W **Monitor for withdrawal symptoms:** Dizziness, CNS depression, psychosis.

- Instruct patient not to discontinue the therapy suddenly, it may cause spasticity, hallucination and tachycardia; teach about tapering of doses as per physician's order.
- Assist patient during ambulation if drowsiness and dizziness occur.
- Instruct patient not to use any OTC drug without physician's order (e.g., antihistamines); do not take this drug with alcohol or other CNS depressant.

A Advise patient to report if he/she experiences any of the following: Nausea, tinnitus, headache, confusion, insomnia, painful urination, constipation.

OTHER MUSCLE RELAXANTS

DICYCLOMINE

Dicyclomine is a tertiary amine having direct smooth muscle relaxant action. Additionally, it has weak anticholinergic action.

For details, Refer to Section G: Gastrointestinal System; Chapter 35: Antiemetics, Antispasmodics, Prokinetics and Drugs Used in Irritable Bowel Syndrome; page no. 660.

SECTION B

CENTRAL NERVOUS SYSTEM

4

Sedatives and Hypnotics

SEDATIVE

Sedative is a drug that reduces activity, decreases excitement and calms the person without inducing sleep.

HYPNOTIC

Hypnotic is a drug that produces drowsiness and promotes the onset and maintenance of a state of sleep. The sleep resembles natural sleep from which the patient can be aroused easily.

The sedatives and hypnotics are usually CNS depressants with somewhat different dose-response relationships. The drugs having faster onset and steeper dose-response effects are preferred as hypnotics while the drugs having slower onset and flatter dose-response effects are preferred as sedatives. A hypnotic at lower doses may function as a sedative. Hence, sedation-hypnosis-general anesthesia may be considered as increasing levels of CNS depression.

Some of the important sedatives and hypnotics can be classified as follows:

A. Barbiturates	a. *Long acting:* Phenobarbitone b. *Short acting:* Pentobarbitone c. *Ultra-short acting:* Thiopentone, Methohexitone.
B. Benzodiazepines	a. *Hypnotic:* Diazepam, Flurazepam, Nitrazepam, Triazolam, Temazepam, estazolam b. *Antianxiety:* Diazepam, Chlordiazepoxide, Alprazolam, Lorazepam, Oxazepam, Etizolam* c. *Anticonvulsant:* Diazepam, Lorazepam, Clobazam, Clonazepam, Midazolam
C. Nonbenzodiazepines	a. *Hypnotic:* Zaleplon, Eszopiclone b. *Antianxiety:* Zolpidem, Zopiclone
D. Benzodiazepine antagonist	Flumazenil
E. Other drugs	Melatonin, Ramelteon, Chloral hydrate.
F. Benzodiazepines (according to the duration of action)	a. *Short-acting, (<8 hours):* Triazolam, Oxazepam, Midazolam b. *Intermediate-acting (8–24 hours):* Alprazolam, Etizolam, Estazolam, Temazepam, Lorazepam c. *Long-acting (>24 hours):* Diazepam, Flurazepam, Clonazepam, Chlordiazepoxide, Nitrazepam

*Etizolam is a thienodiazepine, not a true benzodiazepine

Considerations in

Pregnancy	• Similar to diazepam
Lactation	• Drug is excreted in breast milk • Use during lactation should be avoided
Elderly	• Similar to diazepam
Children	• Not recommended for use in children

Nursing Considerations

Similar to those mentioned for Diazepam *(Refer to page no. 56)*

ALPRAZOLAM

Alprazolam is a short-acting, a triazolo analog of benzodiazepine. It is mainly used in anxiety disorder and panic disorder.

It also has some mood-elevating effect in mild depression and is, therefore, particularly useful in anxiety states associated with depression.

Brand Names

• Alark • Alprax • Alprocontin • Alrif • Alzolam • Alzam • Alzolam/ Alzolam SR • Alzy-1 SR • Alzy • Anzilum • Ateez • Kaprolam • Pralam • Restyl • Sowel • Trika • Tranisol • Xyclalm • Zany • Zenax • Zolam Zoldac • Zolax • Zolipax SR

Mechanism of Action: Alprazolam exerts CNS depressant effect, which occurs due to its potentiation of the action of inhibitory neurotransmitter GABA in the CNS. Alprazolam acts at GABA receptor to open chloride channel allowing chloride ions to flow into neurons resulting in an inhibitory potential that reduces ability of neurons to depolarize.

The effects of alprazolam may result from action in the limbic and subcortical levels of the CNS.

Available Forms: **Tablets:** 0.25 mg, 0.5 mg, 1 mg
Tablets (extended-release): 0.5 mg, 1 mg, 1.5 mg

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	1–2 hours	12–15 hours	Not known
Oral (Extended-release)	Not known	Not known	11–16 hours	Not known

Indications and Dosage

Indications	Dosage
Anxiety disorders and short-term relief from anxiety symptoms, anxiety associated depression, panic disorders.	Start with 0.25–0.5 mg orally 3 times a day; maximum dose usually ≤4 mg/day (higher only under specialist care).

Drug Interactions

- *Opioids:* Concurrent use of benzodiazepines may result in profound sedation, respiratory depression, coma and death.
- *Alcohol/CNS depressants:* Concurrent use may cause additive CNS depression.

Adverse Effects: The adverse effects, if they occur, are generally observed at the beginning of therapy and usually disappear on continued therapy or decreased dosage. The common adverse effects include drowsiness ♦ Light-headedness ♦ Headache ♦ Depression and GIT adverse effects.

Contraindications

- Hypersensitivity to alprazolam or any other benzodiazepine.
- Acute narrow-angle glaucoma.
- Concurrent use with strong CYP3A inhibitors (e.g., ketoconazole, itraconazole).

Considerations in

Pregnancy	• Drug may cause fetal harm when used during pregnancy. Use not recommended • If used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus • There have been reports of neonatal hypotonia, hypoactivity, respiratory and feeding difficulties, hypothermia, and withdrawal symptoms in children born to mothers who received benzodiazepines late in pregnancy
Lactation	• Drug appears in breast milk • Use during lactation is not recommended
Elderly	• Use with caution, initiate therapy in reduced dosage
Children	• Not recommended in children. Safety and effectiveness have not been established.

Mechanism of Action: Similar to Chlordiazepoxide

Available Forms: **Tablets:** 1 mg, 2 mg **Injection:** 2 mg/mL

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	1 hour	2 hours	12–18 hours	12–24 hours
IV	5 minutes	1–1.5 hours	12–18 hours	6–8 hours

Indications and Dosage

Indications	Dosage
Anxiety disorders and short-term relief from anxiety symptoms, Short-term treatment of insomnia, preoperative sedation, status epilepticus	2–3 mg/day in divided doses; maximum 10 mg/day **or debilitated patients:** 1–2 mg orally daily in divided doses, to be adjusted as required and tolerated.

Drug Interactions

- Concurrent use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma and death.
- Concurrent use with CNS depressants drugs/alcohol may cause additive CNS depression.
- Use with *Clozapine* may cause marked sedation, excessive salivation, hypotension, ataxia and delirium.
- Valproate may inhibit glucuronidation of Lorazepam and increase its plasma levels.

Adverse Effects: Similar to those mentioned for diazepam.

Contraindications

- Hypersensitivity to Lorazepam or any other Benzodiazepine.
- Severe respiratory insufficiency, sleep apnea syndrome.
- Acute narrow-angle glaucoma.

Considerations in

Pregnancy
- There have been reports of neonatal hypotonia, hypoactivity, respiratory and feeding difficulties, hypothermia, and withdrawal symptoms in children born to mothers who received benzodiazepines late in pregnancy.
- Avoid use during pregnancy except in life-threatening conditions (such as status epilepticus) where safer drugs cannot be used or are ineffective.

Lactation
- Drug appears in breast milk
- Use during lactation is not recommended

Contd...

MIDAZOLAM

Midazolam is a faster and short-acting benzodiazepine. It is 3 times more potent than diazepam. It is being preferred over diazepam for use during anesthesia.

Brand Names

• Fulsed • Mezolam • Midaz • Midosed • Sedoz • Shortal

Mechanism of Action: Midazolam exerts CNS depressant effect, which occurs due to its potentiation of the action of inhibitory neurotransmitter GABA in the CNS. It acts at GABA receptor to open chloride channel allowing chloride ions to flow into neurons resulting in an inhibitory potential that reduces ability of neurons to depolarize. The effects of midazolam may result from action in the limbic and subcortical levels of the CNS.

Available Form: **Injection:** 1 mg/mL, 5 mg/mL

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
IV	1.5–5 minutes	20–60 minutes	2–6 hours	2–6 hours
IM	5–15 minutes	20–60 minutes	2–6 hours	2–6 hours

Indications and Dosage

Indications	Dosage
• **Sedation during preoperative phase, before intubation.** • **Moderate sedation prior to short diagnostic or endoscopic procedures.**	**<60 years:** Preoperative sedation—0.07–0.08 mg/kg IM, up to 1 hour before surgery. **>60 years:** Preoperative sedation—0.02–0.05 mg/kg IM, up to 1 hour before surgery. 0.1–0.15 mg/kg IM, up to a maximum of 10 mg.

Adverse Effects, Contraindications and Considerations in (Pregnancy, Lactation, Elderly and Children)

Similar to those mentioned for Diazepam (*page no. 56*).

Nursing Considerations

- **Assess vital signs:** Pulse, BP, respiration.
- Assess CBC, LFT, RFT and creatinine.
- Assess history of respiratory disorders, cardiac disorder and neurological conditions.

Contd...

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral*	30 minutes	1 hour	1 hour	Not known

*Oral bioavailability is approx. 30% because of extensive first-pass metabolism.

Indications and Dosage

Indications	Dosage
Short-term treatment of insomnia	10 mg orally daily at bedtime, maximum dose should not exceed 20 mg/day. **and debilitated patients:** 5 mg orally daily at bedtime. Dose >10 mg/day are not recommended.

Drug Interactions

- *Opioids:* Concurrent use may result in respiratory depression, coma and death.
- *CNS depressants/alcohol:* Concurrent use may cause additive CNS depression.

Adverse Effects: Headache ♦ Dizziness ♦ Somnolence ♦ Depression ♦ Nervousness ♦ Abnormal thinking ♦ Nausea ♦ Dry mouth ♦ Constipation and abdominal pain.

Contraindications

- Hypersensitivity to Zaleplon.
- Severe hepatic impairment.

Considerations in

Pregnancy	• Use during pregnancy is not recommended
Lactation	• Drug appears in breast milk in small amounts • Use during breastfeeding is not recommended
Elderly	• Use with caution in reduced dosage
Children	• Not recommended in children. Safety and effectiveness have not been established

Nursing Considerations

- **Monitor psychological status:** Anxiety level (precipitating and alleviating factors) mental status (mood, suicidal behavior, sleeping pattern) and memory (short-term and long-term) need to be assessed.
- Assess history of sleep disorder: Sleep pattern, sleeping and waking up time, time spent on bed.
- Instruct patient to avoid OTC drugs, alcohol, other psychotropic drugs

Contd...

Indications and Dosage

Indications	Dosage
Insomnia, elderly patients, severe hepatic impairment	1 mg orally daily immediately before bedtime; maximum dose 3 mg. **In and hepatic impairment:** 1 mg.

Drug Interactions

- Concurrent use with CNS depressants/alcohol may cause additive CNS depression.
- Concurrent use with *Olanzapine* may impair memory or cognitive function.

Adverse Effects: Headache ♦ Dizziness ♦ Somnolence ♦ Nervousness ♦ Abnormal dreams ♦ Dry mouth ♦ Nausea ♦ Unpleasant taste ♦ Respiratory infections ♦ Urinary tract infections ♦ And decreased libido.

Contraindication: Hypersensitivity to Eszopiclone.

Considerations in

Pregnancy	• Use only if potential benefits outweigh the potential risks to the fetus
Lactation	• It is not known if the drug appears in breast milk • Use in breastfeeding women is not recommended
Elderly	• Use with caution in reduced dosage
Children	• Not recommended in children. Safety and effectiveness have not been established.

Nursing Considerations

- **Assess history of sleep disorder:** Sleep pattern, sleeping and waking up time, time spent on bed.
- **Monitor psychological status:** Anxiety level (precipitating and alleviating factors); mental status (mood, suicidal behavior, sleeping pattern) memory (short-term and long-term) need to be assessed.
- Instruct patient to avoid OTC drugs, alcohol, other psychotropic drugs.
- W Inform patient that drowsiness may occur; do not involve in hazardous activities, such as driving and other activities which require alertness; avoid sudden change in position (to prevent postural hypotension).
- **Instruct patient** to avoid use of fat diet during therapy.
- Instruct patient not to change doses (double) or discontinue drug without physician's order; plan and teach patient and family members about tapering of doses gradually.
- Instruct patient to take this drug with meal.

Contd...

- Instruct patient to use additional contraceptive method; to notify if pregnancy occurs.

A Advise patient to report if he/she experiences any of the following: Memory problem, changes in behavior, difficulty or change in sleep/eating/driving.

ZOLPIDEM

Zolpidem is one of the most commonly used drugs for short-term treatment of insomnia.

Brand Names

• Ambiz • Insom-ZD • Nitrest • Sove • Zleep • Zoldem • Zolfresh • Sobrium • Zem • Zolfresh SR • Zolo • Zolvi

Mechanism of Action: Zolpidem preferentially binds to the α_1 subunit of the $GABA_A$ receptor complex and is mainly used for the short-term treatment of insomnia.

Available Form: **Tablets:** 5 mg, 10 mg
Tablets (Extended-release): 6.25 mg, 12.5 mg

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Rapid	1.6 hours	2.6 hours	6–8 hours

Indications and Dosage

Indications	Dosage
Short-term treatment of insomnia.	5 or 10 mg orally once per night immediately before bedtime. Initial 5 mg, maximum 10 mg/day.

Drug Interactions

- Concurrent use with *Opioids* may result in respiratory depression, coma and death.
- Concurrent use with *CNS depressants/alcohol* may cause excessive CNS depression.
- *Use with Rifampicin* decreases the exposure and effectiveness of Zolpidem.
- *Use with Ketoconazole, Itraconazole may* increase the plasma levels of zolpidem.

Adverse Effects: Insomnia ♦ Headache ♦ Drowsiness ♦ Dizziness ♦ Back pain ♦ Chest pain ♦ Urinary tract infection ♦ Dry mouth ♦ Diplopia.

Contraindication: Hypersensitivity to Zolpidem.

D. BENZODIAZEPINE ANTAGONIST

Flumazenil is a competitive antagonist of the BZD receptor and is currently the only member available in this class.

FLUMAZENIL

It is mainly used to reverse the sedative effects of BZDs in conscious sedation, in general anesthesia and in patients with BZD overdose.

Brand Name

- Anexate

Mechanism of Action: Flumazenil, a BZD analog, is a competitive inhibitor of the BZD receptor (antidote for benzodiazepine). It competes with BZD agonists for the BZD receptor and reverses their depressant effect.

Available Form: **Injection:** 0.5 mg/5 mL

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
IV	1–2 minutes	6–10 minutes	Initial—4–11 minutes Terminal—40–80 minutes	Not known

Indications and Dosage

Indications	Dosage
Reversal of conscious sedation and Reversal of general anesthesia	Initially, 0.2 mg (2 mL) administered IV over 15 seconds
Reversal of conscious sedation	**>1 year:** Initially, 0.01 mg/kg (up to 0.2 mg) administered IV over 15 seconds
Benzodiazepine overdose	Initially, 0.2 mg (2 mL) administered IV over 30 seconds. • If the desired level of consciousness does not occur after waiting for 30 seconds, a further dose of 0.3 mg (3 mL) can be given over another 30 seconds. • Further doses of 0.5 mg (5 mL) can be given over 30 seconds at 1 minute interval up to a cumulative dose of 3 mg.

Drug Interactions

Flumazenil reverses/antagonizes the central effects of BZDs as well as nonbenzodiazepine agonists acting *via* the benzodiazepine receptor (such as zopiclone), by means of competitive interaction at the receptor level. However, flumazenil does not block the effect of medicines that do not act *via* BZD receptors.

6 Antidepressant and Antianxiety Drugs

ANTIDEPRESSANT DRUGS

Depression and anxiety are common mental disorders. Around 10–15% of people experience depression at some point in life. Depression may be classified into either major depression (unipolar depression) or manic-depressive illness (bipolar depression). The important classes of drugs used in the treatment of depression are classified here and details analysis of important classes are given.

CLASS	DRUGS
I. Selective serotonin reuptake inhibitors (SSRIs)	Fluoxetine, Fluvoxamine, Paroxetine, Sertraline, Citalopram, Escitalopram, it is used for premature ejaculation
II. Serotonin-norepinephrine reuptake inhibitors (SNRIs)	Venlafaxine, Desvenlafaxine, Duloxetine, Levomilnacipran
III. Tricyclic antidepressants (TCAs)	Amitriptyline, Nortriptyline, Imipramine, Clomipramine, Trimipramine, Dothiepin, Doxepin, Amoxapine, Reboxetine, Desipramine
IV. Reversible inhibitors monoamine oxidase (RIMAs)	Moclobemide
V. Atypical/Newer antidepressants	Bupropion, Mianserin, Mirtazapine, Tianeptine, Trazodone, Amoxapine, Amineptine, Atomoxetine, Maprotiline, Reboxetine

I. SELECTIVE SEROTONIN REUPTAKE INHIBITORS

Selective serotonin reuptake inhibitors (SSRIs) are a class of drugs whose main action is to increase the level of serotonin in the synaptic cleft. SSRIs selectively inhibit the serotonin reuptake transporter (SERT), thereby inhibiting the reuptake (clearance) of serotonin. SSRIs/SNRIs are known as second-generation antidepressant drugs.

FLUOXETINE

Fluoxetine is the prototype of SSRIs. It is longest-acting drug as compared to other SSRIs.

Contd...

Indications	Dosage
Depressive episodes associated with bipolar I disorder (with olanzapine)	Start with 20 mg fluoxetine orally + 5 mg olanzapine orally, once daily in the evening. Dose adjustments may be made, if required (as per efficacy and tolerability) within dose ranges of fluoxetine 20–50 mg and olanzapine 5–12.5 mg. **10–17 years:** Start with 20 mg fluoxetine orally + 2.5 mg olanzapine orally, once daily in the evening. Dose adjustments may be made, if required (as per efficacy and tolerability) within dose ranges of fluoxetine 20–50 mg and olanzapine 5–12 mg.
Treatment resistant depression (with olanzapine)	Start with 20 mg fluoxetine orally + 5 mg olanzapine orally, once daily in the evening. Dose adjustments may be made, if required (as per efficacy and tolerability) within dose ranges of fluoxetine 20–50 mg and olanzapine 5–20 mg.

Drug Interactions

- Use of this drug with *MAO inhibitors, serotonergic drugs (e.g., Triptans, TCAs, other SSRIs or SNRIs, fentanyl, amphetamines, buspirone, lithium, tramadol, tryptophan)* may cause serotonin syndrome and signs and symptoms of neuroleptic malignant syndrome.
- Use of this drug with *NSAIDs, aspirin, warfarin may increase the risk of bleeding.*
- Use of this drug may increase the plasma *levels Anticonvulsants (phenytoin, carbamazepine, tamoxifen) and the risk of toxicity of these anticonvulsant drugs.*
- In patients on insulin and oral hypoglycemic drugs, fluoxetine may alter glycemic control.

Adverse Effects: Insomnia ♦ Somnolence ♦ Nervousness ♦ Anxiety ♦ Headache ♦ Tremor ♦ Fatigue ♦ Palpitations ♦ Nausea ♦ Diarrhea ♦ GI complaints ♦ Sweating ♦ Sexual dysfunction.

Contraindications: Hypersensitivity, lactation—use with caution, not absolute contraindication.

Considerations in

Pregnancy	• Fluoxetine should be used during pregnancy only if the potential benefits clearly outweigh the potential risks to the fetus
Lactation	• Drug appears in breast milk • Use during breastfeeding is not recommended
Elderly	• Can be used with caution
Children	• Not recommended for use in children <8 years in major depression and <7 years in OCD

Nursing Considerations

- **Assess mental status examination and mental health history:** Mood, affect, memory, behavior, sensorium, suicidal thoughts, psychiatric symptoms, depression, panic, seizures, s/s of obsessive-compulsive disorder.
- **Assess s/s of serotonin syndrome:** Elevated body temperature, hypertension, muscle rigidity/cramps, nausea/vomiting, facial flush, sweating, delirium, decreased LOC, agitation, tremors, and metal change.
- Assess CBC (platelets, s/s of bleeding), LFT (Bilirubin, ALT, AST), RFT (creatinine, BUN); cardiac enzymes and daily weight.
- Assess vitals: Pulse, BP (standing and lying position) every 4 hours, respiration; drop in BP and respiration should be informed to the treating consultant.
- Assess the level of appetite and constipation during therapy; use of this drug may reduce appetite and can cause constipation.
- **Sexual problems:** Ejaculation dysfunction, decreased libido, erectile problem and orgasm dysfunction.
- W Instruct patient NOT to involve in machinery or hazardous activities, such as driving and other activities which require alertness; there may be drowsiness or dizziness.
- Educate and instruct patient not to discontinue drug abruptly; therapeutic effects may take >7 days.
- Instruct patient not to change doses or discontinue drug without physician's order; plan and **teach patient and family members** about tapering of doses gradually as per physician's instructions.
- Instruct patient to avoid OTC drugs, alcohol, CNS depressant.
- **Educate patient and family** to increase green leaf and bulk diet to prevent and manage constipation.
- A Advise patient to report if he/she experiences any of the following: Headache, nausea, vomiting, impotence, anxiety, depression, seizures, suicidal behavior, hallucination, coma, agitation, tachycardia, tremors and pregnancy occur.

CITALOPRAM

Brand Names

• Citadep • Citara • Citopam • Cytop • C-Talp • Celica • Citadelm • Freepram • Feliz • Madam • Zetalo

Mechanism of Action: Similar to Sertraline

Available Form: **Tablets:** 10 mg, 20 mg, 40 mg

Pharmacokinetics

Route*	Onset of effect	Peak effect	Half-life	Duration
Oral	1–4 weeks	4 hours	35 hours	Not known

*Oral bioavailability is around 80%.

Lactation	• Drug appears in breast milk • Discontinue breastfeeding or discontinue drug, taking into account the risks of citalopram exposure for the infant and its benefits for the mother.
Elderly	• Can be used with caution in reduced dosage
Children	• Not recommended for use in children. Safety and efficacy have not been established.

Nursing Considerations

- Similar to those mentioned for Sertraline *(Refer to page no. 140)*
- Educate and instruct patient not to discontinue drug abruptly; therapeutic effects may take 1–1.5 months.
- Monitor for erectile dysfunction, decreased libido.

ESCITALOPRAM

Brand Names

• Articalm • Atpram • Censpram • Cetaram • Cipralex • Citalop-S • Depranex • Depser • Dipwell • Enzycare • Ésilo • Escitapax • Esdep • Esivan • Esizol • Eslika • Esopram • Esty • Eszen • Excita • Feliz-S • Maxtol • Mucita X • Mucita 5 • Nexito • Recita • Recitol • Rexipra • Santo-10 • S-Citadelm • S Citadep • Seatle • Silital • S Zetalo • SC-Talo • Stalotip • Stalopam • Terilom • Vesci • Vesopram

Escitalopram + Clonazepam: • Depran-L • Depser Plus • Dipwell LS • Dipwell Plus Enzycare LC • Enzycare Plus • Escitapax Plus • Esizol-Plus • Esyza-Forte

Mechanism of Action: Similar to Sertraline

Escitalopram is the S(+) enantiomer of citalopram with similar pharmacological properties.

Available Form: **Tablets:** 5 mg, 10 mg, 20 mg

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	5 hours	27–32 hours	Not known

Indications and Dosage

Indications	Dosage
Depression potentially relapse/recurrence. Panic disorder with or without agoraphobia.	Initially, 20 mg orally once daily, in morning or evening, with or without food. *Maximum recommended dose for elderly patients (>60 years) and patients with hepatic impairment 20 mg/day.*

A Advise patient to report if he/she experiences any of the following: Headache, nausea, vomiting, impotence, anxiety, depression, seizures, suicidal behavior, hallucination, coma, agitation, tachycardia, tremors, urinary retention.

W **Overdose intervention:** Monitor vital signs, activated charcoal, symptomatic care, serotonin antagonist (always follow institutional policy).

II. SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS

Serotonin-norepinephrine reuptake inhibitors (SNRIs) are a class of drugs whose main action is to increase the level of serotonin and norepinephrine in the synaptic cleft. SNRIs inhibit the serotonin reuptake transporter (SERT) and norepinephrine reuptake transporter (NET), thereby inhibiting the reuptake (clearance) of serotonin as well as norepinephrine. SNRIs are known as second-generation antidepressants drugs.

SNRIs are often useful in those patients in whom SSRIs are not effective. Moreover, depression that is accompanied by chronic painful symptoms (including backache, myalgia) often responds to SNRIs. The SNRIs include venlafaxine, desvenlafaxine, duloxetine, etc.

VENLAFAXINE

Brand Names

• Dalium • Envelaf • Flavix • Flavix-XR • Nutraport • Sentosa • Sentosa-ER • Valfax-75 ER • Velor • Venfax-PR • Venflexa-Xt-50 • Veniz • Veniz-XR • Venla • Venla-XR • Venlift-OD • Venlor • Venlor-XR • Vijoy-XR • Vinfax

Mechanism of Action: Venlafaxine is the potent neuronal reuptake inhibitor of serotonin and norepinephrine, and weak reuptake inhibitor of dopamine. This results in prolonged stimulation of neuroreceptors.

Available Forms: **Tablets:** 25/37.5/75 mg
Tablets (Extended-release): 37.5/75/150 mg
Capsules (Extended-release): 37.5/75/150 mg

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	2 hours	3–7 hours	Not known
Oral (Extended-release)	Not known	5.5 hours	3–7 hours	Not known

Nursing Considerations

- **Assess mental status examination and mental health history:** Mood, affect, memory, behavior, sensorium, suicidal thoughts, psychiatric symptoms, depression, panic, seizures.
- **Assess vitals:** Pulse, BP (standing and lying position) every 4 hours, respiration; drop in BP and respiration should be informed to the treating consultant.
- Assess CBC, LFT (Bilirubin, ALT, AST), RFT (creatinine, BUN); cardiac enzymes and daily weight.
- Assess the level of appetite, check daily weight, and observe for bingeing, vomiting, peripheral edema.
- **Assess s/s of serotonin syndrome:** Elevated body temperature, hypertension, muscle rigidity/cramps, delirium, decreased LOC, agitation, tremors, and metal change.
- Assist in ambulation during early stage of treatment.
- **Assess allergic reaction:** Itching, skin rash, tachycardia, urticaria, syncope, nausea, vomiting.

W Instruct patient NOT to involve in machinery or hazardous activities, such as driving and other activities which require alertness; there may be drowsiness or dizziness.

- Instruct patient to avoid OTC drugs, alcohol, CNS depressant.
- Instruct patient not to change doses or discontinue drug without physician's order; plan and **teach patient and family members** about tapering of doses gradually as per physician's instructions.
- Instruct patient to notify if pregnancy occurs (in 3rd trimester, this drug can cause birth defect); avoid breastfeeding.

A Advise patient to report if he/she experiences any of the following: Flu-like symptoms, headache, nausea, vomiting, impotence, anxiety, depression, seizures, suicidal behavior, hallucination, coma, agitation, nervousness, tachycardia, tremors, urinary retention.

W **Overdose intervention:** Monitor vital signs, ECG; gastric lavage; activated charcoal; anticonvulsant; bowel irrigation (always follow institutional policy).

DESVENLAFAXINE

Desvenlafaxine (O-desmethylvenlafaxine) is the major active metabolite of venlafaxine. The pharmacological properties are therefore expected to be similar to venlafaxine.

Brand Names

• Desivert • D-Veniz • D-Venlor • MOD-XR • Newven • Prestiq • Venpower • Ventab-DXT • Venz-OD • Vijoy-DXT • Zyven-OD

Contd...

Indications	Dosage
Generalized anxiety disorder	40–60 mg/day in divided doses. **7–17 years:** Start with 30 mg once a day for 2 weeks, after which the dose may be increased to 60 mg once a day.

Drug Interactions

- Use of this drug with *MAO inhibitors (phenelzine, selegiline, tranylcypromine), and serotonergic drugs (e.g., triptans, TCAs, other SSRIs or SNRIs, fentanyl, amphetamines, buspirone, lithium, tramadol, tryptophan)* may cause serotonin syndrome and signs and symptoms of neuroleptic malignant syndrome.
- Use of this drug with *NSAIDs, aspirin, warfarin* may increase the risk of bleeding.
- Used with heavy *alcohol* intake may increase the risk of liver damage.

Adverse Effects: Headache ♦ Dizziness ♦ Insomnia ♦ Somnolence ♦ Tremors ♦ Cramps ♦ Blurred vision ♦ Acne ♦ Skin rash ♦ Nausea/vomiting ♦ Dry mouth ♦ Anorexia ♦ Constipation ♦ Gastritis ♦ Hyperhidrosis ♦ Ejaculation disorder and orgasm dysfunction.

Contraindications: Alcohol intoxication, closed-angle glaucoma, hepatic disease, hypersensitivity

Considerations in

Pregnancy	• Use only if clearly indicated and the potential benefit outweighs the potential risk to the fetus. • Neonates exposed to the drug late in the 3rd trimester have been reported to develop complications requiring prolonged hospitalization, respiratory support and tube feeding.
Lactation	• Drug appears in breast milk • Use with caution in lactating women and only when benefits outweigh potential risks
Elderly	• Can be used with caution
Children	• Not recommended for use in children <7 years

Nursing Considerations

- Similar to those mentioned for Sertraline *(Refer to page no. 140)*
- Monitor for erectile dysfunction, decreased libido.

III. TRICYCLIC ANTIDEPRESSANTS

Until the introduction of SSRIs during 1984–1997, the tricyclic antidepressants (TCAs) were the first line of treatment for depression. Currently, the TCAs are used in the treatment of depression that does not respond to SSRIs or SNRIs. This is because TCAs have poor tolerability and narrow therapeutic window and may cause fatality in overdose.

The main action of TCAs is to increase the level of serotonin and norepinephrine in the synaptic cleft. TCAs inhibit SERT and NET in the presynaptic membrane, thereby preventing the reuptake (clearance) of serotonin and norepinephrine.

AMITRIPTYLINE

Brand Names

• Ambival • Amicon • Amidon • Amirise • Amitone • Amitrol
• Amixide 5/10 • Amixide-H • Amixsil-H • Amline • Amonurite
• Aptric Forte • Aptric Plus • Arixide • AT-10 • Atline-F • Atline-P
• Eliwel • Gabantip-AT • Libotryp • Libotryp DS • Libotryp-XL
• Maxgalip-AT • Mitrip • Neugatrip • Relidep • Ristryl • Ristryl Forte
• Sarotena • Tadamit • Tryptomer • Tryptomer-SR • Trypty • Vitryp
• Weltrip

Mechanism of Action: Inhibits or blocks the reuptake of neurotransmitters (serotonin, norepinephrine) in presynaptic nerve endings, resulting in increased action of these neurotransmitters in neurons.

Available Form: **Tablets:** 10 mg, 25 mg, 50 mg, 75 mg

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	2–6 hours	10–50 hours	Not known

Indications and Dosage

Indications	Dosage
• **Major depressive disorders, depression accompanied by anxiety, agitation, sleep disturbance.** • **Other/unlabeled uses:** Chronic pain, (e.g., cancer, central pain syndrome, neuropathic pain), fibromyalgia.	75 mg/day, orally, in three divided doses or 50–100 mg orally given as a single dose at bedtime. Maximum dose is 150–300 mg/day. **Geriatric:** 10–25 mg/day in three divided doses or 25 mg orally given as a single dose at bedtime. Maximum dose is 150 mg/day. Taper the dose when withdrawing medicine.

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	2–6 hours	19–37 hours	Not known

Indications and Dosage

Indications	Dosage
• **Obsessive-compulsive disorder** • **Other/unlabeled uses:** Autism, depression, premature ejaculation.	25 mg orally daily with meals. Maximum dose in adult 250 mg/day and in children 100 mg/day (or 3 mg/kg/day).

Drug Interactions, Adverse Effects and Contraindications

Similar to those mentioned for Amitriptyline.

Considerations in

Pregnancy	• Use only if the potential benefit outweighs the potential risk to the fetus
Lactation	• Drug appears in breast milk • Discontinue breastfeeding or discontinue drug
Elderly	• Use with caution in reduced dosage
Children	• Not recommended for use in children <10 years

Nursing Considerations

- **Assess vitals:** Pulse, BP (standing and lying position) every 4 hours, respiration; drop in BP and respiration should be informed to the treating consultant.
- Assess s/s of serotonin syndrome: Elevated body temperature, hypertension, muscle rigidity/cramps, delirium, decreased LOC, agitation, tremors, and metal change.
- Monitor ECG for T wave flattening, QT prolongation, bundle branch block, and atrioventricular block (AV block), dysrhythmias among cardiac patient.
- Assess CBC (platelets, s/s of bleeding), LFT (Bilirubin, ALT, AST), RFT (creatinine, BUN); cardiac enzymes and daily weight.
- **Assess mental status examination and mental health history:** Mood, affect, memory, behavior, sensorium, suicidal thoughts, psychiatric symptoms, depression, panic, seizures, s/s of obsessive-compulsive disorder.
- Assess the level of appetite and constipation during therapy; use of this drug may reduce appetite and can cause constipation.
- Instruct patient to avoid OTC drugs, alcohol, CNS depressant.

Contd...

Drug Interactions

- Use of this drug with *MAO inhibitors (phenelzine, selegiline, tranylcypromine)* may cause serotonin syndrome.
- *Strong CYP3A4 inhibitors (e.g., ketoconazole, nefazodone, erythromycin, fluvoxamine, indinavir)*: In vitro metabolism studies indicate that reboxetine is mainly metabolized by CYP3A4. Hence, these drugs would be expected to increase reboxetine levels. Simultaneous use is not recommended.

Adverse Effects: Insomnia ♦ Dizziness ♦ Anxiety ♦ Agitation ♦ Akathisia ♦ Dysgeusia ♦ Vertigo ♦ Palpitations ♦ Hypotension ♦ Dry mouth ♦ Erectile dysfunction ♦ Hyperhidrosis.

Contraindication: Hypersensitivity to Reboxetine.

Considerations in

Pregnancy	• Should be used in pregnancy only if the potential benefits to the mother outweigh the possible risks to the fetus.
Lactation	• Drug appears in breast milk. • Use during lactation only if the potential benefits outweigh the risks to the child.
Elderly	• Can be used with caution in reduced dosage.
Children	• Not recommended for use in children.

Nursing Considerations

Similar to those mentioned for Mianserin *(Refer to page no. 166)*

IV. REVERSIBLE INHIBITORS OF MONOAMINE OXIDASE-A

MOCLOBEMIDE

Moclobemide is a reversible and selective MAO-A inhibitor having a short duration of action. It does not have sedative, anticholinergic, cognitive and cardiovascular adverse effects seen with TCAs. These features make it a good option for elderly patients and also for the patients who are suffering from heart disease.

Brand Names

• Morex • Rimarex • Trima

Mechanism of Action: Moclobemide acts as a selective, reversible inhibitor of MAO-A. It lowers the metabolism and destruction of monoamines in the neurotransmitters, resulting in increase in monoamines, alleviate depressive symptoms.

7 Antipsychotic and Antimanic Drugs

ANTIPSYCHOTIC DRUGS

Psychosis is a symptom of mental disease in which the sense of reality is lost. The patient also has distorted perception (delusions and hallucinations), thought and behavior. Schizophrenia occurs in around 1% of population worldwide and is considered the prototypic disorder for psychosis. The antipsychotic drugs are effective against schizophrenia and other psychotic disorders. The classification of some of the antipsychotic drugs is as follows:

CLASS	DRUGS
I. Phenothiazines (Typical) *Aliphatic side chain*: *Piperidine side chain*: *Piperazine side chain*:	 Chlorpromazine, Triflupromazine, Thioridazine, Trifluoperazine, Fluphenazine
II. Butyrophenones (Typical)	Haloperidol, Penfluridol
III. Thioxanthenes and other heterocyclics (Typical)	Pimozide, Loxapine, Flupenthixol
IV. Atypical neuroleptics or antipsychotics	Aripiprazole, Clozapine, Amisulpiride, Olanzapine, Quetiapine, Risperidone, Paliperidone, Ziprasidone, Zotepine

Mesolimbic pathway → increased dopamine → positive symptoms. Mesocortical pathway → decreased dopamine → negative symptoms. Other neurotransmitters such as serotonin and norepinephrine are also thought to play a role in pathogenesis of the disease.

The antipsychotic drugs exert beneficial effects by the following mechanisms:

- **Typical antipsychotics:** Mainly reduce dopaminergic neurotransmission (i.e., they mainly block D_2 receptors).
- **Atypical antipsychotics:** Atypical antipsychotics block D_2 and 5-HT_{2A} receptors, improving positive and negative symptoms with fewer extrapyramidal side effects.

I. PHENOTHIAZINES (TYPICAL)

Phenothiazines are potent blockers/antagonists of dopamine D_2 receptors. Their capacity to block D_2 receptors correlates well with antipsychotic potency.

CHLORPROMAZINE

Chlorpromazine is the prototype drug of the phenothiazine class. All typical antipsychotics reduce the positive symptoms of schizophrenia but have minimal effect on the negative symptoms and cognitive effects.

Brand Names

• Chlorpromazine • Clozine • CPZ • Emetil • Megatil • Relitil • Tranchlor

Mechanism of Action: Chlorpromazine blocks postsynaptic dopamine receptors in the brain.

Available Forms: **Tablets:** 10 mg, 25 mg, 50 mg, 100 mg, 200 mg
Injection: 50 mg/2 mL, 25 mg/mL

Pharmacokinetics

Route	Onset of effect	Peak effect	Half-life	Duration
Oral	Not known	1–4 hours	~23–37 days	Not known

Indications and Dosage

Indications	Dosage
• **Psychotic disorder, Schizophrenia, Mania, Anxiety, Interactable hiccups, Nausea, Vomiting (in terminally ill patients), Anxiolytic in preoperative patients, Tetanus.** • **Other/unlabeled uses:** Agitated patient, vascular headache, neonatal abstinence syndrome.	10–25 mg/day in 3–4 divided doses orally or 75 mg in a single dose at bedtime. Maximum dose—800–1000 mg/day. **up to 5 years:** 0.5–1 mg/kg/day.

Drug Interactions

- Additive CNS depression if used with CNS depressant drugs.
- Administration along with antihypertensive drugs may increase the effects of antihypertensive drugs and may cause postural hypotension.
- Administration along with anticholinergic drugs may increase the anticholinergic effects.

Adverse Effects: Sedation ♦ Somnolence ♦ Akathisia ♦ Tardive dyskinesia ♦ Hypertonia ♦ Seizures ♦ Anxiety ♦ Restlessness ♦ Postural hypotension ♦ ECG changes ♦ QT prolongation ♦ Dry mouth ♦ constipation ♦ Cholestatic jaundice ♦ Leukopenia ♦ Agranulocytosis ♦ Miosis ♦ Mydriasis ♦ Corneal opacities ♦ Nasal congestion ♦ Respiratory depression ♦ Weight gain ♦ Hyperprolactinemia ♦ Amenorrhea ♦ Galactorrhea ♦ Gynecomastia ♦ Urinary retention

SECTION M

IMMUNE SYSTEM

60

Immunomodulating Drugs

BACTERIAL VACCINES

BCG VACCINE

Bacillus Calmette-Guerin (BCG) vaccine contains a live, attenuated strain of *M. bovis*. It is supplied as 0.5–1 mg of dry powder, to be dissolved in 1 mL of sterile water for injection.

Brand Names

• BCG Vaccine • Tubervac

Mechanism of Action: BCG vaccination activates the innate immune system and induces changes in the pattern of histone modifications of specific genes in innate immune cells.

Available Form: **Injection:** For Intradermal use.

Indications and Dosage

Indications	Dosage
Prevention of tuberculosis in persons not previously infected with *M. tuberculosis* who are at high risk for exposure	**>1 year:** Single dose of 0.1 mL *via* slow injection intradermally, into the deltoid muscle. **Infants <1 year:** Single dose of 0.05 mL *via* slow injection intradermally, into the deltoid muscle.

Adverse Effects: BCG vaccination often causes local skin reactions; however, it rarely causes serious or long-term complications.

After vaccination, a red, painless papule appears after 7–10 days, which reaches around 8 mm size in 5 weeks. This is often accompanied with axillary or cervical lymphadenopathy. These reactions can persist for as long as 3 months after vaccination, after which it usually scales, dries, and heals with a scar.

Contraindications

- Hypersensitivity to any component of the vaccine.
- Immunocompromised states (congenital or acquired), e.g., AIDS, leukemia, steroid use, etc.
- Patients with tuberculin positive skin tests.
- BCG vaccination must not be given to persons previously infected with *M. tuberculosis*.

TYPHOID VACCINE

There are 2 types of vaccines available for prevention of typhoid infection—injectable Vi Typhoid polysaccharide vaccine and Typhoid Ty21A oral vaccine.

1. **Injectable Vi Typhoid polysaccharide vaccine:** It contains purified Vi capsular antigen of *Salmonella typhi*. The overall protective efficacy has been reported to be 74% for blood culture confirmed typhoid cases for 20 months and 55% for blood culture confirmed typhoid cases for 3 years. An increase in serum anti-capsular antibodies is thought to be the mechanism for protection provided by this vaccine.
2. **Oral Typhoid Ty21A vaccine:** It is a live attenuated oral vaccine prepared from the Ty21a strain of *Salmonella typhi*, which lacks the Vi capsular polysaccharide and is nonpathogenic. It induces protection by stimulating intestinal mucosal and systemic immunity. Immunization results in approximately 50–80% reduction in the incidence of typhoid fever, with protection lasting for about 5 years. The vaccine is well tolerated. Selective immunization against typhoid fever is recommended in the following situations:
   - Travelers to areas where a recognized risk of exposure to typhoid exists, especially ones who will have prolonged exposure to potentially contaminated food and water.
   - Persons with intimate exposure, i.e., continued household contact to a documented typhoid carrier.
   - Persons working in laboratories who frequently work with *S. typhi*.

Brand Names

Injection: • Biovac Typhoid • Typbar • Typherix • Typhim VI • Typhivax • Typhibev • Shantyph • Typbar TCV • Vactyph • Zyvac TCV
Oral capsules: • Typhoral

Mechanism of Action: Typhoid vaccine causes a local immune response in the intestinal tract. The attenuated strain causes lipopolysaccharide biosynthesis inducing a protective immune response.

Available Forms

Injection: 25 µg/0.5 mL
Oral capsules: 10^9 *S. typhi* strain Ty21A organisms per capsule.

• **Priorix**	1000 $TCID_{50}$ of measles virus + 1000 $TCID_{50}$ of rubella virus + 5000 $TCID_{50}$ of mumps virus
• **Tresivac**	5000 $TCID_{50}$ of measles virus + 4000 $TCID_{50}$ of rubella virus + 5000 $TCID_{50}$ of mumps virus
• **Trimovax Merieux**	1000 $TCID_{50}$ of measles virus (Schwarz strain) + 1000 $TCID_{50}$ of rubella virus (Wistar RA 27/3M strain) + 5000 $TCID_{50}$ of mumps virus (Urabe AM-9 strain)

Mechanism of Action: The measles, mumps and rubella (MMR) vaccine stimulates the immune system to protect against measles, mumps, and rubella.

Available Forms: The MMR vaccine is available as a subcutaneous injection.

Indications and Dosage

Indications	Dosage
Routine immunization against measles, mumps and rubella infection	**≥12 months:** *Primary immunization* • Single dose of 0.5 mL SC (into upper arm) at 12–15 months of age. • Children first vaccinated before 12 months of age must receive another dose between 12–15 months of age. • In some countries, a second dose is given at 4–6 years of age, prior to elementary school entry.

Note: Consult the applicable guidelines/national protocols regarding routine revaccination, vaccination during outbreaks and vaccination in high-risk adult populations.

Adverse Effects: Mild fever, rash, local injection site induration, as well as enlargement of cervical/occipital lymph nodes and parotid glands may occur after ~5 days of vaccination.

Contraindications

- Hypersensitivity to any component of the vaccine.
- Pregnancy (If vaccination is given to postpubertal females, pregnancy must be avoided for at least 3 months after vaccination)
- Immunodeficiency conditions (congenital or acquired).
- Febrile respiratory illness or other active febrile infections.

Warnings

The MMR vaccine must be used cautiously in persons with a history of cerebral injury, individual or family history of seizures or any other condition in which stress due to fever must be avoided.

Adverse Effects: Injection site reactions such as pain ♦ Soreness ♦ Swelling ♦ Redness and induration ♦ Fever ♦ Drowsiness ♦ Irritability and loss of appetite.

Contraindications

- Hypersensitivity or severe allergic reaction to any component of the vaccine.
- Encephalopathy within 7 days of administration of a previous pertussis containing vaccine.
- Progressive neurologic disorders.

Nursing Considerations

- Clean the site with alcohol swab, allow it to dry before administration.
- Ask for history of hypersensitivity or allergic reaction.
- **Inform parents** that child may develop fever, soreness, redness and swelling at the site of administration of vaccine.
- **Instruct and educate parents** about the use of warm compression/heating pad at the site of vaccination to reduce pain and soreness.
- Acetaminophen or ibuprofen can be administered as per physician's order if pain or fever develops.

IMMUNOGLOBULINS

ANTITHYMOCYTE GLOBULIN (EQUINE)

Brand Names

• Atgam (Equine) • Grafalon • Lymphoglobulin (Equine)
• Thymogam (Equine) • Thymoglobuline (Rabbit) • Thymogam

Mechanism of Action: It has immunosuppressive effect on lymphocytes.

Available Form: **Injection:** 100 mg/5 mL, 250 mg/5 mL

Indications and Dosage

Indications	Dosage
Lymphoglobulin **Acute kidney transplant rejection**	10–15 mg/kg/day IV for 14 days. • Administration may then be continued every other day, up to a total of 21 doses (i.e., a total of 21 doses in 28 days). • Used in conjunction with concurrent immunosuppression.

Contd...