Lactulose: Uses, MOA, Side effects, Dosage and Interactions

Lactulose is a synthetic disaccharide used primarily as an **osmotic laxative** and for the management of **hepatic encephalopathy** . It is classified as a **category B** drug in pregnancy, indicating no evidence of risk in human studies.

Formulation

Lactulose is available as a syrup or oral solution, typically containing:

- **>62% w/v lactulose**
- Minor sugars: **lactose** , **galactose** , **epilactose** , and **fructose**
- Preservatives for microbial control

Pharmacological Classification

- **Chemical class:** Synthetic disaccharide sugar (galactose + fructose)
- **Therapeutic class:**
  - Osmotic laxative
  - Ammonia reducer (used in hepatic encephalopathy)

Indications

1. **Chronic constipation** – especially in elderly patients and children
2. **Hepatic encephalopathy** – to reduce serum ammonia levels
3. **Adjunct therapy (less common use):**
   - In seizure disorders like **Lennox-Gastaut syndrome** and **primary generalized tonic-clonic seizures** , though this is not a standard or first-line indication.

Mechanism of Action

In Constipation

- Lactulose **resists digestion** in the small intestine due to absence of lactulase enzyme in humans.
- Reaches the **colon unchanged** , where it is metabolized by **colonic bacteria** into **lactic acid** , **acetic acid** , and **formic acid** .
- These acids:
  - Lower colonic pH (acidify contents)
  - Increase **osmotic pressure** , drawing water into the lumen
  - Soften stool and stimulate **peristalsis**

In Hepatic Encephalopathy

- Acidification of the colon **traps ammonia (NH?)** by converting it to **ammonium (NH??)**, which cannot be absorbed.
- Also accelerates colonic transit, decreasing time for ammonia absorption.
- Result: **Reduced serum ammonia** and **improved mental status**

Pharmacokinetics

- **Onset of action:** 24–48 hours
- **Absorption:** Minimal; remains in the GI tract
- **Excretion:** Trace amounts in urine; most excreted in feces after bacterial fermentation

Dosage and Administration

Adults:

- **Constipation:** 15–30 mL orally once or twice daily; max ~60 mL/day
- **Hepatic Encephalopathy:** 30–45 mL orally 3–4 times/day; titrate to achieve 2–3 soft stools daily

Children:

- **1–5 years:** 2.5–10 mL twice daily
- **5–10 years:** 10 mL twice daily

Retention enema (for hepatic encephalopathy):

- **300 mL lactulose in 700 mL NS**
- Retain for **30–60 minutes**, repeat **q4–6h** if needed

Side Effects

Common adverse effects include:

- **Abdominal bloating and cramps**
- **Flatulence**, belching
- **Nausea**, especially at high doses
- **Diarrhea** (with prolonged use) leading to:
  - **Hypokalemia**
  - **Hypernatremia**
  - **Dehydration**
- **Unpleasant taste** may affect adherence
- Rare: **Hyperglycemia**, especially in diabetic patients

Contraindications

Avoid or use with caution in patients with:

- **Intestinal obstruction**
- **Low-galactose or lactose-free diets**
- **Disaccharidase deficiency**
- **Known hypersensitivity** to lactulose or excipients

Precautions

- Monitor electrolytes during prolonged use
- Use cautiously in **diabetics** (contains galactose/fructose)
- Risk of **lactic acidosis** in patients with **ileus**
- Can worsen dehydration in pediatric or elderly patients

Drug Interactions

Decreased efficacy with:

- **Antacids**
- **Oral neomycin** (both reduce colonic acidification)
- **Sodium bicarbonate, calcium carbonate**
- **Citrate salts** (e.g., sodium citrate)

Avoid administering other oral drugs within **1 hour** of lactulose to minimize reduced absorption.

Diagnostic Use

Sugar Absorption Test

- Used to assess **intestinal permeability**
- Lactulose combined with **mannitol** or **rhamnose** helps detect **mucosal damage** in conditions like celiac disease

Lactulose Breath Test

- Measures **hydrogen gas in breath** after ingestion
- Assesses **orofecal transit time** and **carbohydrate malabsorption**
- Limited by lactulose's own effect on gut motility

Clinical Pearls

- **First-line treatment** for hepatic encephalopathy
- Helps reduce **mortality and hospitalization** in cirrhotics
- **Safe in pregnancy** (Category B)
- **Titrate dose** to stool consistency, not volume
- **Avoid overuse** due to risk of electrolyte imbalance

Alternatives

- **Rifaximin** (often used with lactulose in hepatic encephalopathy)
- **Polyethylene glycol (PEG)** – for chronic constipation
- **Sorbitol** – another osmotic laxative, less commonly used

Patient Education

- Encourage **adequate fluid intake**
- Expect **delayed onset** (24–48 hours)
- Inform about potential for **gas and bloating**
- Advise to report persistent **diarrhea or cramps**