Pharma1: Histamine & Histamine Antagonists

	First genaration(sedation) [mine]	Second genaration [ine]
Example	• Ethanolamines: Diphenhydramine، Clemastine • Dimethindene • Ethylenediamine: Triprolidine • Alkylamine: Chlorpheniramine • Phenothiazine: Promethazine • Piperazines: Hydroxyzine Cyclizine، Meclizine	• Cetirizine • Fexofenadine • Loratadine • Desloratadine • Azelastin
Uses	*Anaphylaxis (with H2 Antagonists, epinephrine) *Antiallergy *Sedative/sleep aid (Diphenhydramine) *prevent motion sickness (meclizine, cyclizine) *Antiemetic: (promethazine) *Antivertigo (meclizine) safe in pregnancy *Local anesthetic: (diphenhydramine) * Antitussive (diphenhydramine)	Antiallergy
Adverse affect	• Sedation (but in children excitation) • Dizziness • Fatigue • Tachydysrhythmias • Allergic with topical use • Peripheral antimuscarinic effects ➢ dry Mouth ➢ blurred Vision ➢ constipation ➢ urinary Retention	^^Lower incidence of adverse effects than the first generation agents. • terfenadine and astemizole removed from the market due to→effects on cardiac K+ channels – prolong QT interval →fatal arrhythmia "to rsades de pointes" • fexofenadine is active metabolite of terfenadine • Cetirizine appears to have more CNS actions (sedative) than fexofenadine or loratadine. So that cetirizine not be used by Pilots • Erythromycin and ketoconazole inhibit the Metabolism of fexofenadine and loratadine

	First genaration	Second genaration
Drug interaction	• additive ❖antimuscarinics • Potentiate CNS depressants ❖opioids ❖sedatives ❖general and narcotic analgesics ❖alcoho	
PK	• All H1 blockers are active by the oral route. •topical use (in the eye or nose) • Cross BBB and placenta •metabolized in the liver (induce hepatic microsomal enzymes) • Half-lives (4 to 12) h	• Cetirizine , loratadine ,fexofenadine *absorbed and excreted unmetabolized *less lipid soluble than the first Generation *half-lives of 12–24 h. *induce Cyt P450 liver enzymes

*Diphenhydramine ⇒ sedative /sleep aid

Local anesthetic

Antitussive

*Meclizine ⇒ prevent motion sickness

Antivertigo

*Histamine H2- antagonists

-Cimetidine → prototype
-Ranitidine , famotidine and Zatidine
(fewer adverse effect than cimetidine)
-Pk orally active, T1/2 (1- 3)h
-All avalible OTC
-Clinical use → (H2 related to gastric problem)
1-Acid-peptic disease
2-Zollinger-Ellison syn
3-Gastro esophageal reflex (GERD)
4-Prevent gastric erosions and hemorrhage

**PPIS are preferred in Zollinger-Ellison syn, And GERD