



- **What are the problems which you will face when using antiviral drugs?**
  - **Selective toxicity is difficult (why?)** → because it is difficult to find the target that is different from host cells (especially that viruses are intracellular thus they can hide and escape from effects of these drugs). Another reason is that viruses change their structure/configuration from time to time.
  - **An effective antiviral drug must:**
    - ✓ Block the entry of the virus to the host cell.
    - ✓ Block the exit of viruses from the infected host cell.
    - ✓ Inhibit replication of the virus.
- **What are the possible targets of antiviral drugs (sites where they can exert their mechanism of action)?**
  - **This depends on your knowledge of phases of viral replication:**
    - ✓ Attachment: blocked mainly by drugs which work against HIV virus.
    - ✓ Penetration: blocked by interferons.
    - ✓ Uncoating: blocked by two influenza drugs (Amantadine & Rimantadine).
    - ✓ Gene expression & genome replication.
    - ✓ Synthesis of viral components.
    - ✓ Assembly.
    - ✓ Release: blocked by two influenza drugs (Oseltamivir & Zanamivir).
- **Amantadine & Rimantadine**
  - **Against influenza (A) only.**
  - **Mechanism of action:** they inhibit the uncoating of viral RNA by interfering with M2 protein (an integral membrane protein which functions as an ion channel). Therefore, the influx of protons through the ion channel will be inhibited and uncoating will not occur.
  - **Administration must be as early as possible (within 48 hours).**
  - **Route of administration:** these drugs are given orally.
  - Rimantadine is metabolized extensively but not amantadine.
  - **Adverse effects:**
    - ✓ Gastrointestinal disturbances (such as nausea and vomiting).
    - ✓ They may affect the nervous system.
  - **These drugs can be used for treatment and prophylaxis (vaccines).**
- **Oseltamivir & Zanamivir (neuraminidase inhibitors):**
  - **Against influenza (A) and (B).**
  - **Mechanism of action:** they inhibit the release of viruses from the infected host cell.
  - **Administration must be as early as possible (within 48 hours).**
  - **Route of administration:** oseltamivir is given orally while zanamivir is inhaled.
  - **These drugs can be used for treatment and prophylaxis (vaccines).**
- **Oseltamivir (details):**
  - **It is a prodrug:** which means that it is in an inactivated form. It will be activated in the liver by hepatic esterases.
  - **Adverse effects include:**
    - ✓ Nausea, vomiting, diarrhea and abdominal pain.
    - ✓ Headache, fatigue... etc.
- **Zanamivir (details):**
  - It is delivered directly to the respiratory tract.
  - Dose adjustment is not required.
  - **Adverse effects include:**
    - ✓ Cough and bronchospasm.

This explains why it is not suitable for patients with asthma.



## Anti-viral agents for influenza viruses

	<b>Amantadine (oral)</b>	<b>Rimantadine (oral)</b>	<b>Oseltamivir* (oral)</b>	<b>Zanamivir (oral/intranasal inhalation )</b>	<b>Peramivir (IV)</b>
Mode of action	M2 proton ion channel blockade	M2 proton ion channel blockade	Neuraminidase inhibition	Neuraminidase inhibition	Neuraminidase inhibition
Anti viral spectrum	Influenza A	Influenza A	Influenza A & B	Influenza A & B	Influenza A & B
Metabolism and excretion	Mainly excreted unchanged in urine (dosage adjustment is required for renal insufficiency)	Extensive metabolized in liver (dosage adjustment is required in renal and hepatic insufficiency)	Extensive metabolized in liver to oseltamivir carboxylate**	Not significantly metabolized	Dose adjustment is required for renal insufficiency; kidney is the major route of elimination
Adverse effects	Neuropsychiatric disorders	Similar to amantadine but much less common	Nausea and vomiting which may decrease by food.	Oropharyngeal or facial edema; bronchospasm & dyspnea; not recommended in patients with asthma, COPD	Diarrhea, serious skin reactions, neuropsychiatric events
Uses Therapeutic chemoprophylaxis	No longer be used	No longer be used	Any age 3 months & older	7 years & older 5 Years & Older	≥ 2 years & older Not applicable
Uses in pregnancy	Pregnancy category C	Pregnancy category C	Pregnancy category C	Pregnancy category C	Pregnancy category C