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Pharmacology
Chapter 12 : Chemotherapeutic Agents

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Chapter 12

Chemotherapeutic Agents

I. The Chemical substances (Drugs) used for treatment of diseases caused by microorganism and tumor Cell are called Chemotherapeutic Agents.
II. Nowadays it refers to treatment of cancer usually .
III. The Chemical substances used as Chemotherapeutic agents are also called antibiotics and anti-neoplastic Agents.
IV. Now antibiotics can further classified into Bactericidal (kil ls the Bacteria) and Bacteriostatic (Prevents the growth of Bacteria).
V. Even though Antibiotics are referred to bactericidal and Bacteriostatic , But antiviral , antifungal anthelmintic , antiprotozoal are also called antibiotics.
VI. The Chemotherapeutic agents that are used to treat infection and infestation may be other than antibiotics also.

Basic Principle of Chemotherapy of Infections and Infestations

- **Diagnosis** : Before Chemotherapy diagnosis should be performed for determination of type of microorganism and site of infection.
- **Selection of drug :** Drug should be select according to the type of pathogen , and should consider which is required whether Narrow or broad spectrum.
- **Frequency and duration of administration :** low dose can develop resistance , intermediate dose may not cure infection , so optimum dose should be used.
- **Continue therapy** : Acute infection treated for 5-10 days , but some takes a long time like Tuberculosis , thyroid.
- **Prophylactic Chemotherapy** : Chemotherapy is also used as prophylaxis to avoid surgical site infection.

Classification of Chemotherapeutic agents

1) Antibiotics

a) **B-Lactam Antibiotics :** Penicillins. Monobactams, Cephalosporins, Carbapenems etc.
b) **Aminoglycosides** : Streptomycin, Gentamycin, Framycetin, Neomycin, etc.
c) **Macrolides** : Erythromycine , Roxithromycin, Erythromycin, Clarithromycin,
d) **Tetracyclines :** Oxytetracycline, Doxycycline, Minocycline, etc.
e) **Nitrobenzene Derivatives :** Chloramphenicol, etc.
f) **Polypeptide Antibiotics :** Polymyxin-B, Colistin, Bacitracin, Tyrothricin, etc
g) **Polyene Antibiotics :** Nystatin, Hamycin, Amphotericin-B, etc.
h) **Miscellaneous Agents** : Rifampicin, Lincomycin, Vancomycin, Fusidic acid, Cycloserine, Viomycin, Griseofulvin, etc.

2) Chemotherapeutic Agents other than Antibiotics :

a) **Sulphonamides and Related Agents :** Sulfadiazine, Sulfamethoxazole, Sulfones (Dapsone) , Para aminosalicylic acid (PAS), etc.
b) **Diaminopyrimidines :** Pyrimethamine.
c) **Quinolones and Fluoroquinolones :** Nalidixic acid, Norfloxacin, Ciprofloxacin, ofloxacin, etc.
d) **Nitrofuran Derivatives :** Nitrofurantoin, Furazolidone, etc.
e) **Nitroimidazoles :** Metronidazole, Tinidazole etc.
f) **Imidazole Derivatives :** Miconazole, Clotrimazole, Ketoconazole, Fluconazole, etc.
g) **Nicotinic Acid Derivatives :** Isoniazid, Pyrazinamide, Ethionamide, etc.
h) **Miscellaneous Agents :** Ethambutol, Thiacetazone, Clofazimine, etc.

3) According to the Types of Organisms Against which they are Primarily Active:

a. **Antibacterial :** Penicillins, Aminoglycosides (Streptomycin, Gentamycin, Framycetin, Neomycin) , Erythromycin, etc.
b. **Antifungal :** Griseofulvin, Amphotericin B, Ketoconazole, etc.
c. **Antiviral** : Acyclovir, Amantadine, Zidovudine, etc
d. **Antiprotozoal :** Chloroquine, Pyrimethamine, Metronidazole, Diloxanide, etc. v) Anthelmintic: Mebendazole, Niclosamide, Diethylcarbamazine, etc.

4) Classification of Chemotherapeutic Agents According to their Range of Action:

I. **Broad Spectrum Antibiotics :** Those effective against Gram +ve, Gram -ve, rickettsia and chlamydia. For example, Tetracycline,Chloramphenicol etc.
II. Narrow Spectrum Antibiotics
    a. Those effective only against gram +ve bacteria, e.g., Penicillin, Erythromycin group, Vancomycin.
    b. Those effective only against gram -ve bacteria, e.g., Streptomycin and other aminoglycoside antibiotics, Colistin, Polymyxin-B.
III. **Relative Broad Spectrum Antibiotics :** Those effective against +ve and gramve bacteria. For example, Ampicillin group, Cephalosporins, Rifamycins, etc.

Penicillin

- → Penicillin is the first antibiotics which was clinically used in 1941 firstly it was obtained from fungus penicillium notatum , but presently it is obtained from P. Chrysogenum
- → Penicillins work by preventing the bacteria from forming a cell wall, which is essential for their survival. This causes the bacteria to burst and die.

Classification

- **Penicillin G :** Penicillin G (Benzyl Penicillin) , Procaine Penicillin G , Benzathine penicillin G.
- **Acid resistant penicillin :** Phenoxymethylpenicillin (Penicillin V)
- **Penicillin With ß lactamse inhibitor :** Amoxycilin , Clavulanic acid .
- **Penicillin effective against Gram + and gram Negative Organism :** Ampicillin , Talampicillin .

Indications

- Upper respiratory infections
- Otitis media
- Pneumonia
- Rheumatic fever
- Erysipelas
- Skin and soft-tissue infections
- Gonorrhea
- Syphilis

Contraindications

- Previous history of allergic reactions
- In Stevens johnson syndrome
- In lactation

Dose

- ✓ Penicillin G : 0.5-5 MU im/iv

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Cephalosporins

- → Cephalosporins are largest group of Beta lactam antibiotics ,
- → Five generation of cephalosporin are available .
- → It is a broad spectrum antimicrobial agent and used to treat infection gram positive and gram negative bacteria .

Classification

1) First Generation Cephalosporins

- Cefazolin,
- Cephalexin,
- Cefadroxil

2) Second Generation Cephalosporins

- Cefuroxime,
- Cefaclor,
- Cefprozil
- Cefoxitin

3) Third Generation Cephalosporins

- Ceftriaxone,
- Cefotaxime
- Ceftazidime,
- Cefixime
- Cefpodoxime
- Ceftibuten

4) Fourth Generation Cephalosporins

- Cefepime
- Cefpirome

5) Fifth Generation Cephalosporins

- Ceftaroline
- Ceftobiprole

Indications

- Skin or soft tissue infections.
- Urinary tract infections (UTIs)
- Strep throat.
- Ear infections.
- Pneumonia.
- Sinus infections.
- Meningitis.
- Gonorrhea

Contraindications

- Allergic reaction history

Dose

- ✓ **Ampicillin :** 250-500 mg / 6 hours
- ✓ **Cefexime :** 400 mg /d

Aminoglycosides

→ Aminoglycosides have a broad spectrum of activity against Gram negative and mycobacterium
→ It is used to treat serious infection . aminoglycocides are called Bactericidal antibiotics .

Classifications

- ➢ **First generation :** Streptomycin , kanamycin , Neomycin.
- ➢ **Second generation :** Gentamicin , tobramicin .
- ➢ **Third generation :** Amikacin , sisomicin .

Indications

- They are used in the treatment of severe infections of the abdomen, urinary tract, skin and soft tissue, bone, cervix, blood, eye ear, lungs, and heart. tuberculosis , UTIs , gonorrhoea , etc.

Contraindications

- Renal and Hepatic diseases
- Pregnancy

Dose

- ✓ **Streptomycin :** 1-2 g /d
- ✓ **Amikacin :** different according to infections

Fluoroquinolones

- → Fluoroquinolones are highly effective antibiotics with many advantageous pharmacokinetic properties including high oral bioavailability, large volume of distribution, and broad-spectrum antimicrobial activity. With widespread use, antimicrobial resistance to fluoroquinolones has grown.
- → Fluoroquinolones are active against a wide range of aerobic gram positive and gram negative organism . They are commonly used to treat respiratory and urinary tract infections

Classification

- **First generation :** Nalidixic acid , Cinoxacin
- **Second generation :** Norfloxacin , Ofloxacin , ciprofloxacin
- **Third generation :** Levofloxacin , Sparfloxacin.
- **Fourth generation :** Trovafloxacin.

Indications

- Urinary tract infections (UTIs)
- Throat infection .
- Ear infections.
- Pneumonia.
- Sinus infections.
- Meningitis.
- Gonorrhea.

Contraindication

- In lactation
- In Hypersensitivity

Dose

- ✓ **Ofloxacin :** 250-750 / BD
- ✓ **Levofloxacin :** 250 -500 /d

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Macrolides

→ Macrolides are naturally occurring compounds , they have broad spectrum activity against gram positive and gram negative bacteria . these are used in patients who were allergic to penicillin or whose infections were penicillin resistant .

Classification

1) **Macrolides**
   - Erythromycin
   - Clarithromycin
   - Azithromycin
   - Roxithromycin
   - Spiramycin
2) **Ketolides**
   - Telithromycin

Indications

- Pneumonia
- Inflammation of nasal cavity
- Pertussis (Respiratory tract infection)
- Diphtheria (inflammation of mucus membrane of throat)
- Pharyngitis
- Covid-19
- Syphilis and Gonorrhoea
- Tetanus
- Skin infection ointment.

Contraindications

- Hypersensitivity
- Liver or kidney disease
- Myasthenia gravis
- Pregnancy and breastfeeding

Dose

✓ **Erythromycin :** 250 mg /d
✓ **Azithromycin :** 500- 1500 mg /d

Tetracyclines

- → Tetracycline is used to treat infections caused by bacteria including pneumonia and other respiratory tract infections; ; certain infections of skin, eye, lymphatic, intestinal, genital and urinary systems; and certain other infections that are spread by ticks, lice, mites, and infected animals.
- → It is also used along with other medications to treat acne.
- → Tetracycline will not work for colds, flu, or other viral infections.

Classification

- **Short acting (6 hours half life) :** Chlortetracycline , Oxytetracycline
- **Intermediate Acting (16 hours half life) :** Demeclocycline .
- **long acting (18-24 hours) :** Doxycycline , minocycline .

Indications

- Acne
- Chlamydia
- Non-gonococcal urethritis
- Trachoma
- Lymphogranuloma venereum
- Plague
- Respiratory tract infections
- Certain infections of skin
- Eye
- Lymphatic
- Intestinal, genital and urinary system

Contraindications

- Pregnancy and lactation
- Hypersensitivity
- In renal and hepatic failure

Dose

- ✓ **Chlortetracycline :** 250 mg /6 h
- ✓ **Doxycycline :** 100 -200 mg /d

Sulphonamides

- → Sulphonamides were the first antimicrobial agents (AMAs) , they are also known as Sulfa Drugs .
- → Sulfonamides (sulphonamides) are a group of man-made (synthetic) medicines that contain the sulfonamide chemical group .
- → They are bacteriostatic .
- → Many people use the term sulfonamide only for antibiotics However, there are several non-antibiotic sulfonamides that have been developed by observations These are used for a range of conditions such as diabetes and pain relief.

Classification

- ➢ **Short acting (4-8 hours) :** Sulfadiazine .
- ➢ **Intermediate acting (8-12 hours) :** Sulfamethoxaole , Sulfamoxole .
- ➢ **Long acting (7 days) :** Sulfadoxine , sulfamethopyrazine .

Indications

- **Bacterial infections :** eg, sulfamethoxazole / trimethoprim, sulfisoxazole
- **Crohn's disease :** eg, sulfasalazine
- **Diabetes :** eg, glyburide, tolbutamide
- **Fluid retention :** eg, chlorothiazide, furosemide, hydrochlorothiazide
- **Gout :** eg, probenecid
- **High blood pressure :** eg, chlorothiazide, hydrochlorothiazide
- **Pain and inflammation :** eg, celecoxib
- **Rheumatoid arthritis :** eg, sulfasalazine
- **Ulcerative colitis :** eg, sulfasalazine.

Contraindications

- ⮝ Pregnancy and lactation
- ⮝ Hypersensitivity

Dose

- ✓ **Sulfamethoxazole / trimethoprim :** 800 mg 160 mg / d
- ✓ **Sulfones (Dapsone) :** 50-100 mg /d

Anti-Tubercular Drugs

→ Anti-tubercular drugs are a group of medications used in the treatment of tuberculosis (TB), a bacterial infection caused by Mycobacterium tuberculosis.

Classification

1) First Line Drugs
   - Isoniazid (H), Rifampin (R), Pyrazinamide (Z),
   - Ethambutol (E), Streptomycin (S).
2) Second Line Drugs
   - Thiacetazone (Tzn), Paraaminosalicylic acid (PAS),
   - Ethionamide (Etm), Cycloserine (Cys),
   - Kanamycin (Kmc),Capreomycin(Cpr). Amikacin (Am),
3) Newer Drugs
   - Ciprofloxacin, Ofloxacin, Clarithromycin,
   - Rifabutin. Azithromycin,

Indications

- Tuberculosis
- Gaucher's disease
- Mycobacterium avium

Contraindications

- Hypersensitivity,
- Acute and chronic alcoholism,
- Acute liver disease,
- People above 35 years,
- Seizure disorders,
- Lactating women
- Patients with kidney disorders,
- Pregnancy
- Hepatitis

Dose:

✓ **Isoniazid (INH) :**
- Adult dose: 5 mg/kg to 15 mg/kg of body weight, up to a maximum of 300 mg per day
- Pediatric dose: 10 mg/kg to 20 mg/kg of body weight, up to a maximum of 300 mg per day

✓ **Rifampin (RIF) :**
- Adult dose: 10 mg/kg to 20 mg/kg of body weight, up to a maximum of 600 mg per day
- Pediatric dose: 10 mg/kg to 20 mg/kg of body weight, up to a maximum of 600 mg per day

Anti Fungal Drugs

- → The drugs are used to treat Fungal Infections are called antifungal drugs .
- → Fungi most commonly affect Skin , hair and nails .
- → Fungi are neither plants nor animals, and are classified as their own kingdom.
- → Fungi grow either as yeasts (single round cells) or as moulds (many cells forming long, thin threads called hyphae).
- → Some fungi even go through both the forms during their life cycle. Many fungi, including bread moulds and mushrooms, can be seen with the naked eye.
- → Fungal infections are often caused by fungi present in the environment.
- → Most fungi are not dangerous, but some of them can be harmful.

Classification

I. **Antibiotics: (Systemic)**
   - **Polyenes :** Amphotericin B (AMB), Nystatin, Hamycin, and Natamycin (Pimaricin).
   - **Heterocyclic Benzofuran :** Griseofulvin.

II. **Antimetabolite :** Flucytosine (5-FC).

III. **Azoles:**
   - **Imidazoles (Topical) :** Clotrimazole, Econazole, and Miconazole. (Systemic): Ketoconazole.
   - **Triazoles (Systemic) :** Fluconazole , Itraconazole.
   - **Allylamine :** Terbinafine.

Indications

- Fungal infections
- Onychomycosis
- Tinea capitis
- Cryptococcosis
- Prophylaxis

Contraindication:

- Hypersensitivity
- Hepatic dysfunction
- Endocrine or fertility problems

Dose:

- ✓ **Fluconazole :** 150-400 mg orally once daily
- ✓ **Itraconazole :** 200-400 mg
- ✓ **Posaconazole :** 300 mg orally twice daily
- ✓ **Amphotericin B :** Given intravenously, and the dose can range from 0.3-1.5 mg/kg/day.
- ✓ **Caspofungin :** 70 mg intravenously once on the first day.

Anti-Viral Drugs

- → The drugs are used to treat viral infections are called antiviral drugs . Viruses are tiny capsules (smaller than bacteria) containing genetic material.
- → They cause common infectious diseases like common cold, flu, and warts; while they may also cause severe illnesses such as HIV/AIDS, smallpox, and haemorrhagic.
- → Viruses invade (enter , attack and take control of) the living, normal cells of an individual, and use them to multiply.
- → This ultimately kills the cells, and the individual becomes sick.
- → Since the viruses live inside the body's cells, treatment of viral diseases is hard.
- → Antibiotics cannot cure viral diseases, and a few antiviral drugs are available.
- → However, vaccines can prevent the occurrence of many viral diseases.

Classification

1. **Anti-Herpes Virus :** Idoxuridine, Acyclovir, Trifluridine, Ganciclovir, and Foscarnet. Famciclovir, Valacyclovir, Penciclovir, Docosanol,
2. **Anti-Retrovirus**
    - **Nucleoside Reverse Transcriptase Inhibitors (NRTIs) :** Zidovudine (AZT), Stavudine, Lamivudine, and Abacavir.
    - **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) :** Nevirapine, Efavirenz, and Delavirdine.
    - **Retroviral Protease Inhibitors :** Ritonavir, Indinavir, Nelfinavir, Saquinavir, Amprenavir, and Lopinavir.
3. **Anti-Influenza Virus :** Amantadine, and Rimantadine.
4. **Non -Selective Anti - Viral drugs :** Ribavirin , Lamivudine,

Indications

- Influenza A viruses, Herpes viruses
- Cytomegalovirus (CMV) Infection, HIV Infection
- Hepatitis B and C viruses, Some viruses cause warts and Eye infections.

Contraindications

- ⅄ Previous history of allergy to the drug, Renal impairment
- ⅄ Pregnancy and lactation,
- ⅄ Severe CNS disorders
- ⅄ Hepatic dysfunction, Bone marrow suppression

Dose

- ✓ **Acyclovir :** Adults is 200 mg five times daily or 400 mg three times daily for 5-10 days.
- ✓ **Oseltamivir :** Adults and adolescents weighing 40 kg or more is 75 mg twice daily for 5 days.
- ✓ **Ribavirin :** Oral dose for adults is 600 mg twice daily for 3-7 days.

Anti- Amoebic Agents

→ The drugs are used to treat Amoebiasis Infection are called Anti- Amoebic agent.

→ Amoeba is a Parasite which affects intestine and extraintestinal parts of the body including lungs , liver and brain.

Classification

1) Tissue amoebicides

a. For intestinal and Extraintestinal amoebiasis :

- **NItroimidazoles :** *Metronidazole , Tinidazole , Ornidazole .
- **Alkaloids :** *Emetine and Dehyroemetine .

b. For extraintestinal Aboebiasis only : *Chloroquine .

2) Luminal Amoebicides :

a. **Amides :** Diloxanide furomate , Nitazoxanide .

b. **Antibiotics :** Tetracycline , Paramomycin .

Indication

- Amoebiasis
- Giardiasis
- Trichomoniasis (sexually T . D.)
- Anaerobic bacterial Infection
- H. Pylory Infection

Contraindication

- Individuals who have encountered certain blood disorders, pregnant women, and alcoholics are advised against consuming antiamoebic agents

Dose

- ✓ Metronidazole: Adults—500 or 750 milligrams (mg) 3 times a day for 5 to 10 days
- ✓ IV: 15 mg/kg
- ✓ Capsule: 375mg

Anthelmintic Drugs

- → Anthelmintics are a type of medicine that kills helminths. Helminths are worm-like parasites such as flukes, roundworms, and tapeworms.
- → It is important that anthelmintics are selectively toxic to the parasite and not the host.
- → Some work by inhibiting metabolic processes that are vital to the parasite but absent or not vital in the host.

Classification

- ➢ **Benzimidazoles** : Albendazole , Mebendazole .Flubendazole .
- ➢ **Hetrocyclics :** Oxamniquine .
- ➢ **Piperazine derivatives :** Piperazine citrate.
- ➢ **Amides :** Niclosamide
- ➢ **Natural Product :** Ivermectin

Indications

- Hookworm
- Roundworm
- Pinworm
- Liver Fluke
- Tapeworm

Contraindications

- ⅄ Pregnancy
- ⅄ Breastfeeding
- ⅄ Severe diarrhea
- ⅄ Malnourishment
- ⅄ Hepatic or renal diseases

Dose:

- ✓ Albendazole 400 mg taken once daily for 1-3 days for most types of infections.
- ✓ Mebendazole is 100 mg taken twice daily for 3 days for most types of infections. For whipworm infections
- ✓ Pyrantel is 11 mg/kg (up to a maximum of 1 g) taken as a single dose for most types of infection

Anti- Malarial Agents

- → The drugs are used to treat malaria are called anti- malarial drugs .
- → Malaria is a life-threatening disease, transmitted through the bite of an infected female Anopheles mosquito, carrying the Plasmodium parasite.
- → The infected mosquito releases the parasite in the blood by biting an individual

Classification

- **4-Aminoquinolines :** Chloroquine, Amodiaquine, and Piperaquine.
- **Quinoline-Methanol :** Mefloquine.
- **Cinchona Alkaloid :** Quinine and Quinidine.
- **Biguanides :** Proguanil (Chloroguanide) and Chloroproguanil.
- **Diaminopyrimidines :** Pyrimethamine.
- **8-Aminoquinolines :** Primaquine and Bulaquine.
- **Sulfonamides and Sulfone :** Sulfadoxine, Sulfamethopyrazine, and Dapsone.
- **Tetracyclines :** Tetracycline and Doxycycline.
- **Sesquiterpene Lactones :** Artesunate, Artemether, and Arteether.
- **Amino Alcohols :** Halfofantrine and Lumefantrine.

Indications

- Malaria
- Chloroquine is used with metronidazole in amoebiasis .
- It is used in giardiasis
- Chloroquine is used in Arrhythmias
- In rheumatoid arthritis

Contraindication

- Nausea and vomiting
- Headache
- Dizziness
- Fatigue
- Malaise (feeling of discomfort)
- Muscular pain (Myalgia)
- Diarrhea, Cough, Fever and chills

Dose:

- ✓ **Chloroquine :** Adults- 500 mg once a week for malaria.
- ✓ **Quinine :** Adults- 600 mg every 8 hours for 7 to 10 days for treatment of malaria.
- ✓ **Mefloquine :** Adults- 250 mg once a week.

Anti -Neoplastic Agents

→ The drugs are used to treat cancer are called anti-neoplastic agents . Cancer is a disease characterised by abnormal and uncontrolled cell division attacking the surrounding tissues and organs, and also the other body parts by circulating with blood and lymph

Classification

1) Alkylating agents

- Nitrogen mustards : Mechlorethamine (Mustine HCI), Ifosfamide, Cyclophosphamide, Chlorambucil, and Melphalan
- Ethylenimine : Thio-TEPA
- Alkyl sulfonate : Busulfan
- Nitrosoureas : Carmustine (BCNU) and Lomustine (CCNU)
- Triazine : Dacarbazine (DTIC)

2) Antimetabolites

- Folate antagonist : Methotrexate (Mtx)
- Purine antagonist : 6-Mercaptopurine (6-MP), 6-Thioguanine (6 -TG), and Azathioprine
- Pyrimidine antagonist : 5-Fluorouracil (5-FU) and Cytarabine (cytosine arabinoside)

3) Natural Products

- Vinca alkaloids : Vincristine (Oncovin) and Vinblastine
- Taxanes : Paclitaxel and Docetaxel
- Epipodophyllo toxin : Etoposide
- Camptothecin analogues : Topotecan and Irinotecan

4) **Antibiotics:** Actinomycin D, Dactinomycin, Doxorubicin, Daunorubicin, Rubidomycin, Mitoxantrone, Bleomycin, Mitomycin C, and Mithramycin

5) **Enzymes:** Asparaginase

6) **Miscellaneous:** Hydroxyurea, Procarbazine ,L-Asparaginase, Cisplatin, and Carboplatin

7) **Hormone** Balance altering gents

- Glucocorticoids : Prednisolone
- Estrogens : Fosfestrol and Ethinylestradiol
- Antiestrogen : Tamoxifen
- Antiandrogen : Flutamide
- 5-α reductase inhibitor : Finasteride
- GnRH (Gonadotropin Releasing Hormone) analogues: Nafarelin and Goserelin

8. Radioactive Isotopes : Sodium phosphate, Sodium iodide, and Radio gold solution

Indications

- Breast Cancer
- Ovarian cancer
- Cervical cancer
- Blood cancer
- Neck carcinomas (cancer of epithelia tissues)
- Certain lymphomas
- Bladder cancer
- Mechlorethamine is used in Bone Marrow Cancer Like Polycythemia , Leukemia Thrombocythemia .
- Cyclophosphamide is mostly used for treating different cancers .
- Vinblastine sulphate is used to treat neuroblastoma(cancer of adrenal gland) , testicular cancer , kapsosi's sarcoma (cancer of soft tissues with lesions)

Contraindications

- Previous history of allergy
- Pregnancy and lactation
- Bone marrow suppression
- Renal and hepatic disorders
- GI ulceration

Doses

- ✓ Cisplatin : 20mg/m^2 I.V
- ✓ Tamoxifen : 20-40 mg/day
- ✓ Doxorubicin 50 mg/m^2 I.V 4 Weeks

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