Trastuzumab (Herceptin)

Drug type
- Recombinant DNA-derived humanized anti-HER2 (human epidermal growth factor receptor 2 protein) monoclonal antibody
- Antineoplastic agent

Indications
- HER2-positive carcinoma of the breast
  - Used in combination with standard adjuvant chemotherapy for treating operable HER2-positive breast cancer
  - Prescribed as monotherapy for treating metastatic breast cancer that has recurred after prior chemotherapy in patients with tumors that overexpress the HER2 protein
  - Also used along with paclitaxel for initial treatment of metastatic breast cancer in patients with tumors that overexpress the HER2 protein

Mechanism of action and pharmacology
- Inhibits proliferation of tumor cells that overexpress HER2, binding specifically to extracellular domain of HER2 receptor or HER2/neu protein
  - Overexpression of HER2 receptor contributes to neoplastic transformation
  - HER2 receptor participates in receptor-receptor interactions that regulate cell differentiation, growth, proliferation

How to administer
- IV infusion with initial dose infused over 90 minutes
  - If first dose is well-tolerated, subsequent doses may be infused over 30 minutes
  - Do not administer by rapid IV injection, IV push, or bolus
- Prior to administration
  - Do not dilute solutions for infusion in, or administer through, an IV line containing 5% dextrose injection
  - Do not mix or dilute with other drugs
  - Inspect trastuzumab solutions for particulate matter and discoloration
- Premedication
  - None needed
  - If patients have had a prior sensitivity, acetaminophen, diphenhydramine, and/or a corticosteroid may be given

Common IV compatibilities (via Y-site)
- Medications compatible with trastuzumab include granisetron (Kytril), diphenhydramine hydrochloride, dexamethasone sodium phosphate, calcium gluconate, magnesium sulfate, potassium chloride
- These medications may not be compatible with each other
- These medications should be in normal saline; they are not compatible if in D5W

Pregnancy category: B

Lactation
- Unknown if excreted in breast milk
- Breast-feeding while on this agent is not recommended

Cautions and adverse effects
- Common adverse effects associated with trastuzumab include fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue,

paresthesia, dyspnea, rash, neutropenia, anemia, myalgia
- Serious adverse effects include cardiotoxicity, ventricular dysfunction, and heart failure; cardiomyopathy; pulmonary toxicities such as respiratory failure, pneumonitis, pulmonary infiltrates; infusion reactions such as angioedema or anaphylaxis; febrile neutropenia; exacerbation of chemotherapy-induced neutropenia
- Anaphylaxis, infusion reactions, and pulmonary events tend to occur with the first infusion; pulmonary events tend to occur within the first 24 hours
- Emetogenic potential: moderate

Monitoring
- Ejection fraction: echocardiography or multiple gated acquisition scan at baseline and then every 3 months during therapy
- Observe for signs and symptoms of hypersensitivity reactions, including anaphylaxis, urticaria, bronchospasm, angioedema, and/or hypotension
- Monitor patients for potential infusion reactions, including fever, chills, nausea, vomiting, pain, rigors, headache, dizziness, dyspnea, hypotension, hypertension, rash, and asthenia

Drug interactions
- No formal drug interaction studies of trastuzumab have been done; most common adverse effects are increased in patients receiving combination chemotherapy
  - Anthracycline antineoplastic agents
    - Trastuzumab-induced cardiotoxic effects can be increased in patients receiving an anthracycline concomitantly; concomitant use not recommended in the treatment of metastatic breast cancer
  - Paclitaxel
    - A 1.5-fold increase in mean trough serum concentrations of trastuzumab was reported in clinical studies when the drug was administered concomitantly with paclitaxel versus an anthracycline and cyclophosphamide; in primate studies, administration of trastuzumab in combination with paclitaxel resulted in a two-fold decrease in trastuzumab clearance
    - Clinical importance of the interaction between trastuzumab and paclitaxel is not known

What to tell your patient
- Trastuzumab is used by itself or with other medications to treat breast tumors that produce excess amounts of the HER2 protein
- This medication is a *monoclonal antibody*
  - It attaches to the HER2 cancer cells and blocks them from dividing and growing
  - It may also destroy the cancer cells directly or signal the body's immune system to destroy the cancer cells
- Side effects
  - Although this medication may cause side effects, its benefits may be greater than that risk, which is why it was prescribed for you
  - Many people do not have serious side effects
  - Some of the side effects are muscle, joint, or back pain; redness at the IV site; stomach pain; trouble sleeping; diarrhea, nausea, vomiting, and loss of appetite
  - Since the nausea and vomiting can be severe, your doctor may prescribe medication to prevent or relieve it
  - Tell your nurse or doctor immediately if you experience any of these unlikely but more serious side effects: swelling; tingling or numbness in your hands, feet, ankles, or legs; trouble breathing; unusual tiredness; severe headache or dizziness; bone pain; increased coughing; changes in mood; fast or pounding heartbeat
  - Seek immediate medical attention if any of these rare but very serious side effects occurs: weakness on one side of the body, slurred speech, vision changes, confusion
  - You may be able to lessen side effects by not eating before treatment, eating several small meals, or limiting your activity
  - If these side effects don't go away or they get worse, tell your nurse or doctor ■

Prepared by **Bette Weinstein Kaplan**. Reviewed by **Maribel Pereiras, PharmD, BCPS, BCOP**.