Administration of Subcutaneous Injections
Six recommendations that may minimize injection site reactions

1. Needle should be changed after drawing up the drug before injection
Before administration, make sure the needle used during preparation has been changed and the needle should be changed after drawing up the drug before injection.

2. Use abdomen and thighs as injection sites
Site rotation between the abdomen and thighs is suggested as it may prevent contact of medication with the skin.

3. Ensure medication is deposited in the subcutaneous tissue
Ensure medication is deposited in the subcutaneous tissue and not intravenously.

4. Instruct patients to inject slowly and steadily
Inject slowly and steadily (1-0 mL for 10 seconds) allowing absorption by the surrounding tissue and avoiding fluid back up the needle into the tissue.

5. Educate your patients and their families
It is important to educate your patients and their families about the side effects that they may experience with subcutaneous injections.

Additional considerations
• For all subcutaneous injections, it is important to maintain aseptic procedures.
• Nurses must wash their hands before giving the injection and following the administration of VELCADE.
• Gloves should be worn; however, they may not protect from needlestick injuries.

References:
2. Noncoated needles should be carefully and immediately disposed of at the point of administration.
3. This information is not meant to replace institutional policies and procedures.
4. It is important to educate your patients and their families about the side effects that they may experience with subcutaneous injections.

ADVERSE REACTIONS

Tumor lysis syndrome:
Closely monitor patients with high tumor burden and take appropriate precautions.

Hepatic toxicity:
Women should avoid breast-feeding or becoming pregnant while on VELCADE.

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Embryo-fetal risk:
Embryo-fetal risk is present in VELCADE during all trimesters. Women of child-bearing potential should be advised to avoid becoming pregnant during VELCADE treatment. If pregnancy occurs, VELCADE should be immediately stopped and the woman should be referred to a gynecologist. Women should be counseled about the potential for fetal harm. Women of child-bearing potential should be advised to use effective contraception during and for at least 3 months after treatment with VELCADE.

Indication and Important Safety Information for VELCADE® (bortezomib)
CONTRAINDICATIONS: VELCADE is contraindicated in patients with hypersensitivity (including local reactions) to bortezomib, boron, or mannitol, including anaphylactic reactions. VELCADE is contraindicated for intrathecral administration. Fatal events have occurred with intrathecral administration of VELCADE.

WARRANTINGS AND PRECAUTIONS: VELCADE is for subcutaneous or IV administration only. Because each route of administration has a different recombinant formulation, caution should be used when calculating the doses to be administered intraocularly versus subcutaneously.

Peripheral neuropathy, including severe cases, may occur. Patients should be monitored for symptoms and managed with dose modification or discontinuation. Patients with preexisting symptoms may experience worsening peripheral neuropathy. (See table below: Grade 3: Starting with VELCADE subcutaneous may be considered for patients who either have pre-existing or are at high risk for peripheral neuropathy.

Hypersensitivity: Caution should be used when treating patients receiving antihypersensitivities, those with a history of syncope, and those who are debilitated.

Cardiovascular toxicity, including acute development or exacerbation of congestive heart failure and new onset of decreased left ventricular ejection fraction, has occurred, isolated cases of QT-interval prolongation have been reported. Patients with risk factors for, or existing, heart disease should be monitored closely.

Pulmonary toxicity: Acute respiratory distress syndrome (ARDS) and acute diffuse infiltrative pulmonary disease of unknown etiology (Al-DIP) have been reported. Patients with preexisting symptoms may experience worsening pulmonary toxicity. (See table below: Grade 4: For severe or worsening cases of respiratory distress, interrupt VELCADE until a prompt and comprehensive diagnostic evaluation is conducted.

Protease reversible encephalopathy syndrome has occurred. Consider MRI imaging for onset of visual or neurological symptoms; discontinue VELCADE if suspected.

Gastrointestinal toxicity, including nausea, diarrhea, constipation, and vomiting, has occurred and may require use of antiepileptics and antiemetic medications or fluid replacement. Interrupt VELCADE for severe symptoms.

Thrombocytopenia/Neutropenia: Manage with dose and/or schedule modifications. Complete blood counts should be monitored frequently during treatment. These have been reported of gastrointestinal and intracerebral hemorrhage. Support with transfusions and supportive care, according to published guidelines.

Tumor lysis syndrome: Closely monitor patients with high tumor burden and take appropriate precautions.

Hepatic toxicity: Monitor hepatic enzymes during treatment. Upon occurrence, interrupt therapy with VELCADE to assess reversibility.

Embryo-Fetal Risk: Women should avoid breast-feeding or becoming pregnant while taking VELCADE.

Patients with diabetes may require close monitoring and adjustment of the antidiabetic medications.

DRUG INTERACTIONS: Closely monitor patients receiving VELCADE in combination with strong CYP3A4 inhibitors. Avoid concurrent use of strong CYP3A4 inducers.

ADVERSE REACTIONS

Previously untreated multiple myeloma (MM): In the phase 3 study of VELCADE administered intravenously with melphalan and prednisolon (VP-16) to patients with previously untreated MM, the most commonly reported adverse reactions (AEs) were thrombocytopenia (18% vs 42%), neutropenia (17% vs 60%), peripheral neuropathy (16% vs 11%), nausea (23% vs 46%), and anemia (25% vs 28%).

Relapsed MM: In the phase 3 study of VELCADE administered intravenously vs dexamethasone, the most commonly reported AEs were nausea (21% vs 3%), diarrhea (25% vs 25%), neutropenia (31% vs 4%), thrombocytopenia (30% vs 5%), constipation (6% vs 8%), and vomiting (7% vs 3%). The most commonly reported serious AEs were diarrhea (3%), constipation (2%), and vomiting (2%). The incidence of neurologic AEs was similar in the two groups. The most commonly reported AEs in the relapsed MM arm were neuropathy (4%), peripheral neuropathy (4%), and anemia (2%). The most commonly reported serious AEs were neuropathy (2%) and peripheral neuropathy (1%). The incidence of neurologic AEs was similar in the two groups. The most commonly reported serious AEs were neuropathy (2%) and peripheral neuropathy (1%).

In the phase 3 study of VELCADE administered subcutaneously vs intravenously in patients with relapsed MM, the incidence of grade 3 and 4 neutropenia, peripheral neuropathy, and anemia were similar in the two groups.

Injection site reactions: Injection site reactions may occur. Injection sites should be rotated and the drug administered at least 1 inch from an old injection site. Use abdomen and thighs as injection sites.

Site rotation between the abdomen and thighs is suggested as it may prevent the formation of indurations and abscesses.

Inject slowly and steadily (≈1.0 mL for 10 seconds) allowing absorption by the surrounding tissue and avoiding fluid backtrack up the needle into the skin.

Insert needle at a 90-degree angle. Generally, when using a 25-gauge needle that is 5/8 inch in length, insert the needle at a 90-degree angle.

Before administration, make sure the needle used during preparation has been changed to a new, clean, sharp, dry needle. This practice may reduce the chance of topical contact of medication with the skin.

After administration, dispose of the used needle immediately.

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