Guidelines for the use of Linezolid (Revised 5-26-04)

A number of studies have shown vancomycin and linezolid to have equivalent efficacy for a variety of infections due to gram positive organisms (1-5). The 100% bioavailable oral dosage form of linezolid makes it an attractive option for outpatient management of serious infections due to resistant gram positive organisms. One group of investigators has suggested linezolid may be superior to vancomycin for MRSA nosocomial pneumonia (6). The data from these investigators represent a retrospective and multiple subgroup analysis that is in marked contrast to the overwhelming majority of the available data which show equivalence. Recent data regarding emergence of resistance to linezolid in both *Enterococcus* spp. and *Staphylococcus aureus* create a significant concern over the durability of this agent with widespread use (7,8). Also, recent reports of toxicity including bone marrow suppression, neurotoxicity, serotonin-syndrome, uveitis and peripheral neuropathy create concerns over long term use (9-12). Toxicities may increase when the drug is given for longer than 2 weeks.

For initiation of linezolid therapy, patients must meet one of the following criteria:

1) Culture-directed therapy of serious vancomycin-resistant *Enterococcus* infections (NOT stool colonization or uncomplicated urinary tract infections susceptible to an alternative agent such as doxycycline, nitrofuratoin.)

2) Treatment of serious culture-documented MRSA infections in patients with severe adverse reactions to vancomycin as such as defined below:

Stevens-Johnson syndrome

Anaphylaxis or accelerated allergic reactions

Interstitial nephritis

The above statement does NOT include the following: red-man's syndrome, renal insufficiency, mild rash during previous therapy.

3) In cases of **mild to moderate** skin and soft tissue infections due to culture proven MRSA, susceptibility- directed therapy with clindamycin, trimethoprim-sulfamethoxazole, doxycycline, or minocycline should be utilized when appropriate.

Outpatient therapy of culture documented **severe** MRSA skin and soft tissue infections or pneumonia where the alternative therapy would be intravenous vancomycin. Duration of therapy should not exceed 2 weeks due to toxicity concerns.

4) Patients with serious culture-documented MRSA infections failing vancomycin who have clearly documented vancomycin troughs of 15-20 mcg/ml after 3 to 5 days of therapy.

5) For patients in whom the attending physician feels that linezolid is indicated but do not meet the above criteria, written approval from the Infectious Diseases consult service or the Anti-Infectives Management Team is required.

References:

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