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CDC Health Advisory

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CDC Recommends against the Use of Amantadine and Rimantadine for the Treatment or Prophylaxis of Influenza in the United States during the 2005–06 Influenza Season

Recent evidence indicates that a high proportion of currently circulating Influenza A viruses in this country are resistant to these medications

While the primary strategy for preventing complications of influenza infections is annual vaccination, antiviral medications with activity against influenza viruses can be effective for the prophylaxis and treatment of influenza. Two classes of antivirals are currently available—the M2 ion channel inhibitors (i.e., the two adamantanes amantadine and rimantadine) and the neuraminidase inhibitors (i.e., oseltamivir and zanamivir). The neuraminidase inhibitors are effective for the treatment and prophylaxis of influenza A and B, while the adamantanes are only active against influenza A viruses. This alert provides new information about the resistance of influenza viruses currently circulating in the United States to the adamantanes, and it makes an interim recommendation that these drugs not be used during the 2005–06 influenza season. Amantadine is also used to treat the symptoms of Parkinson's disease, and should continue to be used for this indication.

Viral resistance to adamantanes can emerge rapidly during treatment because a single point mutation at amino acid positions 26, 27, 30, 31, or 34 of the M2 protein can confer cross-resistance to both amantadine and rimantadine. The transmissibility of adamantane-resistant viruses is not impaired by any of these amino acid changes. A recent report on the global prevalence of adamantane-resistant influenza viruses showed a significant increase (from 1.9% to 12.3%) in drug resistance over the past 3 years. In the United States, the frequency of drug resistance increased from 1.9% in 2004 to 14.5% during the first 6 months of the 2004–05 influenza season.

For the 2005–06 season, 120 influenza A (H3N2) viruses isolated from patients in 23 states have been tested at CDC through January 12, 2006; 109 of the isolates (91%) contain an amino acid change at position 31 of the M2 protein, which confers resistance to amantadine and rimantadine. Three influenza A(H1N1) viruses have been tested and demonstrated susceptibility to these drugs. All influenza viruses from the United States that have been screened for antiviral resistance at CDC have demonstrated susceptibility to the neuraminidase inhibitors.

On the basis of available antiviral testing results, CDC is providing an interim recommendation that neither amantadine nor rimantadine be used for the treatment or prophylaxis of influenza A in the United States for the remainder of the 2005–06 influenza season. During this period, oseltamivir or zanamivir should be selected if an antiviral medication is used for the treatment and prophylaxis of influenza. Testing of influenza isolates for resistance to antivirals will continue throughout the 2005–06 influenza

season, and recommendations will be updated as needed. Annual influenza vaccination remains the primary means of preventing morbidity and mortality associated with influenza.

Additional information about the prevention and control of influenza is available at <http://www.cdc.gov/flu/>. Specific information regarding the use of the neuraminidase inhibitors is available at <http://www.cdc.gov/flu/protect/antiviral/index.htm>. These websites will be updated as new information becomes available.

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