Emerging Drug List
PLECONARIL

CANADIAN COORDINATING OFFICE FOR HEALTH TECHNOLOGY ASSESSMENT

NO. 15 SEPTEMBER 2001

Generic (Trade Name)**:** Pleconaril (Picovir™)

Manufacturer: ViroPharma

Indication: For the treatment of viral respiratory infections (common cold) in adults.

Current Regulatory Status: ViroPharma announced on July 31, 2001 that they had submitted a new drug application with the U.S. FDA for the clearance of pleconaril for the treatment of viral respiratory infection (common cold) in adults. ViroPharma has not filed a submission with Health Canada but will be discussing that possibility with Aventis in the near future. Globally, pleconaril has not been approved by any regulatory body. Pleconaril is currently in Phase II clinical trials for treatment of the common cold in children, as well as treatment of otitis media and asthma. Pleconaril has also been studied for the treatment of viral meningitis and other potentially life-threatening enteovirus infections.

Description: Pleconaril is an antipicornavirus agent. Picornaviruses include enteroviruses and rhinoviruses (the two types of viruses that account for the majority of human viral infections). Pleconaril integrates within a hydrophobic pocket inside the virion. This results in the viral capsid becoming compressed and rigid. This effect interrupts the viral infection cycle by preventing the virus from attaching to cells and/or releasing viral RNA from the capsid.

For the treatment of the common cold in adults, the dose of pleconaril has ranged from 300 to 400 mg (orally) three times daily for five to seven days. Pleconaril should be given with a fat containing meal to enhance absorption.

Current Existing Treatments: No products are indicated for the treatment of the common cold. Presently, treatment of the common cold consists of agents that target a specific symptom (i.e., antihistamines, decongestants, antipyretics). Pleconaril is the first antiviral agent to be evaluated as a treatment that would target the causative agent.

Cost: No information on cost could be located at this time.

Evidence: Studies of pleconaril for the treatment of the common cold have not been published. Limited data on its effectiveness for this indication were obtained from press-releases from ViroPharma. Pleconaril 400 mg TID for five days was compared to placebo for the treatment of the common cold in two studies with a total of 2096 patients. A total of 65% of these patients had a viral respiratory infection caused by a picornavirus. The primary endpoint of these studies was complete resolution of rhinorrhea and reduction in all other evaluated disease symptoms to absence or mild levels for 48 hours. When only the patients infected with a picornavirus were evaluated, pleconaril

significantly reduced the time to achieve the primary endpoint when compared to placebo (i.e., 6.2 vs 7.7 days in the first study [p=0.001] and 6.6 vs 7.2 days in the second study [p=0.037]). When data from all patients (i.e., intention-to-treat analysis) were evaluated, only one study produced a significant difference in the primary endpoint (i.e., 6.2 vs 7.1 days [p=0.015] and 6.4 vs 6.9 days [p=0.201]).

The effectiveness of pleconaril was evaluated in a small (n=33) study in an experimentally induced coxsackievirus A21 respiratory infection. The dose of pleconaril was 400 mg on Day 1 followed by 200 mg BID for 7 days. Subjects received a nasal inoculation of 100 plaque-forming units of coxsackievirus A21, 14 hours after receiving the first dose of pleconaril. In this study, pleconaril resulted in significant reductions in viral shedding in nasal secretions ($p<0.001$), nasal mucous production ($p=0.004$), and total respiratory illness symptom scores ($p=0.013$) when compared to placebo subjects. The results of this study are significant; however, this data cannot be extrapolated to the normal population, since the researchers controlled the source and timing of the infection and subjects were started on the pleconaril before symptoms of the common cold could have a chance to develop.

Symptoms of the common cold tend to subside naturally with time. A comparison of minimal-symptom days towards the end of therapy is necessary before the true impact of pleconaril can be established. Although individual symptoms improved somewhat faster with pleconaril, the clinical significance of this finding may be questioned.

Adverse Effects: Pleconaril appears to be well tolerated with no systemic adverse effects being reported. Crystalluria has been reported in some healthy patients who received a 1000 mg single dose. There was no pleconaril found in the crystals; however, urinalysis is recommended if pleconaril is going to be used over a prolonged period of time. Since clinical use of pleconaril is limited, other adverse effects may be identified with further experience.

Conclusion: The development of pleconaril will be of great interest to many individuals. Significantly more research is needed to better determine its impact on the common cold. The common cold is a relatively benign condition that resolves spontaneously. It is generally considered more of an annoyance than a disease. It is currently managed with agents that target specific symptoms. Trials which show whether pleconaril use can significantly reduce lost time at work or increase productivity, instead of simply speeding up the disappearance of symptoms when used to treat a cold, would be required to substantiate any real benefit.

References:

Schiff GM, Sherwood JR. Clinical activity of pleconaril in an experimentally induced coxsackievirus A21 respiratory infection. **J Inf Dis** 2000;181(1):20-6. Abstract available: http://www.journals.uchicago.edu/JID/journal/issues/v18n1/990366/brief/990366.abstract.html

Rotbart HA, Webster AD, Pleconaril Treatment Registry Group. Treatment of potentially life-threatening enterovirus infections with pleconaril. **Clin Inf Dis** 2001;32(2):228-35.

Pleconaril DRUGDEX® drug evaluation. In: Hutchison TA, Shahan DR, editors. DRUGDEX® System. Greenwood Village, CO: Micromedex, 2001.

ViroPharma Incorporated. **March 15, 2001: ViroPharma announces successful Phase 3 trial results** [press release]. Available: http://www.viropharma.com/Press/010315Press.htm (accessed 2001 Sept 6).

ViroPharma Incorporated. **July 31, 2001: ViroPharma files new drug application for Picovir™ (pleconaril) for the treatment of viral respiratory infection in adults.** Available: http://www.viropharma.com/Press/010731%20Press.htm (accessed 2001 Sept. 5).

The contents of this bulletin are current as of September 2001.

This series highlights drugs not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

ISSN 1496-8398 (online only)