Bayer Receives FDA Approval for the Intravenous Form of Its Antibiotic Avelox® (moxifloxacin HCl)

--Potent fluoroquinolone targeted against key respiratory pathogens in hospitals--

--Avelox and Cipro® (ciprofloxacin) together cover hospitals' fluoroquinolone needs--

West Haven, CT, December 4, 2001 – The U. S. Food and Drug Administration (FDA) today approved an intravenous (I.V.) formulation of *Avelox*® (moxifloxacin hydrochloride in sodium chloride for injection) for the treatment in adults of community-acquired pneumonia (CAP)[i], acute bacterial sinusitis (ABS)[ii], acute bacterial exacerbations of chronic bronchitis (ABECB)[iii], and uncomplicated skin and skin structure infections (uSSSI)[iv]. Avelox was first approved in tablet form in December, 1999, for treating common adult respiratory tract infections.

After two years and nearly ten million patient uses worldwide, *Avelox* has a proven record of safety and efficacy. "From all of the data I have seen in patients treated with *Avelox*, I am confident that the drug is safe and generally well tolerated," said Paul Iannini, MD, Clinical Professor of Medicine at Yale University, Chairman, Department of Medicine, Danbury Hospital in Connecticut. "*Avelox* I.V. is an excellent choice in the hospital setting for treating respiratory tract infections such as CAP because it provides potent, targeted activity against the key respiratory pathogens -- most importantly *Streptococcus pneumoniae*."

The most recent guidelines from the Infectious Disease Society of America recommend anti-pneumococcal quinolones as first-line therapy in patients presenting to the hospital with CAP.[v] CAP is the most common form of pneumonia, with more than five million cases annually. It is also the sixth leading cause of death overall and the number one cause of death due to an infectious disease.[vi] More than one million patients are hospitalized each year with CAP where treatment with an I.V. antibiotic may be required.[vii]

"*Avelox* I.V. provides us a significant and important new option for very effective and safe treatment of respiratory and other infections in the hospital setting," said Charles Fogerty, MD, Medical Director, Respiratory Therapy at Spartenburg Regional Medical Center, South Carolina, and a lead investigator of *Avelox* I.V. trials. He added that, "because the I.V. and tablet forms of *Avelox* are bioequivalent, no dosing adjustment is required. Physicians can switch a patient from I.V. to oral *Avelox*, facilitating earlier patient discharge and potential cost savings while maintaining excellent clinical outcomes."

Dosing

The recommended therapeutic dose for both *Avelox* I.V. and *Avelox* tablets is 400 mg once-daily for seven to fourteen days for CAP, five and ten days for ABECB and ABS, respectively, and seven days for uSSSI. *Avelox* I.V. is available as a ready-to-use dose in a latex-free pre-mixed flexibag. When switching from intravenous to oral administration of *Avelox*, no dosage adjustment is necessary. Additionally, dosing adjustments are not required in patients with renal impairment or mild to moderate hepatic insufficiency. The pharmacokinetics of *Avelox* in severe hepatic insufficiency has not been studied.

Coverage Against Bacterial Infections in the Hospital Setting

Avelox I.V. joins Cipro® (ciprofloxacin), the well-known fluoroquinolone also from Bayer, for use in treating bacterial infections in the hospital. *Cipro* was launched more than 14 years ago and is available on hospital formularies nationwide.

"The addition of Avelox I.V. to our anti-infective portfolio greatly strengthens our ability to meet a hospital's fluoroquinolone needs," said Dr. Wolfgang Plischke, President of Bayer Corporation's Pharmaceutical Division. "Now, *Cipro* and *Avelox*, between them, have the broadest range of approved indications among the fluoroquinolones and offer *in vitro* coverage of gram-positive, gram-negative, atypical and anaerobic bacteria."

Additionally, the American Thoracic Society guidelines identify *Avelox* as the most active anti-pneumococcal quinolone *in vitro*.[viii]

Approval Based on Pivotal Studies

Bayer submitted data to the FDA from two large, randomized, controlled trials for the treatment of CAP. Each trial compared the efficacy of sequential I.V./oral *Avelox* therapy to that of other leading antibiotics. A double-blind study showed similar efficacy to the comparator fluoroquinolones. An open-label study demonstrated a clinical success rate with *Avelox* therapy that was superior to the comparator beta-lactam given with or without a macrolide.[ix] Approval of *Avelox* I.V. also was based on numerous past studies demonstrating the safety and efficacy of *Avelox* tablets in treating CAP, ABS, ABECB, and uSSSI.

About *Avelox*

Avelox tablets are marketed in 65 countries and approved in 70 countries. To date, nearly ten million patient uses have been reported worldwide since it was approved in September 1999. *Avelox* is the fastest growing quinolone in the United States according to audited data from IMS HEALTH. This respiratory season, *Avelox* is once again the fastest growing quinolone. From January–October 2001, *Avelox* prescriptions grew 160% vs. January – October 2000.

In addition to the current indications for CAP, ABS, ABECB and uSSSI, *Avelox* is currently being studied for use in intra-abdominal and complicated skin infections.

Incidence of Side Effects with *Avelox*

Avelox is generally well tolerated. In clinical trials involving 7,900 patients, the most common adverse events, which were reported in 3% or more patients with *Avelox*, were nausea (7%), diarrhea (6%) and dizziness (3%).

Important Safety Considerations of *Avelox*

Moxifloxacin is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antimicrobial agents.

Anaphylactic reactions, some following the first dose, have been reported in patients receiving quinolone therapy including moxifloxacin.

The safety and effectiveness of moxifloxacin in pediatric patients, adolescents (less than 18 years of age), pregnant women, and lactating women have not been established.

Moxifloxacin has been shown to prolong the QT interval of the electrocardiogram in some patients. The drug should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving Class IA (e.g., quinidine, procainamide) or Class lll (e.g., amiodarone, sotalol) antiarrhythmic agents, due to limited clinical experience. Moxifloxacin should be used with caution when given together with drugs that may prolong the QT interval (e.g., erythromycin, antipsychotics, antidepressants) and in patients with ongoing proarrhythmic conditions, such as clinically significant bradycardia, acute myocardial ischemia.

As with all quinolones, moxifloxacin should be used with caution in patients with known or suspected CNS disorders or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold.

Important Safety Information About *Cipro*

Serious and fatal reactions have been reported in patients receiving concurrent administration of ciprofloxacin and theophylline. Monitor theophylline levels if concurrent administration cannot be avoided. The safety and effectiveness of ciprofloxacin in children and adolescents less than 18 years of age -except for inhalational anthrax (post-exposure) - pregnant women and lactating women have not been established. Ciprofloxacin is contraindicated in persons with a history of hypersensitivity to ciprofloxacin or any member of the quinolone class of antimicrobial agents. Ciprofloxacin should be discontinued at the first sign of an allergic reaction.

Most frequently reported adverse events (>1%) without regard to drug relationship were: CIPRO® Tablets and Oral Suspension: nausea, diarrhea, vomiting, abdominal pain/discomfort, headache, rash, restlessness. CIPRO® I.V.: nausea, diarrhea, CNS disturbance, local I.V. site reactions, abnormalities of hepatic enzymes, eosinophilia, headache, rash, restlessness.

Antacids containing magnesium, aluminum or calcium, or other products containing metal cations should be taken 2 hours after or 6 hours before oral administration of CIPRO®.

About Bayer

Best known for its flagship product, *Bayer Aspirin*, Bayer Corporation produces a broad range of health care, life sciences and chemical products that help diagnose and treat diseases, purify water, preserve local landmarks, protect crops, advance automobile safety and durability and improve people's lives.

Headquartered in Pittsburgh, Bayer Corporation had sales of $10.1 billion in 2000 and is one of *Fortune* magazine's Most Admired Companies. The company employs approximately 23,200 people. It is a member of the worldwide Bayer Group, a $29 billion international health care and chemicals group based in Leverkusen, Germany. The Bayer Group (BAYG.DE) stock is a component of the DAX, and is listed on multiple foreign exchanges.

---

[i] Caused by *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Staphylococcus aureus, Klebsiella pneumoniae, Mycoplasma pneumoniae or Chlamydia pneumoniae.*

[ii] Caused by *Streptococcus pneumoniae, Haemophilus influenzae*, or *Moraxella catarrhalis*.
[iii] Caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, or *Moraxella catarrhalis.*
[iv] Caused by *Staphylococcus aureus* or *Streptococcus pyogenes.*
[v] Infectious Disease Society of America. Practice Guidelines for the Management of Community-Acquired Pneumonia in Adults. August, 2000.
[vi] American Thoracic Society. Guidelines for the Management of Adults with Community-Acquired Pneumonia. March 9, 2001.
[vii] Ibid., op cit.
[viii] American Thoracic Society. Guidelines for the Management of Adults with Community-Acquired Pneumonia. March 9, 2001.
[ix] Note that while oral amoxicillin/clavulanate and oral clarithromycin are approved for use in the United States, the I.V. formulations of these products are not approved.

Forward-Looking Statements

This news release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group management. Various known and unknown risks, uncertainties and other factors could lead to substantial differences between the actual future results, financial situation, development or performance of the company and the estimates given here. The company accepts no obligation to continue to report or update these forward-looking statements or adjust them to future events or developments.

# # #