ANTIVIRAL AGENTS

Amantadine

Mechanism of action.

When influenza viruses replicate within the host cell, a viral

membrane protein known as M2 forms an ion-channel for H+ influx from theendosome into the virion prior to fusion of the viral membrane with the endosomal

membrane. Amantadine binds to M2 protein and blocks its ion channel activity and thus inhibits viral uncoating and replication.

In addition to its antiviral activity, amantadine antagonizes the N-methyl-Daspartate(NMDA) receptor in the CNS.

NMDA receptors are important in pain sensation, especially chronic pain.

Amantadine combined with other analgesics such as opiates or NSAIDs alleviates chronic pain.

. Therapeutic uses. The primary use of amantadine in veterinary medicine is as an adjunct to NSAIDs for the treatment of chronic pain in dogs and cats.

It is effective for treating some, but not all, influenza viruses. Because oral absorption in horses is variable, it has been used IV to treat equine-2 influenza but its potential for inducing seizures when administered by this route limits its use.

. Pharmacokinetics. Given orally, ~50% of the dose of amantadine is absorbed in horses and high levels are attained in secretions. It is excreted unchanged by the kidneys.

The elimination t 1/2 in horses is ~3.5 hours. The information for dogs and cats is not available.

. Administration. As an adjunct to chronic pain therapy, amantadine is administered orally once a day to dogs and cats.

. Resistance. Develops quite rapidly.

. Adverse effects. Infrequently, the following signs are seen: agitation, loose stools, flatulence, or diarrhea, particularly early in therapy.

Acyclovir

. Chemistry. Acyclovir is a guanosine derivative with selectivity for particular herpes

viruses.

. Mechanism of action. Acyclovir is metabolized to the monophosphate by thymidine kinase, which is more active in the virus than in the host cell. The host cell then converts the monophosphate to the triphosphate that inhibits the viral DNA polymerase, ending the nucleotide chain prematurely.

. Therapeutic uses. Acyclovir is used to treat ocular and respiratory infections of herpes virus 1 of cats.

Although acyclovir is active against equine herpes virus type-l

in vitro, oral absorption is poor in horses and therapeutic levels are not attained

. Pharmacokinetics. Acyclovir is poorly absorbed (~20%) after oral administration. It is widely distributed throughout body tissues and fluids, including the brain, semen, and CSF. It has low protein binding and crosses the placenta.

Acyclovir is primarily metabolized by the liver and has a t 1/2 of ~3 hours in humans. No information is available for animals.

. Administration. Acyclovir is administered orally twice a day to cats.

6. Adverse effects. Leucopenia and anemia may occur. These are reversible if therapy is discontinued.

Zidovudine (AZT)

. Chemistry. Zidovudine is an analog of thymidine.

. Mechanism of action. Zidovudine is phosphorylated by host cell enzymes to AZT

5————————————-triphosphate, which competes with host 5——— -thymidine, which is essential for

proviral DNA formation by reverse transcriptase of the virus. The incorporation of the 5 -triphosphate zidovudine into the viral DNA chain produces the termination of viral DNA synthesis. Mammalian α-DNA polymerase does not incorporate the zidovudine.

. Therapeutic uses. Zidovudine may be used in cats to treat FIV infection where it produces temporary alleviation of the clinical signs and increase in quality of life and survival time in most cats, particularly when clinical signs of immunodeficiency are evident.

It does not inhibit the viremia. Clinical improvement occurs 14 days

after the start of treatment.

Zidovudine is not effective against feline leukemia virus at nontoxic doses.

4. Pharmacokinetics. Zidovudine is well absorbed orally and has a t 1/2 of ~2 hours in cats.

It is metabolized in the liver by glucuronide conjugation and excreted in

urine. t 1/2 may be extended in cats that have low levels of glucuronyl transferase. 5. Administration. Zidovudine is administered orally 2–3 times a day for a minimum of 4 weeks.

. Resistance. Mutation of virus target sites may result rapidly and resistance to zidovudine is expected with long-term use.

. Adverse effects. Anemia and reduction in hemoglobin are the most common side effects observed in cats. Diarrhea and weakness may also occur. Reduced dosage should be employed in cats with renal or hepatic insufficiency.

interferon

. Chemistry. Interferons are cytokines, proteins produced by host cells when they are attacked by viruses.

Cat omega interferon is produced by genetic engineering and is

a type 1 interferon closely related to alpha interferon.

. Mechanism of action.

Interferon's mechanism of action is not a direct attack on the

virus but by altering host cell metabolism to induce proteins that protect against viral invasion by several methods including destruction of mRNA and blockade of translational proteins resulting in the inhibition of viral replication.

. Therapeutic uses. Feline omega interferon can be used to treat cat viral infections, including calci virus, FeLF, FIV, and other feline viral infections as well as canine parvovirus.

. Administration. Interferons may be given SC or by other parenteral routes (depending on the virus to be treated) once a day.

. Adverse effects. Transient anorexia and weight loss may occur in cats. Fever, myelotoxicity, and myalgia may develop with parenteral administration at higher dosages.