

Position Statement

Proposed by the NWRA Veterinary Committee: March 10, 2022

Approved by the NWRA Board of Directors: May 13, 2022

Regarding the Use of Human Antiviral Drugs in Wildlife Patients

Avian influenza virus and other emerging viruses (e.g., SARS-CoV-2) are increasingly a significant threat to the health of native wildlife, zoo species, poultry, and people around the world. There are currently four approved antiviral drugs, in two classes, for the treatment or prevention of Influenza A virus in humans. These are the adamantanes (amantadine and rimantadine) and the neuraminidase inhibitors (oseltamivir and zanamivir). The drugs are not approved for use in the treatment or prevention of influenza or other viral infections in animals.

If and when a strain of highly pathogenic avian influenza (HPAI) capable of transmission to humans and adapted to human-to-human spread arrives in the United States, Tamiflu® (oseltamivir phosphate, Roche Laboratories, Inc., Nutley, NJ) will be used as the first line of defense for preventing a catastrophic viral epidemic in humans. On March 22, 2006, the FDA published a final rule prohibiting the extra-label use of adamantane and neuraminidase inhibitor classes of antiviral drugs in chickens, turkeys, and ducks (Regulations.gov and FDA 21 CFR 530.41).

Unfortunately, all currently circulating influenza viruses are **already resistant** to adamantane antiviral drugs (such as amantadine and rimantadine).

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC558527/>

Public health professionals whom we have consulted have recommended in very strong terms that antiviral drugs NOT be used in wildlife. When Tamiflu® is used and then metabolized and excreted by people or other animals, it can persist in the environment for extended periods, potentially leading to avian influenza viruses acquiring drug resistance (Singer et al. 2007). Using these medications in wildlife for the prevention of other viral diseases (parvovirus, distemper, feline leukemia, etc.) might well lead to a highly resistant form of avian influenza and other viruses in the environment for which there would be no useful treatments should humans become sick.

More recently, concerns regarding SARS-CoV-2 and its variants include antiviral selective pressures and mutations in the virus, leading to antiviral drug resistance from animals that may have been exposed to these drugs. RNA viruses, in general, exhibit high mutation rates and are thus more likely to develop antiviral drug resistance.

The NWRA Veterinary Committee has recently been made aware of some rehabilitators and/or practitioners using acyclovir for the treatment of canine distemper virus (CDV) in raccoons. Acyclovir is an antiviral drug that is used mainly in human herpesvirus infections. Its use in animals' herpesvirus infections has been limited because poor of bioavailability. Canine

distemper virus is not a herpes virus. This Paramyxoviridae family is similar to human measles virus. CDV is an RNA virus, and not a DNA virus that acyclovir targets (Weese 2022). There are no studies that have evaluated proper dosing or safety in raccoons.

Given the regulatory prohibitions, lack of evidence demonstrating efficacy, and global concerns for the potential for a world-wide human health crisis surrounding influenza or other emerging viruses (e.g., SARS-CoV-2), the NWRA Veterinary Committee strongly advises that wildlife rehabilitators not use these drugs in wildlife patients and that veterinarians not prescribe antiviral drugs for extra-label use in free-ranging wild animals.

Further Reading

FDA 21 CFR 530.4. Extra-label drug use in animals. Last updated April 2007. Available at:
<<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=530.41>>

Kumar, M., Kuroda, K., Dhangar, K., Mazumder, P., Sonne, C., Rinklebe, J., Kitajima, M. 2020. Potential emergence of antiviral-resistant pandemic viruses via environmental drug exposure of animal reservoirs. *Environmental Science & Technology* 54(14), 8503-8505. DOI: 10.1021/acs.est.0c03105

Davis, J.L., Smith, G.W., Baynes, R.E., Tell, L.A., Webb, A.I., Riviere, J.E. 2009. Update on drugs prohibited for extralabel use in food animals.
<http://www.farad.org/publications/digests/092009ProhibitedDrugsUpdated.pdf>

Hurt, A.C., Ho, H., Barr, I. 2006. Resistance to anti-influenza drugs: adamantanes and neuraminidase inhibitors. Accessed: <https://pubmed.ncbi.nlm.nih.gov/17140356/>
DOI: 10.1586/14787210.4.5.795

Parry, J. 2005. Use of antiviral drug in poultry is blamed for drug resistant strains of avian flu. *BMJ* 331(7507):10

Singer, A.C., M.A. Nunn, E.A. Gould, and A.C. Johnson. 2007. Potential Risks Associated with the Proposed Widespread Use of Tamiflu. *Environmental Health Perspectives*, Volume 115, Number 1.

Villa, T.G., Abril, A.G., Sanchez, S., de Miguel, T., Sanchez-Perez, A. 2021. Animal and human RNA viruses: genetic variation and ability to overcome vaccines. *Archives of Microbiology* 203, 443-464.

Weese, S. 2022. Use of acyclovir in raccoons for the treatment of canine distemper virus infection. Available at:
<https://www.wormsandgermsblog.com/2022/01/articles/miscellaneous/acyclovir-use-in-raccoons-with-distemper/>