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West Nile Virus

West Nile virus (WNV) is the leading cause of arbovirus encephalitis in horses and humans in the United States. Since 1999, over 24,000 cases of WNV encephalitis have been reported in U.S. horses, with 1,069 cases reported in 2006. In 2006, there was a 14% increase in human cases and new expansion of WNV into 52 U.S. counties. The occurrence of over 2,500 human cases in 2007 indicates widespread viral activity in the environment. 1,086 equine cases were reported in the U.S. in 2006. As of October 2007, 250 equine cases were reported. This decline likely reflects both vaccination and naturally acquired immunity. Nonetheless, horses represent 96.9% of all non-human mammalian cases of WNV disease.

This virus has been identified in all of the continental United States, most of Canada and Mexico. Several Central and South American countries have also identified WNV within their borders. The virus is transmitted from avian reservoir hosts by mosquitoes (and infrequently by other bloodsucking insects) to horses, humans and a number of other mammals. West Nile virus is transmitted by many different mosquito species and this varies geographically. The virus and mosquito host interactions result in regional change in virulence of the virus and no prediction can be made regarding future trends in local activity of the viruses. Horses and humans are considered to be dead-end hosts for WNV; the virus is not directly contagious from horse to horse or horse to human. Indirect transmission via mosquitoes from infected horses is highly unlikely as these horses do not circulate a significant amount of virus in their blood.

The case fatality rate for horses exhibiting clinical signs of WNV infection is approximately 33%. Data have supported that 40% of horses that survive the acute illness caused by WNV still exhibit residual effects, such as gait and behavioral abnormalities, 6 months post-diagnosis.

There are three challenge models that have been used to license currently available vaccines. The mosquito and needle challenge were the two models used in early studies. These challenge models result in 90% of nonvaccinated control horses developing viremia, while only 10% of these horses demonstrated clinical disease. More recently, the intrathecal (infection in the atlanto-occipital space) challenge model has been employed. In this model, 70 to 90% of nonvaccinated control horses become viremic and 90 to 100% develop grave signs of encephalomyelitis.

West Nile virus vaccines are licensed either as 1) an aid in protection against viremia or 2) protective against viremia and clinical disease. The basis for labeling reflects the route of virulent challenge performed at the time of licensure. Recent literature indicates that all licensed vaccines demonstrate approximately 95% efficacy when horses undergo intrathecal challenge 28 days post-vaccination. These studies support the epidemiological studies that have demonstrated high efficacy for vaccination. Thus vaccination for West Nile virus is recommended as a core vaccine and is an essential standard of care for all horses in North America.

Vaccines:

Three licensed vaccines are currently available:

Inactivated whole virus vaccine with an adjuvant. Label instructions call for an initial series of two intramuscular injections administered 3 to 6 weeks apart followed by a 12-month revaccination interval.

- This vaccine was tested in a needle challenge model and 95% of vaccinated horses were considered protected based on their failure to develop viremia when challenged 12 months post-vaccination. The product is labeled as an aid in protection against WNV viremia.
- Severe encephalitis was not observed in horses challenged intrathecally 28-days after vaccination.

Recombinant vector vaccine
with protective antigens expressed in a canary pox vector which does not replicate in the horse. The vaccine contains an adjuvant.Label instructions call for an initial series of two intramuscular injections administered 3 to 6 weeks apart followed by a 12 month revaccination interval. The product is labeled as an aid in protection against WNV viremia.

Additional studies with canary pox vector vaccine have been performed and have demonstrated:

- Initial efficacy studies utilized the mosquito challenge model and 90% of horses were protected against viremia for a duration of 12 months.
- For horses previously vaccinated with another product, revaccination with a single dose of this product induced an antibody response. Vaccines can be interchanged without repeating primary inoculation.
- Naïve horses, having received a single dose of the vaccine, and subsequently challenged 28 days post- vaccination were protected from viremia.
- 90% of vaccinated horses were protected when challenged by the intrathecal model 2 weeks after vaccination.
- Severe encephalitis was not observed in horses challenged intrathecally 28 days after vaccination.

Modified live chimera vaccine
having the protective proteins of WNV expressed in a flavivirus vector. The vaccine does not contain an adjuvant. Label instructions are for a single injection followed by revaccination at a 12 month interval.

Efficacy testing for licensing used the intrathecal challenge model in which disease, in addition to viremia, was produced. Severe encephalitis was not observed in horses challenged intrathecally 28 days after vaccination with 1 dose of vaccine. Therefore, this product is labelled for the prevention of disease. Additional intrathecal challenge tests demonstrated:

- 12-month duration of immunity against clinical disease and an aid to prevention against viremia in 90% of horses.
- Severe encephalitis was not observed in horses challenged intrathecally 12 months after vaccination with 1 dose of vaccine.
- Severe encephalitis was not observed 5/6 in horses challenged intrathecally 10 days after vaccination with 1 dose of vaccine.

Vaccination Schedules:

Adult horses previously vaccinated
Vaccinate annually in the spring, prior to the onset of the insect vector season.

For animals at high risk or with limited immunity, more frequent vaccination or appropriately timed revaccination is recommended in order to induce protective immunity during periods of likely exposure. For instance, juvenile horses (<5 years of age) appear to be more susceptible than adult horses that have likely been vaccinated and/or had subclinical exposure. Geriatric horses (>15 years of age) have been demonstrated to have enhanced susceptibility to WNV disease. Therefore, more frequent vaccination is recommended to meet the vaccination needs of these horses.

Booster vaccinations are warranted according to local disease or exposure risk. Only the modified live chimera WNV vaccine has been tested for protection against signs of clinical disease but protection against disease for 12 months is likely with all WNV vaccines. However, m ore frequent vaccination may be indicated with any of these products depending on risk assessment.

Adult horses previously unvaccinated or having unknown vaccinal history

Inactivated whole virus vaccine: A primary series of 2 doses is administered to naïve horses. A 4- to 6-week interval between doses is recommended. The label recommended revaccination interval is 12 months.

Recombinant canary pox vector vaccine: A primary series of 2 doses is administered to naïve horses with a 4- to 6-week interval between doses. The label recommended revaccination interval is 12 months.

Modified live flavivirus chimera vaccine: Primary immunization is by a single dose administered to horses 5 or more months of age. The label recommended revaccination interval is 12 months.

Pregnant mares
Limited studies have been performed that examine vaccinal protection against WNV disease in pregnant mares. While none of the licensed vaccines are specifically labeled for administration to pregnant mares at this time, practitioners have vaccinated pregnant mares due to the risk of natural infection. It is an accepted practice by many veterinarians to administer WNV vaccines to pregnant mares as the risk of adverse consequences of WNV infection outweighs any reported adverse effects of use of vaccine.

Pregnant mare previously vaccinated
Vaccinate at 4 to 6 weeks before foaling.

Pregnant mares previously unvaccinated
Initiate a primary vaccination series (see *Adult horses previously unvaccinated*) immediately. Limited antibody response was demonstrated in pregnant mares vaccinated for the first time with the killed vaccine. It is unknown if this is true for the other products. Vaccination of naïve mares while open is a preferred strategy.

Foals
Limited studies have been performed examining maternal antibody inference and inhibition of protection against WNV disease. The only data currently available is for the inactivated product in which foals were demonstrated to produce antibody in response to vaccination despite the presence of maternal antibody. No studies have been performed evaluating protection from disease in foals vaccinated in the face of maternal immunity.

Foals of vaccinated mares

Inactivated vaccine: Administer a primary 3-dose series beginning at 4 to 6 months of age. A 4- to 6-week interval between the first and second doses is recommended. The third dose should be administered at 10 to 12 months of age prior to the onset of the next mosquito season.

Data indicates that maternal antibodies do not interfere with this product; however protection from clinical disease has not been provocatively tested in foals.

Animals may be vaccinated more frequently with this product if risk assessment warrants.

Recombinant canary pox vector vaccine: No data are available for the vaccination of foals.

Administration of a 3-dose primary vaccination series beginning at 5 to 6 months of age is based on the assumption that foals of that age respond to vaccination similarly to adults. There should be a 4-week interval between the first and second doses. The third dose should be administered at 10 to 12 months of age prior to the onset of the next mosquito season.

There is no data for this product regarding maternal antibody interference. Protection from clinical disease has not been provocatively tested in foals. Animals may be vaccinated more frequently with this product if risk assessment warrants.

Modified live flavivirus chimera vaccine: This vaccine is labeled for the administration of a single dose to foals 5 months of age or older. A second dose is recommended at 10 to 12 months of age prior to the onset of the next vector season.

There is no data regarding administration of this product to younger foals. It is recommended that the above described schedule be followed to completion should this vaccine be administered to increased-risk foals < 5 months of age. Animals may be vaccinated more frequently with the product if risk assessment warrants.

Foals of unvaccinated mares

The primary series of vaccinations should be initiated at 3 months of age and, where possible, be completed prior to the onset of the high-risk insect vector season.

Inactivated vaccine: Administer a primary series of 3 doses with a 30-day interval between the first and second doses and a 60-day interval between the second and third doses. If the primary series is initiated during the mosquito vector season, an interval of 3-4 weeks between the second and third doses is preferable to the above described interval of 8 weeks.

Recombinant canary pox vaccine:
No data are available for the vaccination of foals and scheduling of the administration of the primary vaccination is based on the assumption that foals at 5 to 6 months of age respond to vaccination similarly to adults. A second dose, given at a 3-4 week interval after the first dose, may be warranted to ensure protective immunity. Animals may be vaccinated more frequently with this product if risk assessment warrants.

Modified live flavivirus chimera vaccine: There is no data regarding administration of this product to foals younger than 5 months of age. Due to presence of vectors and risk of disease, vaccination is warranted at earlier than 5 months of age and the use of this product is likely more appropriate for revaccination of older juveniles having already been administered a primary series.

Horses having been naturally infected and recovered
Recovered horses likely develop life-long immunity. Consider revaccination only if the immune status of the animal changes the risk for susceptibility to infection. Examples of these conditions would include the long term use of corticosteroids and pituitary adenoma.

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