Desmopressin Acetate

- Used to diagnose and treat central diabetes insipidus
- Used to treat von Willebrand’s disease

Desmopressin acetate (1-deamino-8-D-arginine vasopressin; DDAVP) is a synthetic analogue of the antidiuretic hormone vasopressin. It is useful for treating bleeding disorders, such as von Willebrand’s disease, and polyuria related to central diabetes insipidus (DI) in small animals.

PHARMACOLOGY

DDAVP differs in structure from endogenous vasopressin in two places. The amino terminal is absent at position 1, and the D isomer replaces the L isomer at position 8. These differences give DDAVP more antidiuretic potential and fewer vasoressor properties than vasopressin. They also prolong the actions of DDAVP two- to threefold.

The specific mechanism of action of DDAVP is to increase reabsorption of water in the collecting ducts of the kidneys. DDAVP binds to V2 antidiuretic receptors on tubule cells in the kidneys and stimulates an increase in adenylate cyclase activity, leading to increases in cAMP concentrations, which in turn increase renal tubule permeability and free water reabsorption. This results in a decrease in net urine production and an increase in urine osmolality. At therapeutic doses, DDAVP does not interfere with sodium or potassium excretion into the urine.

In addition, DDAVP has a higher capacity compared with vasopressin to increase plasma coagulation factor VIII and von Willebrand’s factor (vWF) on a dose-dependent basis. The increases occur rapidly and appear to result from stimulation and release of endogenous stores of factor VIII and vWF as opposed to increased synthesis of these agents. Thus when repeated doses of DDAVP are given, the response tends to lessen. DDAVP cannot be administered orally because it is destroyed by the gastrointestinal tract.

In dogs, the antidiuretic activities of DDAVP typically begin within 1 hour after administration. The action peaks in 2 to 8 hours and can last up to 24 hours. The distribution and metabolism of DDAVP are not well understood. In humans, intravenous DDAVP has a terminal half-life ranging from 0.4 to 4 hours.

INDICATIONS

DDAVP is used to diagnose and treat central DI in small animals. DDAVP coupled with a water deprivation test can be used to differentiate central DI, nephrogenic DI, and psychogenic polydipsia in animals presenting with polyuria and polydipsia. The purpose of the water deprivation test is to assess the appropriate release of endogenous vasopressin during dehydration and the kidneys’ response to vasopressin. After this test, DDAVP is given (either 2 µg SC or IV or 20 µg intranasally or conjunctivally) if the animal cannot concentrate urine after losing at least 5% of its body weight. Urine osmolality is then measured every 2 hours for 6 to 10 hours. If osmolality increases by at least 10%, central DI is strongly suspected.

Animals with psychogenic polydipsia should have a urine concentration of greater than 1.035 with water deprivation alone. Animals with nephrogenic DI show no response to DDAVP, whereas animals with central DI have a urine concentration of greater than 1.035. Once a diagnosis of central DI is made, DDAVP is a mainstay of treatment. Administration of DDAVP completely corrects
Al-Thus DDAVP can be used
DDAVP is safe
The intranasal formula-
Appropriate dosing for
Other studies have found more
2
2
2
If this occurs, appropriate
Cau-
2
2
2
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For treating central
1
1
Type II von Willebrand’s
tions do not increase dramatically.
DDAVP is most useful when pet
owners are taught to administer it at
the first sign of hemorrhage, such as
epistaxis or hematuria. DDAVP in-
creases levels of vWF more than fac-
or VIII. Factor VIII is important in
the pathogenesis of hemophilia A, and the effects of DDAVP in the rare
cases of dogs with hemophilia A are
unknown. DDAVP could also be
given to a blood-donor dog 30 min-
utes before drawing blood to increase
the concentration of vWF and factor
VIII in the transfused blood if the re-
cipient is deficient in these factors.2

CAUTIONS
Side effects of DDAVP are un-
common in small animals. Caution
should be used when administering
DDAVP to German shorthaired
pointers. Type II von Willebrand’s
disease is common in this breed, and
DDAVP administration could result
in thrombocytopenia when given to
a patient with type II disease.1 Cau-
tion is also needed when adminis-
tering DDAVP to patients at risk for
thrombotic events.1 DDAVP is safe
to use in dogs with central DI. Possi-
ble water intoxication, induced by a
dysfunctional inhibitory thirst mech-
anism, is the major complication of
DDAVP use in patients with central
DI, but this problem is uncommon.2
Likewise, hypersensitivity reactions
are possible but uncommon.1
The safety of DDAVP for use in
canine pregnancy has not been estab-
lished.1 However, no harmful fetal
effects were seen when 125 times
normal human doses were adminis-
tered to rats and rabbits.1

ACUTE TOXICITY
Overdose may result in fluid reten-
tion or overload and subsequent hy-
ponatremia.1 If this occurs, appropri-
te treatment includes dose reduction and
fluid restriction.1 Monitoring of elec-
trolytes is recommended.1

DRUG INTERACTIONS
Concomitant administration of
chlorpropamide, carbamazepine,
clofibrate, fludrocortisone, or urea
has the potential to increase the an-
tidiuretic effects of DDAVP and put
the patient at risk for water
overload.1 The antidiuretic effect of
DDAVP may be decreased with con-
comitant administration of lithium,
epinephrine, demeclocycline, he-
parin, or alcohol.1

DOSE AND ADMINISTRATION
In small animals, DDAVP can be
administered intravenously, subcuta-
neously, intranasally, or intraconju-
ctivally. The intracutaneous route is
preferred for animals with central DI
because of ease of administration.2
Parenteral use is recommended for-
patients with von Willebrand’s dis-
eease because of the need for higher
concentrations.2,4 For treating central
DI in dogs, the recommended dose
is one to four drops of intranasal so-
ution once or twice daily applied to
the conjunctiva indefinitely.2 The
dose should be adjusted to control
signs of polyuria and polydipsia.1
Parenteral dosing is reserved for pa-
tients not responding to or tolerating
DDAVP intraconjectivally or in-
tranasally.3 The intranasal formula-
tion is safe for parenteral use, and the
dose is 0.5 to 2 µg IV or SC
q12–24h.2 Appropriate dosing for
cats with central DI is one to two
drops of the intranasal preparation
q12–24h.1

For von Willebrand’s disease, the
appropriate canine dosage is 1 µg/kg
SC, and the effect lasts 3 to 4 hours.
Subsequent doses within 24 hours
do not add benefit.1 DDAVP can
also be used intravenously in these
patients but must be diluted in 0.9%
normal saline and given over 20 to
30 minutes.2

PREPARATIONS
DDAVP is available as a nasal solu-
tion containing 10 µg/0.1 ml or 1.5
mg/ml.1 The former is available in
2.5- and 5-ml bottles and comes with
either two calibrated rhinal tube ap-
licators (1.5 to 4 µg per drop) or a
nasal compression pump that delivers
10 µg of DDAVP in each spray.2 The
1.5-mg/ml concentration is manufac-
tured only in 2.5-ml bottles.1

DDAVP as a parenteral injection
http://www.VetLearn.com
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is available in 1-ml ampules and 10-ml multiple-dose vials at a concentration of 4 µg/ml. DDAVP tablets (0.1 and 0.2 mg) are also available but are not recommended because they are destroyed in the gastrointestinal tract.

**STORAGE AND HANDLING**

Refrigeration is recommended for both nasal and parenteral DDAVP solutions. However, an unopened bottle of nasal solution is stable for 3 weeks at room temperature. DDAVP should not be frozen. Tablets should be stored at room temperature.

**REFERENCES**


