

Table 4: Characteristics of specific Angiotensin II Type-1 Receptor Blockers and an ARB/neprilysin-inhibitor.

AT ₁ R blocker	Active molecule	Pharmacokinetics: Dog (unless otherwise noted)	Dosage & Doses/Day All dosages are oral
Species	Excretory route (Human data)		
Candesartan cilexetil^{1,2} H, V	Candesartan (U=0.3%; F=99.7%)	Bio: 5% active drug, with peak concentration at 1.3h; ET _{1/2} 4-5h	D: 1mg/kg q24h
Eprosartan³ H	Eprosartan (U=10%; F=90%)	----	----
Irbesartan^{4,5} HV	Irbesartan (U=20%; F=80%)	Peak concentration at 5.5h; ET _{1/2} = 3.7h	D: 5mg/kg q24 to 12h C: 6 mg/kg q24h (experimental)
Losartan^{6,7} V	E-3714; Losartan activity 1/3 of E-3714 (U=10%) <i>Enterohepatic recirculation in dog</i>	Bio: 23-33% with peak concentration at 1h; ET _{1/2} = 1.7-2.5h (single 5 to 20mg/kg dose)	Azotemic dogs: 0.125mg/kg q24h up-titrate to 0.5mg/kg q24h Non-Azotemic dogs: 0.5mg/kg q24h up-titrate to 1 mg/kg q24h
Olmesartan⁸ H	RNH-6270 = active drug (U=40%; F=60%)	----	----
Telmisartan^{7,9} V	Telmisartan Primarily eliminated as unchanged compound in feces (cat)	Dog: ET _{1/2} ~5.4h Cat: 33% bioavailability. Highly protein bound (>99.5%); ET _{1/2} 7.7 hr	D: 2mg/kg q24h C: 1mg/kg q24h (Semintra® label) C: 3mg/kg q24h (experimental)
Valsartan¹⁰ H, V	Valsartan (U=30%; F=70%)	ET _{1/2} ~7.4h At 10 and 30 mg/kg no effect on blood pressure or cardiac output in normal dogs	D: Experimental dosages of 10-30mg/kg
Valsartan and Sacubitril¹¹ (neprilysin Inhibitor) H, V	Valsartan (see above) Sacubitrilat (LBQ657) (U=52-68%)	45mg/kg/day significantly increases cGMP and lowers aldosterone in dogs with RAAS activation from a sodium restricted diet	D: Experimental dosages of 15-45mg/kg/day

AT₁R angiotensin II type-1 receptor; Bio, bioavailability; C, cat; D, dog; ET_{1/2}, elimination half-life; F, fecal excretion; H, human marketed only; h, hour; **V**, veterinary and human marketed; **V**, veterinary research/clinical use – not marketed; U, urinary excretion; (*i*) – italicized in parentheses, human data

References

1. Kondo T, Yoshida K, Yoshimura Y, Motohashi M, Tanayama S. Disposition of the new angiotensin II receptor antagonist candesartan cilexetil in rats and dogs. *Arzneimittelforschung*. 1996;46(6):594–600.
2. Yamane T, Fujii Y, Orito K, Osamura K, Kanai T, Wakao Y. Comparison of the effects of candesartan cilexetil and enalapril maleate on right ventricular myocardial remodeling in dogs with experimentally induced pulmonary stenosis. *Am J Vet Res*. 2008;69(12):1574–9.
3. McClellan KJ, Balfour JA. Eprosartan. *Drugs*. 1998;55(5):713–8.
4. Carlucci L, Song KH, Yun HI, Park HJ, Seo KW, Giorgi M. Pharmacokinetics and pharmacodynamics (PK/PD) of irbesartan in Beagle dogs after oral administration at two dose rates. *Polish J Vet Sci*. 2014;16(3):1–7.
5. Huang X-H, Qiu F-R, Xie H-T, Li J. Pharmacokinetic and pharmacodynamic of irbesartan in renal hypertensive dogs under non-steady-state and steady-state conditions. *Eur J Drug Metab Pharmacokinet*. 2005;30(1-2):121–6.
6. Christ DD, Wong PC, Wong YN, Hart SD, Quon CY, Lam GN. The pharmacokinetics and pharmacodynamics of the angiotensin II receptor antagonist losartan potassium (DuP 753/MK 954) in the dog. *J Pharmacol Exp Ther*. 1994;268(3):1199–205.
7. Jenkins TL, Coleman AE, Schmiedt CW, Brown SA. Attenuation of the pressor response to exogenous angiotensin by angiotensin receptor blockers and benazepril hydrochloride in clinically normal cats. *Am J Vet Res*. 2015;76(9):807–13.
8. Warner GT, Jarvis B. Olmesartan Medoxomil. *Drugs* 2002;62(9):1345–53.
9. Baek IH, Lee BY, Lee ES, Kwon KI. Pharmacokinetics of Angiotensin II Receptor Blockers in the Dog Following a Single Oral Administration. *Drug Res*. 2013;63(07):357–61.
10. Hayashi N, Yamamoto S, Kometani M, Nakao K. Pharmacological profile of valsartan, a non-peptide angiotensin II type 1

- receptor antagonist. 3rd communication: hemodynamic effects of valsartan in rats and dogs. *Arzneimittelforschung*. 1997;47(5):620–5.
11. Mochel J, Burkey BF, Fink M, Garcia R, Peyrou M, Giraudel JM, et al. First-in-class angiotensin receptor neprilysin inhibitor LCZ696 modulates the dynamics of the renin cascade and natriuretic peptides system with significant reduction of aldosterone exposure. *J Am Coll Cardiol*. 2014;63:A806.