

The multi-drug resistance gene (*mdr1*) encodes P-glycoprotein, a protein that functions as a drug-transport pump across cell membranes. A lack of P-glycoprotein means certain drugs cannot be absorbed, distributed or metabolized normally. Dogs with the *mdr1* genetic mutation have a P-glycoprotein deficiency and are extremely susceptible to toxicosis from many common drugs.

## Affected Breeds

The *mdr1* mutation has been documented in many herding breeds and some sighthounds. Affected breeds include Australian Shepherds (all sizes), Collies, English Shepherds, German Shepherds, Longhaired Whippets, McNabs, Old English Sheepdogs, Shetland Sheepdogs, and Silken Windhounds. Researchers are currently testing more than 100 additional breeds for the mutation.

## MDR1 Mutation Test

The Veterinary Clinical Pharmacology Laboratory (VCPL) at Washington State University has developed a commercially available test for the *mdr1* mutation. Any dog of any breed can be tested via DNA collected from a cheek swab. Results are reported as homozygous for the normal *mdr1* allele (normal/normal), heterozygous (mutant/normal), or homozygous for the mutant *mdr1* allele (mutant/mutant). **Dogs carrying the mutant gene or dogs from affected breeds that have not been tested for the mutation should not be given any of the *mdr1* problem drugs.**

## Problem Drugs

P-glycoprotein transports many drugs including antiparasitic agents, opioids, cardiac drugs, immunosuppressants, steroid hormones, and anticancer agents. Research is ongoing to determine which P-glycoprotein substrates cause toxicity in dogs with the *mdr1* mutation. The most commonly used medicines identified so far are acepromazine, butorphanol, cyclosporine, ivermectin, loperamide, and morphine. All of the problem drugs are prescription medicines except for some of the over-the-counter diarrhea medicines like Imodium.

The BusterAlert.org *MDR1 Problem Drugs List* includes the generic problem drugs identified by the *mdr1* researchers along with the brand names under which these drugs are marketed, as compiled by BusterAlert.org. Brand names were obtained from many sources including the FDA, Health Canada, and *Martingale: The Complete Drug Reference*. For drugs with no specific veterinary formulation, human drug brand names were included.

Additional problem drugs will be added to the list as *mdr1* research progresses. For the most up-to-date version of the *MDR1 Problem Drug List*, visit the BusterAlert.org website.

## Additional Information

VCPL MDR1 Research and MDR1 Testing: <http://www.vetmed.wsu.edu/depts%2DVCPL/>

Mealey, KL. Adverse drug reactions in herding-breed dogs: The role of P-glycoprotein. *Compendium*. 2006 Jan; 23-32. CE test available.

Mealey, KL. Therapeutic implications of the MDR-1 gene. *J Vet Pharmacol Ther*. 2004 Oct;27(5):257-64.

Neff MW, Robertson KR, Wong AK, Safra N, Broman KW, Slatkin M, Mealey KL, Pedersen N. Breed distribution and history of canine *mdr1*-1 $\Delta$ , a pharmacogenetic mutation that marks the emergence of breeds from the collie lineage. *Proc Natl Acad Sci USA*. 2004 Aug 10;101(32):11725-30.

Sartor LL, Bentjen SA, Trepanier L, Mealey KL. Loperamide toxicity in a collie with the MDR1 mutation associated with ivermectin sensitivity. *J Vet Intern Med*. 2004 Jan-Feb;18(1):117-8.

Nelson OL, Carsten E, Bentjen SA, Mealey KL. Ivermectin toxicity in an Australian Shepherd dog with the MDR1 mutation associated with ivermectin sensitivity in Collies. *J Vet Intern Med*. 2003 May-Jun;17(3):354-6.

Mealey KL, Bentjen SA, Gay JM, Cantor GH. Ivermectin sensitivity in collies is associated with a deletion mutation of the *mdr1* gene. *Pharmacogenetics*. 2001 Nov;11(8):727-33.

# MDR1 Problem Drugs List

## with North American Brand & Trade Names

**Dogs who test as having a mutated mdr1 gene OR dogs from affected breeds\* who have not been tested for the mutation should avoid these drugs.**

*Drug names in bold are the generic drugs identified as problems by the mdr1 researchers. Below each generic drug is a list of some of the synonyms, brand, and trade names for the generic drug provided by BusterAlert.org. More drugs are likely to be added as mdr1 research progresses.*

### Drugs PROVEN to Cause Problems

<b><u>Acepromazine</u></b>	<b><u>Doxorubicin</u></b>	Equell	Tri-Heart	Lop
Ace	Adriamycin	Equimax	Unimectrin	Loperacap
Acepro	Adriblastina	Equimectrin	Virbamec	Nodiamex
Aceproject	Caelyx	Eqvalan	Zimecterin	Permidal
Acevet	Doxil	Heartgard	<b><u>Loperamide</u></b>	Pramidal
ACP	Doxolem	Ivercare	Acanol	Raxamida
Atravet	Doxotec	Ivercide	Acqta	Rediarin
PromAce	Hydroxydaunomycin	Iverhart	Anti-Diarrheal Formula	Top-Dal
<b><u>Butorphanol</u></b>	Hydroxydoxorubicin	Iver-On	Cryoperacid	Valfam
Dolorex	Hydroxyldaunorubicin	Iversol	Deroser	<b><u>Vinblastine</u></b>
Stadol	Myocet	Ivexterm	Diahalt	Lemblastine
Torbugesic	Oxicina	Ivomec	Diamode	Velban
Torbutrol	Rubex	Mectizan	Diarr-Eze	Velbe
Torphajet	<b><u>Ivermectin</u></b>	Megamectin	Diarrhea Relief	<b><u>Vincristine</u></b>
<b><u>Digoxin</u></b>	Abamectin	Noromectin	Hurplex	Citomid
Digibind	Acarexx	Panomec	Imodium	Leurocristine
Digitalis	Advantage DUO	Phoenectin	Imogen	Oncovin
Lanoxicaps	Avermectin	Primectin	Imotil	Vinblax
Lanoxin	Bimectin	Privermectin	Imperim	Vincasar
Mapluxin	BMD/Ivomec	SparMectin	Kao-Paverin Caps	Vincrex
	Ecomectin	Stromectol		Vintec

### Drugs SUSPECTED to Cause Problems (*research is ongoing*)

<b><u>Cyclosporin</u></b>	Lanoxicaps	<b><u>Morphine</u></b>	RMS	Quinact
Atopica	Lanoxin	Analfin	Roxanol	Quinaglute
Cicloral	Mapluxin	Apokyn	Statex	Quinalan
Ciclosporin	<b><u>Domperidone</u></b>	Astramorph	<b><u>Ondansetron</u></b>	Quinatime
Cyclosporine	Motilium	Avinza	Zofran	Quinidex
Gengraf	<b><u>Etoposide</u></b>	DepoDur	<b><u>Paclitaxel</u></b>	Quinora
Immulem	EPEG	Doloral	Abraxane	<b><u>Rifampicin</u></b>
Modusik-A	Etopophos	Duralmor	Asotax	IsonaRif
Neoral	Etopos	Duramorph	Bris Taxol	Rifadin
Optimmune	Toposar	Graten	Onxol	Rifamate
Restasis	Vepesid	Infumorph	Paclisan	Rifampin
Sandimmune	VP-Tec	Kadian	Praxel	Rifater
SangCya	<b><u>Mitoxantrone</u></b>	M-Eslon	Taxol	Rimactane
Supremunn	Formyxan	MOS	<b><u>Quinidine</u></b>	Rofact
<b><u>Digoxin</u></b>	Mitroxone	MS Contin (MSC)	Biquin	
Digibind	Neotalem	MSIR	Chinidinum	
Digitalis	Novantrone	Oramorph	Cin-Quin	

**For more information and updates, please visit [www.busteralert.org](http://www.busteralert.org)**

\*Affected breeds include Australian Shepherds (all sizes), Collies, English Shepherds, German Shepherds, Longhaired Whippets, McNabs, Old English Sheepdogs, Shetland Sheepdogs, and Silken Windhounds.

**List updated  
9/8/07  
© 2007 MARS, Inc.**