

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019651/S005

PHARMACOLOGY REVIEW(S)

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Summary of Neoplastic Histomorphologic Findings for All Animals
with Similar Tumor Types Combined

TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#
BRAIN:													
ASTROCYTOMA/OLIGODENDROGLIOMA (M)		2	(60)	(59)	(60)	(59)	1	1	(60)	(60)	(60)	(60)	1
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		2	1										
MENINGIOMA (B)				1									
CECUM:		(59)	(60)	(60)	(60)	(60)		(60)	(58)	(60)	(60)	(59)	
HEMANGIOSARCOMA (M)													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		2						1					
COLON:		(59)	(59)	(59)	(60)	(59)		(60)	(60)	(59)	(60)	(60)	
LARGE GRANULAR-CELL LYMPHOMA (M)		1											
DUODENUM:		(59)	(60)	(60)	(60)	(59)		(60)	(60)	(60)	(60)	(60)	
INTESTINAL ADENOCARCINOMA (M)						1							

Figures in brackets represent the number of animals from which this tissue was examined microscopically. In this table, a benign tumor is ignored if a malignant tumor of the same histogenetic origin is also present in the same tissue. The absence of a numeral indicates that the lesion specified was not identified.

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	
DUODENUM:													
LARGE GRANULAR-CELL LYMPHOMA (M)		(59)	(60)	(60)	(60)	(59)		(60)	(60)	(60)	(60)	(60)	
EPIDIDYMI(S):													
EPIDIDYMAL ADENOCARCINOMA (M)		(60)	(58)	(60)	(60)	(59)							
LYMPHOMA (M)			1										
EYE(S):													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(60)	(60)	(60)	(60)		(60)	(60)	(60)	(60)	(60)	
HARDERIAN GLAND(S):													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(60)	(60)	(60)	(60)		(60)	(60)	(60)	(60)	(60)	

Figures in brackets represent the number of animals from which this tissue was examined microscopically in this table, a benign tumor is ignored if a malignant tumor of the same histogenetic origin is also present in the same tissue the absence of a numeral indicates that the lesion specified was not identified

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	
HEART:													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
JEJUNUM:													
INTESTINAL ADENOCARCINOMA (M)		(60)	(59)	(60)	(59)	(59)	#	(60)	(60)	(59)	(60)	(60)	#
LEIOMYOMA (B)					1		#		1				#
LARGE GRANULAR-CELL LYMPHOMA (M)		1					#						#
JOINT(S):		(59)	(59)	(60)	(60)	(60)	#	(59)	(60)	(59)	(59)	(60)	#
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		3					#						#
KIDNEY(S):		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
TUBULAR CARCINOMA/ADENOCARCINOMA OR ADENOMA			1	1			#		1	2			#

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TUMORS	INCIDENCE OF TUMORS (NUMERIC)													
	MALES							FEMALES						
	TREATMENT	0	60	120	360	480	#	0	60	120	360	480	#	
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG		
KIDNEY(S):														
TRANSITIONAL CELL CARCINOMA (M)		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#	
SQUAMOUS CELL CARCINOMA (M)							#		1				#	
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		4	1		2		#		1				#	
LACRIMAL GLAND(S):														
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(55)	(59)	(57)	(60)	(58)	#	(60)	(60)	(59)	(60)	(60)	#	
LIVER:														
HEPATOCELLULAR CARCINOMA OR ADENOMA		2	4		1	3	#	(60)	(60)	(60)	(60)	(60)	#	
HISTIOCYTIC SARCOMA/FIBROUS HISTIOCYTOMA (M)					1	2	#						#	
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		4	2		2	1	#						#	

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#
LUNG:													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (H)		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
MAMMARY GLAND(S):													
MAMMARY ADENOCARCINOMA OR ADENOMA		4	1		1	1	#						#
LARGE GRANULAR-CELL LYMPHOMA (H)		(54)	(55)	(57)	(52)	(53)	#	(60)	(60)	(60)	(60)	(60)	#
FIBROADENOMA (B)		1		3		1	#	17	11	10	8	19	#
MESENTERIC LYMPH NODE(S):													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (H)		1	1	2	4	3	#	36	36	35	35	30	#
HEMANGIOMA (B)		(56)	(58)	(55)	(58)	(58)	#	(60)	(58)	(59)	(59)	(56)	#
NASAL CAVITY/TURBINATE(S):		3	1		1		#						#
SQUAMOUS CELL CARCINOMA (H)		(60)	(59)	(58)	(60)	(59)	#	(59)	(60)	(58)	(60)	(60)	#
		3			2		#	1					#

Figures in brackets represent the number of animals from which this tissue was examined microscopically in this table, a benign tumor is ignored if a malignant tumor of the same histogenetic origin is also present in the same tissue. The absence of a numeral indicates that the lesion specified was not identified.

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)									
		MALES					FEMALES				
		0	60	120	360	480	0	60	120	360	480
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG
NASAL CAVITY/TURBINATE(S):											
HISTIOCYTIC SARCOMA/FIBROUS HISTIOCYTOMA (N)		(60)	(59)	(58)	(60)	(59)		(60)	(58)	(60)	(60)
FIBROSARCOMA (N)				1		1					
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (N)		3	1								
NASAL ADENOMA (B)		1									
OVARY(IES):											
GRANULOSA-CELL/GRANULOSA-THECA CELL TUMOR, BENIGN OR MALIGNANT							(60)	(60)	(60)	(60)	(60)
SERTOLI CELL TUMOR, BENIGN OR MALIGNANT							1		2	1	
PANCREAS:											
ISLET CELL CARCINOMA OR ADENOMA		(60)	(60)	(60)	(60)	(60)	(60)	(60)	(60)	(60)	(60)
		4	2	3	2		3		1	4	1

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#
PANCREAS:													
HISTIOCYTIC SARCOMA/FIBROUS HISTIOCYTOMA (M)		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		2	1	1			#						#
PANCREATIC ADENOMA (B)		2	1	1	1	1	#					1	#
PARATHYROID GLAND(S):		(53)	(56)	(58)	(58)	(55)	#	(54)	(56)	(56)	(56)	(55)	#
PARATHYROID ADENOMA (B)			1		1	2	#	1			1		#
PITUITARY:		(59)	(60)	(58)	(60)	(59)	#	(60)	(60)	(58)	(60)	(60)	#
PITUITARY CARCINOMA OR ADENOMA		33	32	31	39	32	#	47	46	46	51	49	#
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		3					#						#

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG
PREPUTIAL/CLITORAL GLAND(S):													
LYMPHOMA (M)		(58)	(58)	(58)	(56)	(56)	(56)	(51)	(48)	(56)	(54)	(54)	(54)
PROSTATE:													
PROSTATIC ADENOCARCINOMA (M)		(60)	(60)	(57)	(59)	(59)							
HISTIOCYTIC SARCOMA/FIBROUS HISTIOCYTOMA (M)				1									
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		3	1										
SALIVARY GLAND(S):		(60)	(60)	(60)	(60)	(59)		(60)	(59)	(59)	(60)	(60)	
SALIVARY ADENOCARCINOMA (M)									1				
LYMPHOMA (M)		1	1										

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG
SEMINAL VESICLE(S):													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(59)	(57)	(59)	(59)	#						
VESICULAR ADENOMA (B)		2	1				#						
SKELETAL MUSCLE:							#						
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(60)	(60)	(59)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
SKIN/SUBCUTIS:							#						
SQUAMOUS CELL CARCINOMA OR PAPILLOMA OR KERATOCANTHOMA		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
BASOSQUAMOUS CARCINOMA OR BASAL CELL TUMOR		7	3	6	3	6	#	1	1		1	2	#
HISTIOCYTIC SARCOMA/FIBROUS HISTIOCYTOMA (M)			2	3			#			1		1	#

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#
SKIN/SUBCUTIS:													
FIBROSARCOMA OR FIBROMA		(60)	(60)	(60)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
HEMANGIOSARCOMA (M)		0	1	4	4	5	#	3		6	2	4	#
LARGE GRANULAR-CELL LYMPHOMA (M)		1					#	1			1		#
MYXOMA (B)			1				#						#
TRICHOEPITHELIOMA (B)						1	#						#
LIPOMA (B)			1		2		#				3		#
NEURILEMMOMA (B)							#		1				#
SPLEEN:							#						#
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(60)	(59)	(60)	(60)	#	(60)	(60)	(60)	(60)	(60)	#
MYELOLIPOMA (B)		4	2		2	1	#						#
		1					#						#

figures in brackets represent the number of animals from which this tissue was examined microscopically
in this table, a benign tumor is ignored if a malignant tumor of the same histogenetic origin is also present in the same tissue
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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#
STOMACH:													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		(60)	(60)	(60)	(60)	(60)	1	(60)	(60)	(60)	(60)	(60)	
SQUAMOUS PAPILLOMA (B)										1			
SUBMANDIBULAR LYMPH NODE(S):		(58)	(59)	(58)	(60)	(55)	3	(58)	(58)	(59)	(60)	(55)	
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)		3	1		1	1							
TESTIS(ES):		(60)	(58)	(60)	(60)	(59)							
INTERSTITIAL CELL ADENOMA (B)		1	1	2	1	1							
THYMUS:		(53)	(54)	(52)	(55)	(55)		(54)	(59)	(58)	(58)	(56)	
THYMOMA (M)			2		1	1							
HISTIOCYTIC SARCOMA/FIBROUS HISTIOCYTOMA (M)										1			

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		#	0	60	120	360	480	#	0	60	120	360	480
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG
THYMUS:													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)			(53)	(54)	(52)	(55)	(55)		(54)	(59)	(58)	(58)	(56)
		3	1			1			1				
THYROID GLAND:													
FOLLICULAR-CELL CARCINOMA OR ADENOMA			(60)	(60)	(60)	(60)	(58)		(60)	(58)	(60)	(59)	(60)
C-CELL CARCINOMA OR ADENOMA			7	6	3	3	5		3	7	5	3	4
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)			1	1									
URINARY BLADDER:													
LYMPHOMA/LARGE GRANULAR-CELL LYMPHOMA (M)			(60)	(60)	(58)	(58)	(58)		(58)	(60)	(59)	(59)	(59)
		1	1										
UTERUS:													
ENDOMETRIAL ADENOCARCINOMA (M)									(60)	(60)	(60)	(60)	(60)
											1		

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TUMORS	TREATMENT	INCIDENCE OF TUMORS (NUMERIC)											
		MALES						FEMALES					
		0	60	120	360	480	#	0	60	120	360	480	#
		MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#	MG/KG	MG/KG	MG/KG	MG/KG	MG/KG	#
UTERUS:													
ENDOMETRIAL STROMAL SARCOMA OR POLYP													
VAGINA:													
LEIOMYOMA (B)													
HEMANGIOMA (B)													
ZYMBAL'S GLAND(S):													
ZYMBAL'S GLAND CARCINOMA OR ADENOMA													
LARGE GRANULAR-CELL LYMPHOMA (M)													

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