VET 415 Pain Management Drugs

Drug Class	Analgesic effect/ MOA	Use	Side Effects
<u>Opioids</u> *Morphine,* *Methadone* *Fentanyl* *Buprenorphine* *Butorphanol*	Activate opioid receptors (mu, kappa, delta) to produce analgesia Main site of action: brain and spinal cord Full mu agonist (best analgesia): Morphine, Methadone, Fentanyl Partial mu agonists (good analgesia): Buprenorphine Mu antagonists-Kappa agonists (mild analgesia, short duration): Butorphanol Simbadol: High-concentration formulation buprenorphine (NOT sustained-release formulation) labeled for SQ use. *Due to the high dose and SQ route (poor absorption) there is a slower absorption leading to ~24-hour analgesia	Main drug for moderate, severe acute pain (not very much for chronic pain) CNS effects: Sedative in some species (dogs), euphoria to dysphoria (cats, horses) Peripheral: Intra-articular, cornea Epidural/subarachnoid: Morphine and buprenorphine most commonly used because of their longer lasting analgesia Oral transmucosal: Cats (only effective if not swallowed) *Oral buprenorphine has low bioavailability Transdermal: fentanyl patch and extended duration transdermal buprenorphine solution (Zorbium)	Respiratory depression Vagally mediated decrease in heart rate, manageable with anticholinergics GI effects: Emetic and antiemetic effects, decrease GI motility Alters thermoregulatory set-point in hypothalamus, panting in dogs and hyperthermia in cats and horses
<u>Local Anesthetics</u> *Lidocaine* *Bupivacaine* *Mepivacaine* *Ropivacaine*	Bind to voltage-gated sodium channels, reversibly prevent their opening, stop propagation of the action potential along nerve fibers *no nerve transmission → no nociceptive signal to the brain → no pain Un-ionized form easily penetrates nerve membrane and reaches the binding site Ionized form binds to the receptor on the sodium channel, so it is needed at the site of action	Perineural Epidural/subarachnoid injection Wound/skin infiltration Body cavity infusion (pleura, abdomen) Topical skin application Lidocaine patch	CNS toxicity: Nystagmus, muscle twitching, seizures CV toxicity: arrhythmias, hypotension, CV collapse CNS is more sensitive than CV system

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		Intravenous (Lidocaine only) *Can add vasoconstrictors to prolong duration of action by decreasing systemic uptake **do NOT use in tissue with low blood flow	*Cumulative effect when multiple local anesthetics are used Oxidative damage to Hb molecule Neurotoxicity (concentration dependent) Hypersensitivity
<u>Non-Steroidal Anti-Inflammatory Drugs (NSAIDS)</u> Meloxicam Carprofen Robenacoxib Flunixin meglumine	Cyclooxygenase 1 and 2 antagonists → reduces the production of prostaglandins and thromboxane COX-1 enzyme is constitutively expressed in peripheral tissues such as gastric mucosa, kidneys or blood platelets COX-2 enzyme is synthesized in various tissues during inflammatory processes *COX-2 selective NSAIDS are preferred	Analgesia Anit-inflammatory Antipyretic Anti-thrombotic Anti-endotoxin	Due to inhibition of prostaglandins COX-1 inhibition is associated with most of the negative effects *Do NOT administer with corticosteroids or other NSAIDS Vomiting, diarrhea, inappetence, ulceration, renal ischemia, plt disfunction and prolonged bleeding, idiosyncratic hepatocellular necrosis
Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) Grapiprant	Antagonist of prostaglandin E receptor subtype 4 (EP4) Inhibits peripheral EP4 receptors = homeostatic function of PGs is better maintained	Licensed for use in dogs with osteoarthritis	Mild GI signs

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<u>Alpha-2 Receptor Agonists</u> Dexmedetomidine Xylaxine Detomidine	Binds to alpha-2 receptors → reduced neurotransmitter release and nociceptive stimulation in the CNS *synergistic effect with opioid receptors due to the location	Acute and chronic pain Produce sedation and decrease GI motility	Dose-dependent CV depression
<u>NMDA Receptor Antagonists</u> Ketamine	Block NMDA receptors → block calcium currents that are needed for the development and persistence of central sensitization	Chronic pain Analgesic effect can outlast drug's duration of action	
<u>Gabapentonids</u> Gabapentin Pregabalin	Bind to voltage-gated calcium channels leading to a decrease in neurotransmitter presynaptic release and decreased neuronal activity	Recommended as first line of intervention for chronic and neuropathic pain in humans NOT effective for acute pain management	Sedation
<u>Antidepressants</u> Fluoxetine Trazodone	Serotonin or Norepinephrine reuptake inhibitors enhance descending inhibition of pain Tricyclic antidepressants Serotonin-norepinephrine-reuptake inhibitors Selective serotonin-reuptake inhibitors Monoamine oxidase inhibitors	Used exclusively for chronic pain TCAs and SNRIs are recommended as the first line of intervention for chronic and neuropathic chronic pain in humans Weeks required before analgesia is seen, tapering down is recommended before discontinuing	Serotonin toxicity
<u>Antidepressants</u> Tramadol	Weak Ser and NE reuptake inhibitor Produced by its metabolite M1	Dogs produce little M1 → weak analgesic effect M1 production decreases over time so this is not a great choice for chronic administration	

		Cats produce more amounts of M1 metabolite than dogs making this an OK option, (longer-half-life than dogs)	