1. Purpose and scope

To facilitate the safe administration of ranitidine within the Neonatal Intensive Care Unit (NICU).

2. Drug

Drug	**Ranitidine, ranitidine hydrochloride**
Drug action	Ranitidine is a histamine (H_2 receptor) antagonist. It inhibits the secretion of gastric acid from parietal cells in the stomach.[1,2] Onset of action is rapid after injection with peak plasma concentrations achieved within 15 minutes. The oral formulation has a bioavailability of 50% and peak plasma concentrations are reached after 2-3 hours.[2] Ranitidine does not extensively bind to plasma proteins (15%).[1] The major route of elimination is renal after IV administration with a terminal half-life of 3-7 hours in neonates. After oral administration hepatic biotransformation predominates.[3]
Indications	• Gastro-oesophageal reflux (usually oral administration) • Acute upper gastro-intestinal haemorrhage (IV administration)
Presentation	**IV**: Ranitidine 50mg in 2ml solution Clear, colourless to yellow solution pH 6.7-7.3[4] **Oral**: Ranitidine syrup 15mg/ml Clear to pale yellow in colour with a spearmint flavour[5]
Route	• IV via slow push • IM • oral or nasogastric tube
Dose	**IV**: Preterm – 0.5mg/kg every 12 hours Term - 1.5mg/kg every 8 hours[2,3,5] **Oral:** 2 mg/kg every 8 hours[3,5] Contains 7.5% ethanol
Contraindications	• hypersensitivity to ranitidine or any component of the formulation
Precautions	• Caution in hepatic impairment, can elevate ALT. • Adjust dose in renal impairment.[2] • Acid suppression is a risk factor for NEC, gastroenteritis and candidemia and associated with an increased risk of late-onset bacterial and fungal sepsis in preterm infants. • Avoid routine gastric acid suppression.[3] • Cardiac rhythm disturbance. • Avoid rapid administration, can precipitate bradycardia, hypotension or premature ventricular contractions.[4]
Compatibilities & Interactions	• Compatible with sodium chloride 0.9% and glucose 5% and lactated Ringer's (Hartmann's).[4] • Incompatible with insulin, midazolam, phenobarbital[6] and amphotericin B.[3] • Contact a Pharmacist for other medication compatibilities if required. • Ranitidine may decrease the effect of iron salts, ketoconazole and multivitamins.[2]

Adverse effects	• Headache and dizziness. • Skin rash, rare cases of erythema multiforme and alopecia. • Rare reports of bradycardia (resolves on discontinuation), AV block and vasculitis.[1] • Fatigue and irritability.[3] • Blood count changes which are usually reversible e.g. leucopenia, thrombocytopenia, acquired immune haemolytic anaemia[2], rarely agranulocytosis or pancytopenia with marrow hypoplasia or marrow aplasia. • Reversible blurred vision. • Rare cases of diarrhoea and acute pancreatitis.[1] • Abdominal pain, constipation, nausea. • Risk of NEC in very low birth weight infants.[7] • Transient and reversible changes in liver function tests. • Involuntary muscle disturbance.[7] • Pain or itching at injection site.[2]

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse/registered midwife who holds current Waikato DHB Generic Medicine Management competency certification **and** Neonatal specific competency NCV/NAC as well as Guardrails competency.
Preparation & Administration	**IV Infusion** • IV push not recommended because of risk of bradycardia and hypotension.[5] • Draw up 0.2ml and dilute with 4.8ml of sodium chloride 0.9% or dextrose 5% to make a 1mg/ml solution.[8] • From the 1mg/ml solution, draw up prescribed dose and give over 15-30 minutes using Guardrails profiled syringe driver. **Oral** • May be given without regard to timing of feeds.[8]
Observations and management	• Monitor for signs and symptoms of hypersensitivity/anaphylaxis.[4] • Monitor ALT if on IV longer than 5 days.[2] • Monitor for adverse effects. • If bradycardia or arrhythmias occur during administration, discontinue the infusion and notify medical staff.[8] • Gastric pH may be monitored to assess efficacy.[3]
Storage	• IV solution – store below room temperature (below 25°C) and protect from light. • Diluted IV solution – Must be discarded within 24 hours of preparation if not used. Slight darkening of solution does not affect potency.[4] • Oral solution - store below 25°C.[9]
Special considerations	• Oral ranitidine (<8 years of age) and injection (all children) are not approved in New Zealand, therefore its use is considered “off-license” [5]
Rescue medication	• Significant toxicity is not expected after an overdose with ranitidine. • Treatment is symptomatic and supportive.[1,9] • Allergic reactions should be treated with antihistamines, steroids and adrenaline, oxygen and airway management as appropriate.

4. Guardrails Information[10]

Guardrails Drug Name	Ranitidine*			
Pump	CC			
	0.4-1kg	1-2kg	2-3kg	3-5kg
Concentration (mg/ml)				
Minimum	0.12	0.31	0.62	0.93
Maximum	1	2	2.5	2.5
Default	0.12	0.31	2.5	2.5
Administration Rate (mg/kg/hr)				
Soft minimum	1	1	1	1
Default	1	1	1	3
Soft maximum	6	6	6	6
Hard maximum	6.1	6.1	6.1	6.1

5. References

1 The New Zealand Medicines and Medical Devices Safety Authority (Medsafe): Zantac Injection, Data sheet, GlaxoSmithKline NZ Ltd. October 2013. Last accessed 12th October 2016. Available from http://www.medsafe.govt.nz/profs/Datasheet/z/Zantacinj.pdf

2 UpToDate® Ranitidine: Paediatric drug information accessed on 12 October 2016. Available from: https://www.uptodate.com/contents/ranitidine-pediatric-drug-information?source=search_result&search=ranitidine&selectedTitle=2~133

3 Micromedex® 1.0 (Healthcare Series), (electronic version). Paediatrics and Neofax - Ranitidine. Truven Health Analytics, Greenwood Village, Colorado, USA. Last accessed 12th October 2016. Available from : http://www.micromedexsolutions.com/

4 Handbook on injectable drugs, 18th edition, American Society of Health-system Pharmacists 2015.

5 New Zealand Formulary for Children, NZ. Ranitidine. Last accessed 12th October 2016. Available from http://www.nzfchildren.org.nz/nzf_749

6 Handbook on injectable drugs, 18th edition, American Society of Health-system Pharmacists 2015.

7 Pediatric & Neonatal Handbook. 20th edition. American Pharmacists Association. 2013.

8 Auckland NICU Drug Protocols – Ranitidine, August 2007. Last accessed 12th October 2016. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols/RanitidinePharmacology.htm

9 The New Zealand Medicines and Medical Devices Safety Authority (Medsafe): Peptisoothe, Data sheet, AFT Pharmaceuticals Ltd. August 2008. Last accessed 12th October 2016. Available from: http://www.medsafe.govt.nz/profs/Datasheet/p/Peptisoothesyrup.pdf

10 Guardrails Data Sheets, Waikato Hospital, Hamilton, NZ, August 2016