Royal College of Emergency Medicine and National Poisons Information Service Guideline on Antidote Availability for Emergency Departments January 2017

TOXBASE and/or the BNF should be consulted for further advice on doses and indications for antidote administration and, if necessary, the National Poisons Information Service (NPIS) should be telephoned for more patient-specific advice. Contact details for NPIS are available on TOXBASE.

Additional drugs that are used in the poisoned patient that are widely available in ED are not listed in the table – in particular it is important to ensure that insulin, benzodiazepines (diazepam and/or lorazepam), glyceryl trinitrate or isosorbide dinitrate and magnesium are immediately available in the ED.

The following drugs should be immediately available in the ED or any area where poisoned patients are initially treated. <u>These drugs should be held in a designated storage facility</u>* **The stock held should be sufficient to initiate treatment (stocking guidance is in Appendix 1).**	
Drug	**Indication**
Acetylcysteine	Paracetamol
Activated charcoal	Many oral poisons
Atropine	Organophosphorus or carbamate insecticides
	Bradycardia
Calcium chloride	Calcium channel blockers Systemic effects of hydrofluoric acid
Calcium gluconate Calcium gluconate gel	Local infiltration for hydrofluoric acid Hydrofluoric acid
Cyanide antidotes Dicobalt edetate Hydroxocobalamin (Cyanokit®) Sodium nitrite Sodium thiosulphate	Cyanide The choice of antidote depends on the severity of poisoning, certainty of diagnosis and cause of poisoning/source of cyanide. - **Dicobalt edetate** is the antidote of choice in severe cases when there is a high clinical suspicion of cyanide poisoning e.g. after cyanide salt exposure. - **Hydroxocobalamin** (Cyanokit®) should be considered in smoke inhalation victims who have a severe lactic acidosis, are comatose, in cardiac arrest or have significant cardiovascular compromise - **Sodium nitrite** may be used if dicobalt edetate is not available. - **Sodium thiosulphate** is used generally as an adjuvant to other antidotes.
Flumazenil	Reversal of iatrogenic over-sedation with benzodiazepines. Use with caution in patients with benzodiazepine poisoning, particularly in mixed drug overdoses. Should not be used as a "diagnostic" agent and is contraindicated in mixed tricyclic antidepressant (TCA)/ benzodiazepine overdoses and in those with a history of epilepsy.
Glucagon	Beta-adrenoceptor blocking drugs. Other indications e.g. calcium channel blocker (CCB) / TCA
Intralipid 20%	Severe, systemic local anaesthetic toxicity
Methylthioninium chloride (methylene blue)	Methaemoglobinaemia
Naloxone	Opioids
Procyclidine injection	Dystonic reactions
Sodium bicarbonate 8.4% and 1.26% or 1.4%	TCAs & class Ia & Ic antiarrhythmic drugs Urinary alkalinisation
ViperaTAb*	European adder, *Vipera berus*

** ViperaTAb does not need to be held in hospitals in Northern Ireland*

The following drugs should be available within 1 hour (i.e. within the hospital)	
Drug	**Indication**
Calcium folinate	Methotrexate (MTX)
	Methanol, formic acid
Cyproheptadine	Serotonin syndrome
Dantrolene	Neuroleptic malignant syndrome (NMS)
	Other drug-related hyperpyrexia (consult TOXBASE)
Desferrioxamine	Iron
Digoxin specific antibody fragments (Digibind or Digifab)	Digoxin and related glycosides
Fomepizole (*or* Ethanol (IV or oral)) **Fomepizole is the antidote of choice**. Ethanol only needs to be held if fomepizole is unavailable.	Ethylene glycol, diethylene glycol, methanol
Idarucizumab	Dabigatran related active bleeding (discuss with local haematologists and NPIS)
Macrogol '3350' (polyethylene glycol) *Klean-Prep®*	Whole bowel irrigation for agents not bound by activated charcoal e.g. iron, lithium, also for bodypackers and for slow release preparations
Mesna *(in hospitals commonly using cyclophosphamide)*	Cyclophosphamide
Octreotide	Sulphonylureas
Phentolamine#	Digital ischaemia related to injection of epinephrine
Phytomenadione (Vitamin K1)	Vitamin K dependent anticoagulants
Protamine sulphate	Heparin
Pyridoxine, high dose injection	Isoniazid

#There have been recently been availability and supply problems with phentolamine, advice on alternative treatment strategies is available on TOXBASE if phentolamine is not available.

The following drugs are rarely used and are suitable to be held supra-regionally. In the absence of nationally agreed arrangements, this needs to be organised locally. Use of these antidotes should be discussed with NPIS and/or a clinical toxicologist	
Prussian Blue (Berlin Blue)	Thallium
Botulinum antitoxin	Botulism
Glucarpidase	Methotrexate
Pralidoxime chloride	Organophosphorus insecticides
Sodium calcium edetate	Heavy metals (particularly lead)
Succimer (DMSA)	Heavy metals (particularly lead and arsenic)
Unithiol (DMPS)	Heavy metals (particularly mercury)

It is not considered essential to hold the following drugs
Benzatropine, Dimercaprol, Methionine, Penicillamine Physostigmine

** Antivenoms for non-indigenous venomous animals*:* Public Health England (PHE) holds a stock of exotic antivenoms for use in cases of venomous bites from non-indigenous animals. These are held by Movianto UK on behalf of PHE in sites at Bedford and Knowsley to ensure stock is available in good time across the UK. In the event of a bite, advice should be sought from NPIS. If antivenom is indicated an order will be placed with Movianto by either a national antivenom expert or NPIS for both in hours and out of hours delivery. Any unused antivenom should be stored in the fridge for collection by Movianto.

Royal College of Emergency Medicine and National Poisons Information Service
Guideline on Antidote Availability for Emergency Departments (January 2017)

Appendix 1. Stock levels & storage recommendations

Doses and Clinical Advice on the Administration of Antidotes

TOXBASE and/or the BNF should be consulted for further advice on doses and indications for antidote administration. If necessary, the National Poisons Information Service (NPIS) should be telephoned for more patient-specific advice. Contact details for NPIS are available on TOXBASE.

Stock Levels

The recommended minimum stocking levels (rounded up to full "pack-sizes" where necessary) are based on the amount of antidote required to initiate treatment for an adult patient in the ED and to continue treatment for the first 24 hours.

Higher stock levels may be required and individual departments should determine the amount of each antidote they stock based on the epidemiology of poisoning presentations to their department.

Additional drugs that are used in the poisoned patient that are widely available in ED are not listed in the table – in particular it is important to ensure that insulin, benzodiazepines (diazepam and/or lorazepam), glyceryl trinitrate or isosorbide mononitrate and magnesium are immediately available in the ED.

The following drugs should be immediately available in the ED or any area where poisoned patients are initially treated
These drugs should be held in a designated storage facility

Drug	Indication	Presentation	Recommended stock	Special storage conditions
Acetylcysteine	Paracetamol	200mg/mL, 10mL ampoule	20 ampoules	
Activated charcoal	Many oral poisons	50g pack	7 packs	
Atropine	Bradycardia Organophosphorus or carbamate insecticides	600mcg/mL, 1mL ampoule	10 ampoules[1]	
Calcium chloride	Calcium channel blockers Systemic effects of hydrofluoric acid	10mL ampoule	6 ampoules	
Calcium gluconate	Local infiltration for hydrofluoric acid	10mL ampoule	10 ampoules	
Calcium gluconate gel	Hydrofluoric acid	25g pack	1 pack	
Dicobalt edetate	Cyanide	15mg/mL, 20mL ampoule	6 ampoules	
Hydroxocobalamin *(Cyanokit® only suitable product)*		5g pack *(Cyanokit®)*	2 packs	
Sodium nitrite		3% (30mg/mL), 10mL ampoule	5 ampoules	
Sodium thiosulphate		50% (500mg/mL), 10mL ampoule	5 ampoules	

Drug	Indication	Presentation	Recommended stock	Special storage conditions
Flumazenil	Reversal of iatrogenic over-sedation with benzodiazepines. Use with caution in patients with benzodiazepine poisoning, particularly in mixed drug overdoses; contraindicated in mixed TCA/ benzodiazepine overdose.	100mcg/mL, 5mL ampoule	5 ampoules	
Glucagon	Beta-adrenoreceptor blockers. Other indications e.g. calcium channel blockers, seek NPIS advice	1mg vial	50 vials	Store in fridge (can store at room temperature but reduced shelf life must be marked)
Intralipid 20%	Severe systemic local anaesthetic toxicity. Always seek NPIS advice before giving intravenous lipid emulsion therapy.	100mL 20% solution OR 250mL 20% solution OR 500mL 20% solution	1.5 litres	
Methylthioninium chloride (methylene blue)	Methaemoglobinaemia	0.5% (5mg/mL), 10mL ampoules	5 ampoules	
Naloxone	Opioids	400mcg/1mL, 1mL ampoule	30 ampoules	
Procyclidine injection	Dystonic reactions	5mg/mL, 2mL ampoule	5 ampoules	
Sodium bicarbonate 8.4%	TCAs & class Ia & Ic antiarrhythmic drugs Urinary alkalinisation	200mL polyfusor	3 polyfusors	
Sodium bicarbonate isotonic 1.26% or 1.4%	Urinary alkalinisation	500mL polyfusor	12 polyfusors	
ViperaTAb*	European adder (*Vipera berus)*	10ml ampoule	2 ampoules	Store in fridge

*ViperaTAb can be ordered from Public Health England (PHE) through the ImmForm website (https://portal.immform.dh.gov.uk/) and will be delivered by Movianto Ltd on a scheduled delivery day

The following drugs should be <u>available within 1 hour</u> (i.e. within the hospital)				
Drug	**Indication**	**Presentation**	**Recommended stock**	**Special storage conditions**
Calcium folinate	Methotrexate (MTX)	10mg/mL, 30mL ampoule	15 am poules	Store in fridge and protect from light.
	Methanol, formic acid	10mg/mL, 30mL ampoule	5 ampoules	
Cyproheptadine	Serotonin syndrome	4mg tablet	30 tablets	
Dantrolene	Neuroleptic malignant syndrome (NMS)	20mg vial	48 ampoules	
	Other drug-related hyperpyrexia, seek NPIS advice	20mg vial	36 ampoules	
Desferrioxamine	Iron	500mg vial	40 vials	
Digoxin specific antibody fragments Digifab	Digoxin	40mg vial	10 vials	Store in fridge
Fomepizole *OR* Ethanol[2] **Fomepizole is the antidote of choice.** Ethanol only needs to be held if fomepizole is not available.	Ethylene glycol, methanol	5mg/mL, 20mL ampoule *OR* 1g/mL, 1.5mL vial	25 ampoules 4 vials	
		100% ethanol, 5mL ampoule (approx ≈ 4g)	60 ampoules	
Idarucizumab	Dabigatran	2.5g/50mL vials	2 vials	
Macrogol '3350' (polyethylene glycol) *Klean-Prep*®	Gut decontamination for agents not bound by activated charcoal e.g. iron, lithium, bodypackers	4 sachets (reconstituted with 4L water)	12 sachets	
Mesna	Cyclophosphamide	400mg tablet; 1 g/10mL ampoule	Variable, liaise with oncology	
Octreotide	Sulphonylureas	50mcg/mL, 1mL ampoule	5 ampoules	Store in fridge
Phentolamine	Digital ischaemia related to injection of epinephrine	10mg/mL, 1mL ampoule	5 ampoules	
Phytomenadione (Vitamin K1)	Vitamin K dependent anticoagulants[3]	10mg tablet; 10mg/mL, 1mL ampoule	2 tablets 10 ampoules	
Protamine sulphate	Heparin	10mg/mL, 5mL ampoule	10 ampoules	
Pyridoxine (high dose injection)	Isoniazid	50mg/mL, 1mL ampoule	100 ampoules	

Dosages of the rarely used drugs that are suitable to be held supra-regionally are variable & depend on the patient's clinical condition; discuss use of these antidotes with NPIS and/or a clinical toxicologist.

Superscript notes from the tables:

1 Much higher doses may be required in OP poisoning: see TOXBASE for further advice
2 Ethanol needs frequent blood assay, ensure laboratories provide an out of hours service & have sufficient reagent; ethanol should only be used if fomepizole is not available.
3 Larger doses and/or prolonged therapy may be required for long acting anticoagulants

Most antidotes listed in the guidelines are readily available within the UK. Further information is given here for unlicensed products or those with special storage or usage requirements. TOXBASE also contains details for product supply.

Unlicensed Medicines or 'Specials'

These are exempt under Schedule 1 of the Medicines Act from the need for a marketing authorisation as they are used to fill a "special need" in response to an order from a prescriber for use in an individual patient, under that prescriber's direct responsibility. Unlike licensed products, these may not have been assessed by the Licensing Authority against the criteria of safety, quality and efficacy.

A pharmacist in a hospital is allowed to procure a stock of 'specials' in order to meet an anticipated doctor's prescription. There are various companies that import unlicensed medicines/'specials' into the UK. Specific records have to be kept by pharmacy for five years which include details of the product obtained, the prescriber and the patients to which the medicine is dispensed.

'Advanced supply' of unlicensed medicines/specials

As appropriate records must be kept, Chief Pharmacists and Trust Clinical Governance Committees should be involved in any decision to hold unlicensed products as an 'advance supply' in clinical areas (rather than in pharmacy). For any products held as such, that may be required for immediate use, retrospective collection of patient details must be undertaken and systems must be in place to ensure this is completed in a timely manner.

Further Information:

1. The supply of unlicensed relevant medicinal products for individual patients MHRA Guidance Note 14 Revised August 2006
2. Rarely Used Medicines Database. London, Eastern and South Eastern Specialist Pharmacy Services NHS Procurement http://www.londonpharmacy.nhs.uk/Procurement/RUM/default.asp [accessed 25.05.08]
3. United Kingdom Clinical Pharmacists Association Emergency Care Specialist Interest Group. http://www.ukcpa.org/

Version 1, January 2017
For Review January 2020