

Bibliography

SPC Reopro 2 mg/mL solution for injection or infusion (accessed 30 March 2010).

Acetylcysteine

200 mg/mL solution in 10-mL ampoules (20% solution)

- Acetylcysteine is used for the prevention of hepatotoxicity in the treatment of paracetamol (acetaminophen) overdose.
- It protects the liver if infused within 24 hours of paracetamol ingestion. It is most effective if given within 8 hours of ingestion, after which effectiveness declines sharply.
- If more than 24 hours have elapsed since ingestion, advice should be sought from the National Poisons Information Service (NPIS) or from a liver unit on the management of serious liver damage.
- Acetylcysteine can be nebulised (unlicensed) for use as a mucolytic.

Pre-treatment checks

- Administer with caution to any patient with asthma or a history of bronchospasm or peptic ulcer disease (↑risk of GI haemorrhage). However, do not delay necessary treatment in these patients.
- Previous anaphylactoid reaction to acetylcysteine is *not* an absolute contraindication for a further treatment course: NPIS advice is to pretreat with an antihistamine, e.g. chlorphenamine 10 mg IV.
- In pregnancy, appropriate maternal treatment is important for the wellbeing of both the mother and the fetus. If the blood levels of paracetamol indicate that acetylcysteine is required, it should be given.

Biochemical and other tests (not all are necessary in an emergency situation)

Bodyweight

INR

LFTs

The plasma paracetamol concentration in relation to time after overdose is used to determine whether a patient is at risk of hepatotoxicity and should therefore receive acetylcysteine.

As there is a risk of increased acetylcysteine side-effects, it is unwise to institute treatment before paracetamol levels are known unless more than 8 hours have elapsed since ingestion or levels are likely to be delayed.

NB: Blood samples taken <4 hours after a paracetamol overdose give unreliable estimates of the serum paracetamol concentration.

Refer to the poisoning treatment graph (Figure A1) at the end of the monograph:

- Otherwise healthy patients whose plasma paracetamol concentrations fall on or above the 'Normal treatment line' should receive acetylcysteine. If there is doubt about the timing of the overdose, consideration should be given to treatment with acetylcysteine.
- Sufferers from chronic alcoholism and patients taking enzyme-inducing drugs, e.g. phenytoin, phenobarbital, primidone, carbamazepine, rifampicin and St John's wort, are susceptible to paracetamol-induced hepatotoxicity at lower plasma paracetamol concentrations and should be treated if plasma paracetamol concentrations fall on or above the 'High-risk treatment line'.
- The 'High-risk treatment line' should also be used to guide treatment in patients with malnutrition, e.g. patients with anorexia or AIDS, as they are likely to have depleted glutathione reserves.
- In patients who have taken staggered overdoses, blood levels are meaningless in relation to the treatment graph, and these patients should be considered for treatment with acetylcysteine.

Dose

It is essential to consult a poisons information service, e.g. Toxbase at www.toxbase.org (password or registration required) for full details of the management of paracetamol toxicity.

Treatment for paracetamol poisoning by IV infusion (refer to Table A1 below):

Bag 1: 150 mg/kg bodyweight given in 200 mL of infusion fluid over 15 minutes

Bag 2: 50 mg/kg bodyweight in 500 mL infusion fluid over the next 4 hours

Bag 3: 100 mg/kg bodyweight in 1 L infusion fluid over the next 16 hours

Treatment for paracetamol poisoning by the oral route (unlicensed): in the USA, acetylcysteine is licensed for oral use in paracetamol overdose. An initial dose of 140 mg/kg as a 5% solution is followed by 70 mg/kg every 4 hours for an additional 17 doses.

As a mucolytic via nebuliser (unlicensed): the adult dose is 3–5 mL acetylcysteine 20% injection, nebulised 3–4 times daily using air (use of concentrated oxygen causes degradation).

Acetylcysteine may cause bronchospasm. This can be avoided either by giving a lower dose – diluting 1 mL acetylcysteine 20% in 5 mL NaCl 0.9% and giving 3–4 mL – or pre-administering a nebulised bronchodilator.

Intravenous infusion

Preparation and administration

1. Withdraw the required dose and add to the appropriate volume of infusion fluid. Mix well.
2. The solution should be clear and colourless. Inspect visually for particulate matter or discoloration before administration.
3. Give by IV infusion over the time period stated above.

Oral administration (unlicensed)

Preparation and administration

1. Withdraw the required dose.
2. Dilute the injection to 4 times its volume with diet soft drink and give to the patient to drink; if given via a nasogastric tube, water may be used as the diluent.

Nebulisation (unlicensed)

Preparation and administration

1. Withdraw the required dose and dilute with NaCl 0.9% if required (see dose above).
2. Give via a nebuliser using air (not oxygen).

Technical information

Incompatible with	Equipment made of rubber and some metals, e.g. iron, copper and nickel. Otherwise no information.
Compatible with	Equipment made of plastic, glass and stainless steel. Flush: NaCl 0.9% Solutions: Gluc 5% (preferred), NaCl 0.9% (both including added KCl) Y-site: No information
pH	6-7.5
Sodium content	12.8 mmol/10 mL

(continued)

Technical information *(continued)*

Storage	Store below 25°C. A change in colour to light purple is not thought to indicate significant impairment of safety or efficacy.
Stability after preparation	From a microbiological point of view, prepared infusions should be used immediately; however, solutions are known to be stable at room temperature for up to 24 hours.

Monitoring

Measure	Frequency	Rationale
Liver function and INR	To determine completion of antidote	<ul style="list-style-type: none"> • ↑Transaminases (ALT or AST) and ↑INR indicate hepatotoxicity. Acetylcysteine can also cause a marginally elevated INR. • An INR of ≤ 1.3 with normal transaminases does not warrant further treatment. If all measures are raised, then 'bag 3' should be repeated over 16 hours.
ECG	If indicated	<ul style="list-style-type: none"> • ECG changes have been reported in patients with paracetamol poisoning, irrespective of the treatment given.
Renal function and serum K		<ul style="list-style-type: none"> • ↓K has been reported in patients with paracetamol poisoning, irrespective of the treatment given. • Renal failure is a recognised complication of paracetamol overdose.
Serum bicarbonate		<ul style="list-style-type: none"> • Metabolic acidosis can be a complication of paracetamol overdose.

Additional information

Common and serious undesirable effects	<p><i>Immediate:</i> Anaphylactoid or hypersensitivity-like reactions have been reported in 0.3-3% of patients, in patients with hepatic cirrhosis, and in patients with low or absent paracetamol concentrations.</p> <ul style="list-style-type: none"> • Symptoms include nausea/vomiting, injection-site reactions, flushing, itching, rashes/urticaria, angioedema, bronchospasm/respiratory distress, ↓BP and, rarely, ↑pulse or ↑BP. These have usually occurred 15-60 minutes after the start of infusion. Symptoms have often been relieved by stopping the infusion, but occasionally an antihistamine or corticosteroid may be necessary. • Once the reaction has settled, the infusion can normally be restarted at 50 mg/kg over 4 hours. Further reactions are almost unknown. <p><i>Infusion-related:</i> Too rapid administration: Higher incidence of hypersensitivity reactions.</p>
Pharmacokinetics	Elimination half-life of 2-6 hours reported after IV dosing, with 20-30% of the administered dose being recovered unchanged in the urine.
Significant interactions	No known interactions.
Action in case of overdose	<p><i>Symptoms to watch for:</i> effects similar to the anaphylactoid reactions noted above, but they may be more severe.</p> <p>There is a theoretical risk of hepatic encephalopathy.</p>

Risk rating: **AMBER**

Score = 4

Moderate-risk product: Risk-reduction strategies are recommended.



This assessment is based on the full range of preparation and administration options described in the monograph. These may not all be applicable in some clinical situations.

Bibliography

SPC Parvolex (accessed 17 August 2008).

Toxbase at www.toxbase.org (accessed 18 August 2008).

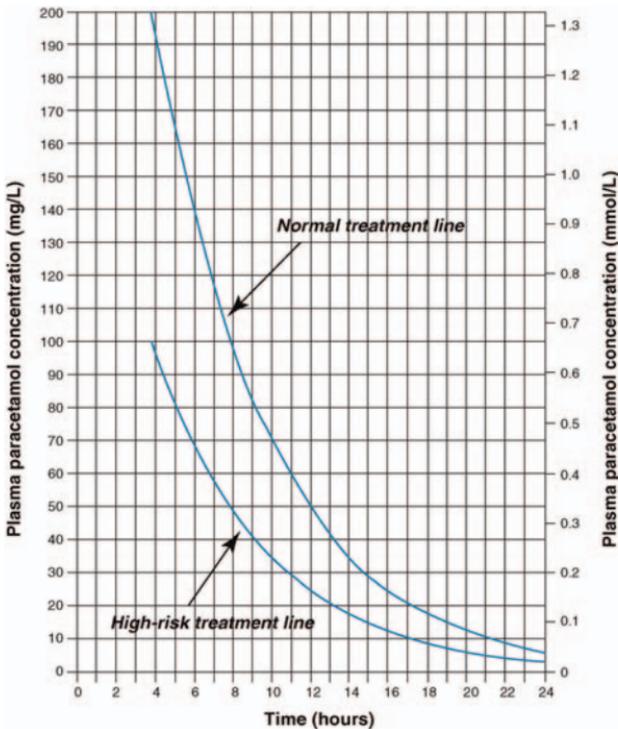


Figure A1 Patients whose plasma paracetamol concentrations are above the normal treatment line should be treated with acetylcysteine by IV infusion (or, if acetylcysteine cannot be used, with methionine by mouth, provided the overdose has been taken within 10-12 hours and the patient is not vomiting).

Patients on enzyme-inducing drugs (e.g. carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, alcohol and St John's wort) or who are malnourished (e.g. in anorexia, in alcoholism, or those who are HIV positive) should be treated if their plasma paracetamol concentration is above the high-risk treatment line.

The prognostic accuracy after 15 hours is uncertain, but a plasma paracetamol concentration above the relevant treatment line should be regarded as carrying a serious risk of liver damage.

(Graph reproduced courtesy of Professor Philip Routledge, Therapeutics and Toxicology Centre, Cardiff and taken from BNF 60 (September 2010).)

Table A1 Acetylcysteine dosing table for paracetamol overdose

Bodyweight (kg)	1st dose 'Bag 1' 150 mg/kg over 15 minutes in 200 mL Gluc 5%		2nd dose 'Bag 2' 50 mg/kg over 4 hours in 500 mL Gluc 5%		3rd dose 'Bag 3' 100 mg/kg over 16 hours in 1 L Gluc 5%	
	Parvolex (dose)	Parvolex (volume)	Parvolex (dose)	Parvolex (volume)	Parvolex (dose)	Parvolex (volume)
40	6.0 g	30.0 mL	2.0 g	10.0 mL	4.0 g	20 mL
42	6.3 g	31.5 mL	2.1 g	10.5 mL	4.2 g	21 mL
44	6.6 g	33.0 mL	2.2 g	11.0 mL	4.4 g	22 mL
46	6.9 g	34.5 mL	2.3 g	11.5 mL	4.6 g	23 mL
48	7.2 g	36.0 mL	2.4 g	12.0 mL	4.8 g	24 mL
50	7.5 g	37.5 mL	2.5 g	12.5 mL	5.0 g	25 mL
52	7.8 g	39.0 mL	2.6 g	13.0 mL	5.2 g	26 mL
54	8.1 g	40.5 mL	2.7 g	13.5 mL	5.4 g	27 mL
56	8.4 g	42.0 mL	2.8 g	14.0 mL	5.6 g	28 mL
58	8.7 g	43.5 mL	2.9 g	14.5 mL	5.8 g	29 mL
60	9.0 g	45.0 mL	3.0 g	15.0 mL	6.0 g	30 mL
62	9.3 g	46.5 mL	3.1 g	15.5 mL	6.2 g	31 mL
64	9.6 g	48.0 mL	3.2 g	16.0 mL	6.4 g	32 mL
66	9.9 g	49.5 mL	3.3 g	16.5 mL	6.6 g	33 mL
68	10.2 g	51.0 mL	3.4 g	17.0 mL	6.8 g	34 mL
70	10.5 g	52.5 mL	3.5 g	17.5 mL	7.0 g	35 mL
72	10.8 g	54.0 mL	3.6 g	18.0 mL	7.2 g	36 mL
74	11.1 g	55.5 mL	3.7 g	18.5 mL	7.4 g	37 mL
76	11.4 g	57.0 mL	3.8 g	19.0 mL	7.6 g	38 mL
78	11.7 g	58.5 mL	3.9 g	19.5 mL	7.8 g	39 mL
80	12.0 g	60.0 mL	4.0 g	20.0 mL	8.0 g	40 mL

(continued)

Table A1 Acetylcysteine dosing table for paracetamol overdose (*continued*)

Bodyweight (kg)	1st dose 'Bag 1' 150 mg/kg over 15 minutes in 200 mL Gluc 5%		2nd dose 'Bag 2' 50 mg/kg over 4 hours in 500 mL Gluc 5%		3rd dose 'Bag 3' 100 mg/kg over 16 hours in 1 L Gluc 5%	
	Parvolex (dose)	Parvolex (volume)	Parvolex (dose)	Parvolex (volume)	Parvolex (dose)	Parvolex (volume)
82	12.3 g	61.5 mL	4.1 g	20.5 mL	8.2 g	41 mL
84	12.6 g	63.0 mL	4.2 g	21.0 mL	8.4 g	42 mL
86	12.9 g	64.5 mL	4.3 g	21.5 mL	8.6 g	43 mL
88	13.2 g	66.0 mL	4.4 g	22.0 mL	8.8 g	44 mL
90	13.5 g	67.5 mL	4.5 g	22.5 mL	9.0 g	45 mL
92	13.8 g	69.0 mL	4.6 g	23.0 mL	9.2 g	46 mL
94	14.1 g	70.5 mL	4.7 g	23.5 mL	9.4 g	47 mL
96	14.4 g	72.0 mL	4.8 g	24.0 mL	9.6 g	48 mL
98	14.7 g	73.5 mL	4.9 g	24.5 mL	9.8 g	49 mL
100	15.0 g	75.0 mL	5.0 g	25.0 mL	10.0 g	50 mL
102	15.3 g	76.5 mL	5.1 g	25.5 mL	10.2 g	51 mL
104	15.6 g	78.0 mL	5.2 g	26.0 mL	10.4 g	52 mL
106	15.9 g	79.5 mL	5.3 g	26.5 mL	10.6 g	53 mL
108	16.2 g	81.0 mL	5.4 g	27.0 mL	10.8 g	54 mL
110	16.5 g	82.5 mL	5.5 g	27.5 mL	11.0 g	55 mL
>110	If weight is >110 kg, dose as for 110 kg					

Risk rating: GREEN	Score = 2 Lower-risk product: Risk-reduction strategies should be considered.
	
This assessment is based on the full range of preparation and administration options described in the monograph. These may not all be applicable in some clinical situations.	

Reference

1. Maling TJB, Cretney MJ. Ethanolamine oleate and acute renal failure. *N Z Med J.* 1975; 82: 269–270.

Bibliography

SPC Ethanolamine Oleate Injection BP, UCB Pharma Ltd (accessed 28 September 2009).

Exenatide

5 micrograms/dose and 10 micrograms/dose solution in pre-filled pen

- Exenatide is a synthetic form of exendin-4, a 39-amino-acid peptide isolated from the venom of the Gila monster lizard. It is an incretin mimetic that ↑insulin secretion, ↓glucagon secretion, and slows gastric emptying.
- It is used for the treatment of type 2 diabetes mellitus in combination with metformin and/or a sulfonylurea, in patients who have not achieved adequate glycaemic control with these drugs alone or in combination. It is also licensed for use with glitazones (with or without other oral agents) in the USA.

Pre-treatment checks

- Do not use in type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Not licensed in combination with insulin in type 2 diabetes.
- Do not use in severe renal impairment (CrCl or eGFR <30 mL/minute).
- Avoid in severe gastrointestinal disease (including gastroparesis) because of GI side-effects.
- Avoid in pregnancy and breast feeding – insulin is a safe alternative.
- Consider reducing the dose of sulfonylurea when starting therapy.
- Ensure that the patient reads and understands the user manual.

Biochemical and other tests

HbA_{1c}

Renal function: U, Cr, CrCl (or eGFR)

Dose

Initiate at 5 micrograms twice daily by SC injection for at least 1 month, in order to improve tolerability. The dose can then be increased to 10 micrograms twice daily to further improve glycaemic control.

- Give the dose **60 minutes or less before the two main meals of the day** (at least 6 hours apart).
- Exenatide **must not** be injected after a meal.

Subcutaneous injection

Exenatide must not be injected after a meal.

Preparation and administration

1. The solution should be clear and colourless, do not use if cloudy or discoloured or if particles are present.
2. Dial up the dose according to the pen-user manual (see package insert).
3. Give by SC injection into the upper outer thigh, abdomen or upper arm. Remove the needle after use and discard according to local guidelines. Although not specifically recommended by the manufacturer, it would be wise to vary the site of the injection.

Technical information

Incompatible with	Not relevant
Compatible with	Not relevant
pH	Not relevant
Sodium content	Negligible
Excipients	Contains metacresol which may cause hypersensitivity reactions.
Storage	<i>Long term:</i> Store at 2-8°C. Do not freeze. If it has been frozen, do not use. <i>In use:</i> Store below 25°C. Do not store the pen with the needle attached. Replace the cap on the pen to protect from light. Each pen contains 60 doses. Discard after 30 days of use even if some medication remains.

Monitoring

Measure	Frequency	Rationale
Hypersensitivity reactions	At the start of treatment	<ul style="list-style-type: none"> • May very rarely cause hypersensitivity reactions including anaphylaxis.
Renal function	Periodically	<ul style="list-style-type: none"> • May exacerbate pre-existing renal impairment.
Capillary blood glucose	As clinically appropriate	<ul style="list-style-type: none"> • Has caused hypoglycaemia with concomitant sulfonylurea therapy.
HbA _{1c}	Every 3-6 months	<ul style="list-style-type: none"> • To assess therapeutic response.

Additional information	
Common and serious undesirable effects	<p><i>Immediate:</i> Hypersensitivity reactions (anaphylaxis, rash, pruritus, urticaria, angioedema) occur very rarely (possibly due to metacresol content).</p> <p><i>Injection/infusion-related:</i> Local: Injection-site reactions.</p> <p><i>Other:</i> GI disturbances: nausea (may improve with time), vomiting, diarrhoea, dyspepsia, abdominal pain and distension, gastro-oesophageal reflux disease, ↓appetite; constipation, flatulence, dehydration, taste disturbance.</p> <p>Hypoglycaemia (particularly when given with sulfonylurea). Headache, dizziness, asthenia, drowsiness, jitteriness, ↑sweating. Pancreatitis has rarely been reported (stop immediately if suspected).</p>
Pharmacokinetics	Following SC injection exenatide reaches peak plasma concentrations in 2 hours. The mean terminal half-life is 2.4 hours. Clearance is principally renal, and is reduced in renal impairment.
Significant interactions	<ul style="list-style-type: none"> • ↑INR has been reported in patients taking warfarin. • Exenatide slows gastric emptying so may reduce the extent and rate of absorption of some oral medicinal products. • In general, oral antibiotics should be taken one hour before exenatide dose. • Proton pump inhibitors should be taken 1 hour before, or 4 hours after exenatide.
Action in case of overdose	<i>Symptoms to watch for:</i> Severe nausea, severe vomiting and rapidly declining blood glucose concentrations. Manage symptomatically.
Counselling	<p>Use and storage of pens, disposal of pen and needles, discard pens that have been frozen.</p> <p>Timing of dose in relation to food and what to do about missed doses.</p> <p>Warn about the ↑risk of hypoglycaemia at the start of therapy in patients being treated with a sulfonylurea.</p> <p>Warn to report symptoms of pancreatitis i.e. persistent, severe abdominal pain, sometimes accompanied by vomiting.</p> <p>Warn about timing of concomitant antibiotic therapy and other medication if appropriate.</p>

Risk rating: GREEN	Score = 0 Lower-risk product: Risk-reduction strategies should be considered.
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This assessment is based on the full range of preparation and administration options described in the monograph. These may not all be applicable in some clinical situations.

Bibliography

- SPC Byetta 5 micrograms solution for injection, prefilled pen (accessed 15 January 2009).
 SPC Byetta 10 micrograms solution for injection, prefilled pen (accessed 15 January 2009).
 MHRA. *Drug Safety Update* March 2009; 2(8).

Additional information	
Common and serious undesirable effects	Dizziness, visual disturbances, headache and nausea.
Pharmacokinetics	Elimination half-life is 7-20 hours.
Significant interactions	<ul style="list-style-type: none"> The following may ↑flecainide levels or effect (or ↑side-effects): amiodarone (halve flecainide doses), artemether/lumefantrine (avoid combination), quinine, verapamil. ↑Risk of arrhythmias with the following drugs: clozapine, dolasetron (avoid combination), tricyclic antidepressants, fosamprenavir (avoid combination), indinavir (avoid combination), lopinavir (avoid combination), mizolastine (avoid combination), ritonavir (avoid combination), tolterodine. Flecainide may ↑levels or effect (or ↑side-effects) of beta-blockers (↑risk of bradycardia).
Action in case of overdose	Life threatening - no specific antidote; there is no known way of rapidly removing flecainide from the body. Stop administration and give supportive therapy as appropriate.

Risk rating: AMBER	Score = 5 Moderate-risk product: Risk-reduction strategies are recommended.
	
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Bibliography

SPC Tambocor injection (accessed 1 October 2009).

Flucloxacillin (floxacillin)

250-mg, 500-mg, 1-g dry powder vials

- Flucloxacillin sodium is a penicillin with a mode of action similar to that of benzylpenicillin, but it is resistant to staphylococcal penicillinase.
- It is particularly useful in infections caused by staphylococci resistant to benzylpenicillin. These include bone and joint infections, endocarditis and soft-tissue infections.
- Dose are expressed in terms of flucloxacillin:
Flucloxacillin 1 g ≡ 1.09 g flucloxacillin sodium.

Pre-treatment checks

- Do not give if there is known hypersensitivity to penicillin.
- Avoid in patients with a history of hepatic dysfunction associated with flucloxacillin.
- Flucloxacillin is considered unsafe in porphyria (associated with acute attacks).

Biochemical and other tests (not all are necessary in an emergency situation)

Bodyweight in certain indications

LFTs

FBC

Renal function: U, Cr, CrCl (or eGFR)

Dose

If used in combination with an aminoglycoside (e.g. amikacin, gentamicin, tobramycin), preferably administer at a different site. If this is not possible then flush the line with a compatible solution between drugs.

Standard dose: 250 mg–2 g by IM or IV injection or IV infusion every 6 hours.

Osteomyelitis: 2 g by IV injection or infusion every 6–8 hours.

Endocarditis: bodyweight ≤ 85 kg: 2 g by IV injection or infusion every 6 hours; bodyweight > 85 kg: 2 g every 4 hours.

Surgical prophylaxis: 1–2 g at induction by IV injection or infusion followed by (for high risk procedures), up to four further doses of 500 mg orally or parenterally every 6 hours. Check local policies.

Intrapleural injection: 250 mg once daily.

Intra-articular injection: 250–500 mg once daily.

Nebulised: 125–250 mg every 6 hours.

Dose in renal impairment: adjusted according to creatinine clearance:¹

- CrCl > 10 mL/minute: dose as in normal renal function.
- CrCl < 10 mL/minute: dose as in normal renal function (maximum total daily dose 4 g).

Dose in hepatic impairment: use with caution (risk of cholestatic jaundice and hepatitis).

Intravenous injection

Preparation and administration

See Special handling below.

If used in combination with an aminoglycoside (e.g. amikacin, gentamicin, tobramycin), preferably administer at a different site. If this is not possible then flush the line with a compatible solution between drugs.

1. Dissolve each 250 mg in 5 mL WFI (i.e. use 10 mL for a 500-mg vial, 20 mL for 1-g vial).
2. Withdraw the required dose.
3. The solution should be clear and colourless. Inspect visually for particulate matter or discoloration prior to administration and discard if present.
4. Give by IV injection over 3–4 minutes.

Intermittent intravenous infusion

Preparation and administration

See Special handling below.

If used in combination with an aminoglycoside (e.g. amikacin, gentamicin, tobramycin), preferably administer at a different site. If this is not possible then flush the line with a compatible solution between drugs.

1. Reconstitute each 250-mg vial with 5 mL WFI (use 10 mL for each 500-mg vial, 20 mL for each 1-g vial).
2. Withdraw the required dose and add to a suitable volume of compatible infusion fluid (usually 100 mL NaCl 0.9%).
3. The solution should be clear and colourless. Inspect visually for particulate matter or discoloration prior to administration and discard if present.
4. Give by IV infusion over 30–60 minutes.

Intramuscular injection (maximum dose 500 mg)

Preparation and administration

See Special handling below.

1. Reconstitute each 250-mg vial with 1.5 mL WFI (use 2 mL for each 500-mg vial).
2. Withdraw the required dose.
3. Give by IM injection into a large muscle such as the gluteus or the lateral aspect of the thigh. Rotate injection sites for subsequent injections.

Other routes

See Special handling below.

- **Intrapleural injection:** dissolve 250 mg in 5–10 mL WFI.
- **Intra-articular injection:** dissolve 250–500 mg in up to 5 mL of WFI. If pain occurs, 0.5% lidocaine may be used for reconstitution (see the Lidocaine monograph for cautions and monitoring)
- **Nebulised:** dissolve 250 mg in 3 mL of WFI.

Technical information

Incompatible with	Sodium bicarbonate. Amikacin, amiodarone, benzylpenicillin, calcium gluconate, ciprofloxacin, clarithromycin, diazepam, dobutamine, erythromycin lactobionate, gentamicin, metoclopramide, midazolam, ofloxacin, tobramycin, verapamil.
Compatible with	Flush: NaCl 0.9% Solutions: NaCl 0.9%, Gluc 5%, Gluc-NaCl, Hartmann's (all with added KCl), WFI Y-site: Adrenaline (epinephrine), aminophylline, ampicillin, bumetanide, ceftazidime, cefuroxime, dexamethasone sodium phosphate, digoxin, hydrocortisone sodium succinate, isosorbide dinitrate, metronidazole, ranitidine, sodium fusidate
pH	5-7
Sodium content	2.3 mmol per 1-g vial
Storage	Store below 25°C in original packaging.
Displacement value	0.2 mL/250 mg
Special handling	Avoid skin contact as may cause sensitisation.

(continued)

Technical information (continued)

Stability after preparation

- From a microbiological point of view, should be used immediately; however:
- Reconstituted vials may be stored at 2-8°C for 24 hours.
 - Prepared infusions may be stored at 2-8°C and infused (at room temperature) within 24 hours.

Monitoring

Measure	Frequency	Rationale
LFTs	Intermittently if on long-term/high-dose treatment and if otherwise indicated	<ul style="list-style-type: none"> • Changes in LFTs may occur; reversible on discontinuation of treatment. • Hepatitis and cholestatic jaundice can occur up to 2 months post treatment; the effects can last several months and are not related to either dose or route of administration. • Older patients and those receiving more than 2 weeks' treatment at higher risk.
Renal function		<ul style="list-style-type: none"> • Reduction of dose or extension of dosing interval is required if CrCl <10 mL/minute.
FBC		<ul style="list-style-type: none"> • Agranulocytosis has been associated rarely with flucloxacillin. Neutropenia and thrombocytopenia can also occur but are reversible when treatment is stopped. • Neutropenia is reported with high doses of beta-lactams with an incidence of from 5% to 15% in patients treated for more than 10 days.

Additional information

Common and serious undesirable effects

Immediate: Anaphylaxis and other hypersensitivity reactions have been reported.

Injection/infusion-related: Phlebitis following IV infusion.

Other: Urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reaction, nausea, vomiting and diarrhoea (pseudomembranous reported rarely). Patients treated for syphilis or neurosyphilis may develop a Jarisch-Herxheimer reaction (occurs 2-12 hours after initiation of therapy - headache, fever, chills, sweating, sore throat, myalgia, arthralgia, malaise, ↑pulse and ↑BP followed by a ↓BP. Usually subsides within 12-24 hours. Corticosteroids may ↓incidence and severity).

Pharmacokinetics

Half-life is approximately 1 hour.

Significant interactions

No significant interactions.

Action in case of overdose

Symptoms to watch for: Large doses have been associated with seizures.

Antidote: None; stop administration and give supportive therapy as appropriate.

Counselling

Women taking the combined contraceptive pill should be advised to take additional precautions during and for 7 days after the course.

Risk rating: **GREEN**

Score = 2

Lower-risk product: Risk-reduction strategies should be considered.



This assessment is based on the full range of preparation and administration options described in the monograph. These may not all be applicable in some clinical situations.

Reference

1. Ashley C, Currie A, eds. *The Renal Drug Handbook*, 3rd edn. Oxford: Radcliffe Medical Press, 2009.

Bibliography

SPC Flucloxacillin 500 mg powder for solution for injection or infusion, Wockhardt (accessed 28 September 2009).

Fluconazole

2 mg/mL solution in 50-mL, 100-mL, 200-mL infusion bags; 25-mL, 100-mL infusion vials

- Fluconazole is a triazole antifungal drug that in sensitive fungi selectively inhibits cytochrome P450-dependent enzymes resulting in impairment of ergosterol synthesis, an essential component of fungal cell membranes.
- It is used IV to treat systemic fungal infections including candidiasis, coccidioidomycosis and cryptococcosis.

Pre-treatment checks

Do not use in acute porphyria.

Biochemical and other tests (not all are necessary in an emergency situation)

Electrolytes: serum K

Renal function: U, Cr, CrCl (or eGFR)

FBC

Consider baseline ECG (caution in susceptibility

LFTs

to QT interval prolongation)

Dose

Invasive candidal infections (including candidaemia and disseminated candidiasis) and cryptococcal infections (including meningitis): 400 mg by IV infusion on first day then 200–400 mg daily; unlicensed doses of 800–1000 mg daily have been used in severe infections with treatment continued according to response (at least 8 weeks for cryptococcal meningitis).

Prevention of relapse of cryptococcal meningitis in AIDS patients after completion of primary therapy: 100–200 mg daily by IV infusion (or orally).

Prevention of fungal infections in immunocompromised patients: 50–400 mg daily by IV infusion (or orally), adjusted according to risk: 400 mg daily if there is high risk of systemic infections,