Digoxin antibody fragments (Fab) (Digifab) Intravenous for Adults

Who can administer

May be administered by registered competent doctor or nurse/midwife

Important information

- **Infusion related reactions or hypersensitivity reactions are possible** - monitor closely for signs of allergic reaction. See Further Information
- Consultation with National Poisons Centre (NPIC) may be advisable in acute overdose situation
- The onset of response is usually within 30 minutes
- See also **Renal impairment** below
- See '**Monitoring**'overleaf
- Stored in **fridge in ED** with back-up stock in the pharmacy

Available preparations

Digifab 40mg vial

Reconstitution

Water for injection

4ml per 40mg vial

Infusion fluids

Sodium chloride 0.9%

Methods of intravenous administration

Intermittent intravenous infusion (preferred route)

- Dilute required dose with a suitable volume of infusion fluid (suggested volume 100ml [ref 2]) and administer over 30 minutes
- If an infusion related reaction occurs, the infusion should be stopped and the patient treated. Consider restarting the infusion at a slower rate [ref 1,2]
- The residual volume in the infusion line must be flushed through at the same rate to avoid significant underdosing

Bolus intravenous injection

- If cardiac arrest is imminent Digifab may be given undiluted by rapid injection [ref 2]
- An increased incidence of allergic reactions may be expected using a bolus intravenous injection

Dose in adults

Doses below are as per Toxbase, rather than the SPC

- Digoxin antidote has previously been used in two doses: one calculated to neutralise all the digoxin

load ('full neutralisation' dose (FND)) and one calculated to neutralise only half of it ('half neutralisation' dose).
- Recent evidence indicates that the 'half neutralisation' dose is adequate for most patients. The doses below are calculated as 'half-neutralisation' doses as per Toxbase

The dose depends on the clinical situation and on whether plasma digoxin concentration is available [ref 1]

A: Cardiac arrest due to digoxin toxicity:

- Urgently administer Digifab as an IV bolus
- Weight greater than 40kg: give 5 vials (200 mg)
- Repeat as necessary after 15 minutes:

B: Other indications (e.g.acute digoxin overdose on top of usual therapy, acute overdose in digoxin-naive patient, digoxin toxicity from chronic therapy) - the following calculations can be used to work out the required dose.

- **B1. When digoxin concentration is available** (measured 6 hours after overdose/last dose, unless urgently indicated in patient with arrhythmia):
  - **Number of vials = {0.781 x serum digoxin concentration (nanomol/L) x weight (kg)} / 200.**
  - Round up to the nearest vial - for convenience, these doses have been worked out in table 1 below

Table 1
• Initial dose - when digoxin concentration is available
• Important: If clinical features persist despite initial dose, then discuss with NPIC (01) 809 2566 or 01 837 9964

Example, a patient who weighs 80kg, with a digoxin level of 5.12nanomoL/L- should receive an initial dose of 2 vials

Patient weight (kg)	**Serum digoxin concentration (nanomol/L)**					
Â	**2.56**	**5.12**	**10.24**	**15.36**	**20.48**	**25.6**
40	1 vial	1 vial	2 vials	3 vials	4 vials	4 vials
60	1 vial	2 vials	3 vials	4 vials	5 vials	6 vials
70	1 vial	2 vials	3 vials	5 vials	6 vials	7 vials
80	1 vial	2 vials	4 vials	5 vials	7 vials	8 vials
100	1 vial	2 vials	4 vials	6 vials	8 vials	10 vials

- **B2. When only ingested dose is available (overdose situation):**
  - **Number of vials = Amount of digoxin ingested (mg) x 0.8**
  - Round up to the nearest vial
  - If clinical features persist despite initial dose, then discuss with NPIC (01) 809 2566 or 01 837 9964
  - Example: if a patient ingested twenty-five tablets of the 0.25mg strength, as an acute single ingestion, (0.25mg x 25 tablets x 0.8) = 5 vials initially

Renal impairment

- It may be expected that excretion of the Fab-digoxin levels complexes from the body is slowed in the

presence of renal impairment, and that digoxin may be released after some days from retained Fab-digoxin complexes

General information

- Erroneous dosage calculations may result from inaccurate estimates of the amount of digoxin ingested or absorbed, **or from non steady-state serum digoxin concentrations**
- Inaccurate serum digoxin concentration measurements are also a possible source of error, especially at high serum values, as **most assay kits are not designed to measure values above 6.4nmol/L** (5ng/ml)
- If after several hours toxicity has not been adequately reversed or appears to recur, re-administration of Digifab at a dose guided by clinical judgement may be required
- If there is no response to an adequate dose of Digifab, the diagnosis of digitalis toxicity should be questioned
- Repeated use: no data available on repeated dosing. May give rise to anaphylactic reactions. Consider risk/benefit if considering repeated dose. This does not apply to the situations given above, where the calculated dose is given in two parts

Monitoring

- Patients should have **continuous ECG monitoring during and for at least 24 hours after** administration of Digifab
- Monitor temperature, potassium, blood pressure during and after administration
- Once Digifab has been administered, serum digoxin levels will no longer be clinically useful, as the level will represent both free and bound digoxin. Because of this, it is important to monitor the cardiac status of the patient for at least 24 hours after administration for signs of recurrent toxicity [ref 1]
- Adverse reactions can occur up to 14 days after the infusion has been administered

Further information

- **Digoxin serum levels are reported in UHG as nanomol/l.** Toxbase refers to levels in nanogram/ml
- To convert nanomol/L to nanogram/ml multiply nanomol/L by 0.781. For example 2.5 nanomol/L = 1.95nanogram/ml
- The likelihood of hypersensitivity reactions is higher in patients who are allergic to sheep-derived proteins, or to papain, an extract of the papaya fruit, dust mites or latex
- The dosage information in this monograph is taken from Toxbase. It recommends the use of 'Half-neutralisation doses'. The manufacturers suggest administration of the second half of the full-neutralisation dose after two hours if clinically indicated

Storage

- Store at 2 to 8^{0}C
- Do not freeze

References

Package insert and SPC December 2017

1: Toxbase, downloaded 13/04/2022

2:Injectable Medicines Administration Guide Medusa downloaded 11/05/2022

Therapeutic classification

Antidote