Public Health England

Protecting and improving the nation's health

# Guidance on the use of diphtheria anti-toxin

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# Diphtheria anti-toxin (DAT)

A single diphtheria anti-toxin (equine) product is currently being supplied in the UK.

Diphtheria Antitoxin (DAT) manufactured by Butantan Institute (Instituo Butanan) in 10ml ampoules containing 10,000 IU per ampoule (at least 1,000 IU DAT per ml).

## Indications

- for treatment of suspected diphtheria cases*
- for treatment of confirmed infections, where clinically appropriate, due to toxigenic Corynebacteria ulcerans or C diphtheriae

*As defined in National Guidelines (1).

### Notes:

- diphtheria anti-toxin should not be used for diphtheria prophylaxis
- unimmunised contacts should be given diphtheria-containing vaccine and antibiotic prophylaxis in line with National Guidelines (1)

## Dosage

Dosage for diphtheria anti-toxin is determined by the severity and duration of the disease as shown in the table below. The dose is the same for adults and children, and the number of ampoules required is also shown.

| Type of diphtheria | Dosage adults and children | Number of ampoules (5,000 IU/ampoule) |
|---|---|---|
| Severe diphtheria, for example extensive membrane and /or severe oedema (‘bull neck’) | 100,000 IU | 10 |
| Laryngeal OR pharyngeal OR nasopharyngeal disease of more than 48 hours | 100,000 IU | 10 |

| | | |
|---|---|---|
| Laryngeal OR pharyngeal disease OR nasopharyngeal disease of less than 48 hours | 70,000 IU | 6 |
| Skin lesions only1 | 40,000 IU | 4 |

The World Health Organization (2) state that antitoxin is of limited value in cutaneous disease. In most cutaneous infections, large-scale toxin absorption is unlikely and therefore the risk of giving anti-toxin is usually considered substantially greater than any benefit. Nevertheless, if the cutaneous ulcer is sufficiently large (more than 2cm squared) and membranous, then anti-toxin may be justified.

**Please note this guidance will differ from the dosage instructions in the SmPC distributed with the product. In this instance this guidance document should be followed.**

**Please read 'Administration' section carefully prior to giving anti-toxin.**

# Administration

## Precautions for Administration:

Prior to administration, a detailed history should be taken including:

- previous administration of equine-derived anti-toxin/immunoglobulins
- known allergy (for example, allergic rhinitis) following exposure to horses or other animals

## Route

The IV route is the preferred route of administration of DAT, especially in severe cases. The antitoxin dose should be mixed in 100 mL of normal saline (i.e. sodium chloride 0.9% injection) and administered slowly over 2 to 4 hours, closely monitoring for anaphylaxis.

## Dosage

1.1 Give the entire treatment dose of antitoxin IV in a single administration, unless there is onset of an allergic response. Divided doses are not recommended as this increases risk of sensitivity reactions (see section on Side Effects).

# Sensitivity testing and desensitisation

Sensitivity testing is not recommended for this product due to the balance of risk between the potential delay to treatment in performing testing and the limited potential to protect from adverse reactions. For individuals with a history of adverse reactions to equine-derived immunoglobulin products, or other sensitivity to horse proteins, pre-medication with antihistamines and corticosteroids fifteen minutes before administering the recommended dose of DAT may be considered at the clinician's discretion.

# Antimicrobial therapy

Appropriate antimicrobial agents in full therapeutic dosages should be started in line with National guidelines (1).

# Pregnancy

Diphtheria anti-toxin (equine) should be used cautiously during pregnancy.

# Side effects

Administration of diphtheria equine anti-toxin may cause hypersensitivity reactions including anaphylaxis. Reactions occur in individuals previously sensitized to equine anti-toxin or horse proteins either through previous administration or in some other way. Reactions to the anti-toxin may manifest as an anaphylactic reaction and/or serum sickness. This is why giving the required dose of anti-toxin in a single administration is recommended.

Anaphylaxis usually occurs within 1 to 2 hours of administration. The dose of adrenaline for anaphylaxis in teenagers and adults is 0.5ml of 1:1000 adrenaline given **intramuscularly**, every 5 minutes. In the event of severe anaphylaxis (no response to 2+ IM injections of adrenaline), an adrenaline infusion may be needed – call for specialist support.

Serum sickness can occur in up to 5% of patients according to historic data, usually around 7 to 12 days after the first injection although accelerated reactions have been reported in patients who have previously received equine anti-toxin preparations, with onset within days or even hours. Symptoms include more generalised erythema, urticaria, itching, and occasionally fever, pain and oedema of the joints and lymph nodes. Treatment is supportive, with anti-inflammatory preparations and antihistamine to provide symptomatic relief; systemic steroids may be needed in more severe cases.

# Storage

Store at 2º to 8º C. Once the ampoule is opened, the preparation must be used immediately.

# References

1. PHE Public Health Control and management of diphtheria (in England and Wales): 2015. Available at https://www.gov.uk/government/publications/diphtheria-public-health-control-and-management-in-england-and-wales

2. WHO (1994) Diphtheria. Manual for the Management and Control of Diphtheria in the European Region. WHO, Copenhagen.

3. CDC (2016) Expanded Access Investigational New Drug (IND) Application Protocol: "Use of Diphtheria Antitoxin (DAT) for Suspected Diphtheria Cases" IND Sponsor: Centers for Disease Control and Prevention (CDC) Protocol CDC IRB # 4167

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