**Publications gateway number: GOV-13702**

## Patient Group Direction (PGD) for the supply of azithromycin for the prevention of diphtheria in high risk settings or during outbreaks

# For the supply of azithromycin 250mg capsules, 250mg tablets, 500mg tablets or 200mg in 5ml suspension for the prevention of diphtheria in high risk settings or during outbreaks by registered healthcare practitioners identified in [Section 3,](#section3) subject to any limitations to authorisation detailed in [Section 2.](#section2)

Reference: Azithromycin\_Diphtheria\_PGD

Version no:02.00

Valid from: 21 November 2022

Review date: 21 May 2024

Expiry date: 20 November 2024

**The UK Health Security Agency (UKHSA) has developed this PGD for local authorisation**

Those using this PGD must ensure it is organisationally authorised and signed in Section 2 by an appropriate authorising person, relating to the class of person by whom the product is to be supplied, in accordance with the Human Medicines Regulations 2012 (HMR2012)[[1]](#footnote-2). **The PGD is not legal or valid without signed authorisation in accordance with** [**HMR2012 Schedule 16 Part 2**](http://www.legislation.gov.uk/uksi/2012/1916/schedule/16/part/2/made)**.**

Authorising organisations must not alter or amend the clinical content of this document (sections 4, 5 and 6); such action will invalidate the clinical sign-off with which it is provided.

As operation of this PGD is the responsibility of commissioners and service providers, the authorising organisation can decide which staff groups, in keeping with relevant legislation, can work to the PGD. Therefore sections 2, 3 and 7 must be completed and can be amended in the editable field provided.

The final authorised copy of this PGD should be kept by the authorising organisation completing Section 2 for 25 years after the PGD expires. Provider organisations adopting authorised versions of this PGD should also retain copies for 25 years after the PGD expires.

**Individual practitioners must be authorised by name, under the current version of this PGD before working according to it.**

Practitioners and organisations must check that they are using the current version of the PGD. Amendments may become necessary prior to the published expiry date. Current versions of the UKHSA PGD for authorisation can be found from: [Immunisation patient group direction (PGD) templates](https://www.gov.uk/government/collections/immunisation-patient-group-direction-pgd)

Any queries regarding the content of this PGD should be addressed to: [immunisation@ukhsa.gov.uk](mailto:immunisation@ukhsa.gov.uk)

**Change history**

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| **Version number** | **Change details** | **Date** |
| 01.00 | Original PGD | 9 November 2022 |
| 02.00 | Removal of Sandoz being the only brand of suspension allowed to be supplied under this PGD  Addition of off-label use for Pfizer brand of the suspension  Additional information under ‘Quantity to be supplied’ regarding expiry for Pfizer brand of the suspension  Advice for those taking the suspension, to shake the bottle well before measuring the dose | 21 November 2022 |

1. **PGD development**

This PGD has been developed by the following on behalf of the UKHSA:

|  |  |  |  |
| --- | --- | --- | --- |
| **Developed by:** | **Name** | **Signature** | **Date** |
| Pharmacist (Lead author) | Jacqueline Lamberty  Lead Pharmacist Medicines Governance, UKHSA |  | 21 November 2022 |
| Doctor (Chair Expert Panel) | Mary Ramsay  Consultant Epidemiologist  Immunisation and Vaccine Preventable Diseases Division, UKHSA | Signature of Mary Ramsay | 21 November 2022 |
| Registered nurse | Kate Wedgwood  Senior Health Protection Practitioner,  East Midlands Health Protection Team  UKHSA |  | 21 November 2022 |

This PGD has been peer reviewed by an expert panel in accordance with the UKHSA PGD Policy. It has been agreed by the UKHSA Medicines Governance Group and ratified by the UKHSA Clinical Quality Oversight Board.

**Expert panel**

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| --- | --- |
| **Name** | **Designation** |
| Dr Nicholas Aigbogun | Consultant in Communicable Disease Control, Yorkshire and Humber Health Protection Team, UKHSA |
| Prof Diane Ashiru-Oredope | Lead Pharmacist, HCAI, Fungal, AMR, AMU & Sepsis Division, UKHSA |
| Dr Colin Brown | Director (Interim): Clinical and Emerging Infections; Deputy Director (Interim): HCAI, Fungal, AMR, AMU, & Sepsis Division, UKHSA; |
| Dr Rebecca Cordery | Consultant in Communicable Disease Control, UKHSA |
| Rosie Furner | Community Services Pharmacist, East Sussex Healthcare NHS Hospital Trust |
| Jo Jenkins | Lead Pharmacist Patient Group Directions and Medicines Mechanisms, Medicines Use and Safety Division, NHS Specialist Pharmacy Service |
| Dr Shamez Ladhani | Consultant Epidemiologist, UKHSA; Paediatric Infectious Disease Consultant, St. George’s Hospital London |
| Rohini Manuel | Consultant Medical Microbiologist, UKHSA |
| Lesley McFarlane | Lead Immunisation Nurse Specialist, Immunisation and Vaccine Preventable Diseases Division, UKHSA |
| Dr Mariyam Mirfenderesky | Consultant in Infectious Diseases and Medical Microbiology  IPC, Outbreaks and Antimicrobial Stewardship (IOS) Team  HCAI, Fungal, AMR, AMU & Sepsis Division, UKHSA |

**2.** **Organisational authorisations**

The PGD is not legally valid until it has had the relevant organisational authorisation.

It is the responsibility of the organisation that has legal authority to authorise the PGD, to ensure that all legal and governance requirements are met. The authorising body accepts governance responsibility for the appropriate use of the PGD.

Insert authorising body name authorises this PGD for use by the services or providers listed below:

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| Authorised for use by the following organisations and/or services |
| Limitations to authorisation |
| For instance, any local limitations the authorising organisation feels they need to apply in line with the way services are commissioned locally. This organisation does not authorise the use of this PGD by …. |

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| Organisational approval (legal requirement) | | | |
| Role | Name | Sign | Date |
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| Additional signatories according to locally agreed policy | | | |
| Role | Name | Sign | Date |
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Section 7 provides a practitioner authorisation sheet. Individual practitioners must be authorised by name to work to this PGD. Alternative practitioner authorisation sheets may be used where appropriate in accordance with local policy, but this should be an individual agreement, or a multiple practitioner authorisation sheet as included at the end of this PGD.

#### Characteristics of staff

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| **Qualifications and professional registration** | To be completed by the organisation authorising the PGD. For instance Registered professional with one of the following bodies:   * Nurses currently registered with the Nursing and Midwifery Council (NMC). * Pharmacists currently registered with the General Pharmaceutical Council (GPhC).   Additional registered healthcare professionals to be added by the organisation authorising the PGD |
| **Additional requirements** | Additionally, practitioners:   * must be authorised by name as an approved practitioner under the current terms of this PGD before working to it * must have undertaken appropriate training for working under PGDs for supply or administration of medicines for example [Patient Group Directions - elearning for healthcare](https://www.e-lfh.org.uk/programmes/patient-group-directions/) * must be competent in the use of PGDs (see [NICE Competency framework](https://www.nice.org.uk/guidance/mpg2/resources) for health professionals using PGDs) * must be familiar with the product and alert to changes in the Summary of Product Characteristics (SPC) * must have undertaken training appropriate to this PGD as required by local policy * must have access to the PGD and associated online resources * should fulfil any additional requirements defined by local policy * authorising organisation to insert any additional requirements   **The practitioner must be authorised by name, under the current version of the PGD, before working according to it.** |
| **Continued training requirements** | Authorising organisation to insert any continued training requirements**.** |

1. **Clinical condition or situation to which this PGD applies**

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| **Clinical condition or situation to which this PGD applies** | Prevention of diphtheria in high risk settings or during outbreaks. |
| **Criteria for inclusion** | Adults and children aged 1 year and older with potential exposure to diphtheria in high risk settings or during outbreaks. |
| **Criteria for exclusion[[2]](#footnote-3)** | Individuals are excluded from this PGD if:   * they have had a known severe allergic reaction to azithromycin, erythromycin, any macrolide or ketolide antibiotic, or to any of the excipients (see [SPC](https://www.medicines.org.uk/emc/)) * they are currently taking ergot derivatives such as ergotamine (Migril®) * they are currently taking any of the following medicines listed in the BNF as severe interactions: * berotralstat * chloroquine * colchicine * dabigatran * digoxin * edoxaban * hydroxychloroquine * rifabutin * talazoparib * ticagrelor * topotecan * vinblastine * vincristine * vindesine * vinflunine * vinorelbine * they have rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption * some brands of azithromycin contain soya or soya lecithin and are therefore contraindicated in individuals with an allergy to soya or peanuts. |
| **Action to be taken if the individual or carer declines treatment** | Advise the individual or their carer of the possible consequences of declining treatment and of alternative options.  Advise about the protective effects of the treatment, risks of infection, risk of spreading the disease to others and disease complications.  Advise on the need for vigilance for symptoms of diphtheria, recognising symptoms and the need to seek urgent medical attention should symptoms occur.  Document the individual has declined treatment and the advice given in their record. |
| **Action to be taken if the individual is excluded** | If the individual is allergic to soya or soya lecithin, check the manufacturer’s information for the brand to be supplied. If the product contains soya or soya lecithin, exclude the individual from the PGD or select an alternative suitable brand if available.  Explain the reasons for exclusion to the individual or their carer.  Individuals who are excluded from the PGD will need individual clinical assessment. If a decision is made to supply azithromycin or alternative antibiotics, another form of authorisation will be needed, such as a Patient Specific Direction (PSD).  Individuals excluded under this PGD should be assessed for symptoms and if symptomatic consider referral for clinical assessment of alternative treatment options. |
| **Cautions including any relevant action to be taken** | Although the SPCs state azithromycin should be used with caution for individuals with certain conditions, on the balance of risk to benefit, these individuals should receive treatment because the benefits outweigh any risk.  Refer to the [SPC](https://www.medicines.org.uk/emc/) or British National Formulary ([BNF](https://bnf.nice.org.uk/drugs/azithromycin/)) for details when appropriate and/or seek advice from the UKHSA Health Protection Team or the Incident Control Team. |

1. **Description of Treatment**

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| **Name, strength & formulation of drug** | Azithromycin 250mg capsules, 250mg tablets, 500mg tablets, 200mg in 5ml powder for oral suspension |
| **Legal category** | POM - Prescription only medicine |
| **Black triangle▼** | No |
| **Off-label use** | Yes  Treatment and prophylaxis of diphtheria with azithromycin is not a licensed indication but is recommended in the [UKHSA](https://www.gov.uk/government/publications/diphtheria-public-health-control-and-management-in-england-and-wales), [World Health Organization (WHO)](https://www.who.int/docs/default-source/documents/publications/operational-protocol-for-clinical-management-of-diphtheria.pdf?sfvrsn=70868342_1) and [Médecins Sans Frontièrs (MSF)](https://medicalguidelines.msf.org/en/viewport/CG/english/diphtheria-16689456.html#section-target-3) guidelines.  For ease of operation of this PGD in the locations required and in recognition weighing individuals may not be practical and some individuals may be malnourished, doses and duration may not be in exact accordance with the licensed doses.  A 6-day in-use shelf-life for the Pfizer brand of the suspension is not supported by the manufacturer’s SPC (see [Quantity to be supplied](#Pfizer)).  Where a product is recommended off-label consider, as part of the consent process, informing the individual or carer that the product is being offered in accordance with national guidance but that this is outside the product licence. |
| **Route / method of administration** | Oral  The tablets and capsules to be swallowed whole with fluid  The tablets and the suspension may be taken with or without food  The capsules should be taken at least 1 hour before or 2 hours after food  Before use, the powder for suspension needs to be reconstituted with water according to the [manufacturers’ instructions](https://www.medicines.org.uk/emc/product/441/smpc#USEHANDLING), into a white to off white, homogenous suspension. After reconstitution the suspension can be administered using a syringe for oral use.  After taking the suspension, a bitter after-taste can be avoided by drinking fruit juice directly after swallowing  Avoid taking simultaneously with antacids |
| **Dose and frequency of administration[[3]](#footnote-4)**  Continued over page  **Dose and frequency of administration** (continued) | **Adults and children aged 12 years and over** (unless severely malnourished)**:**  500mg (one 500mg tablet or two 250mg capsules or two 250mg tablets) once a day  **Children aged one year to under 5 years:** 12mg / kg once a day  10kg: 120mg (3ml of 200mg in 5ml suspension) once a day  12.5kg: 140mg (3.5ml of 200mg in 5ml suspension) once a day  15kg: 180mg (4.5ml of 200mg in 5ml suspension) once a day  20kg: 240mg (6ml of 200mg in 5ml suspension) once a day  **Children aged 5 years and over and adults who appear to be malnourished:** Note some children in the age ranges given below may not fall into the standard weight range given in the BNF.  **5 to 7 years:** 5 ml to 7ml of 200mg in 5ml suspension once a day  Note for those who can swallow tablets or capsules, 250mg tablets or capsules can be supplied. One 250mg capsule or one 250mg tablet is equivalent to 6.25ml of 200mg in 5ml suspension  **8 to 10 years:** 7.5 ml to 10ml of 200mg in 5ml suspension once a day  **11 years and those aged 12 and over who are malnourished:** 11 ml to 12.5ml of 200mg in 5ml suspension once a day |
| **Duration of treatment** | 6 days (see [footnote 3](#footnote3)) |
| **Quantity to be supplied**  Continued over page  **Quantity to be supplied** (continued) | **Adults and children aged 12 years and over (unless severely malnourished:**  6 x 500mg tablets or 12 x 250mg tablets or 12 x 250mg capsules  **Adults and children aged one year to under 5 years:**  The suspension will need reconstitution with water before supply; refer to the [manufacturers’ instructions](https://www.medicines.org.uk/emc/product/441/smpc#USEHANDLING) for reconstitution.  The packs are supplied with a 10ml dosage syringe. Supply this dosage syringe with the product.  The reconstituted suspension can be kept at room temperature, up to 25o C and must be discarded after 10 days.  As the formulations are similar, there is no theoretical reason why the stability of the Pfizer and Sandoz products after reconstitution should differ. There is no theoretical reason to expect loss of potency or increased toxicity from storage and use of the Pfizer product between 6 and 10 days after reconstitution. Given the complex logistics of this outbreak, UKHSA guidance is that the Pfizer suspension can be supplied to cover the 6-day course in children where the Sandoz product is not available.  Supply the quantity of suspension appropriate for the dose and duration.  Weight 10kg: 18ml of 200mg in 5ml suspension  Weight 12.5kg: 21ml of 200mg in 5ml suspension  Weight 15kg: 27ml of 200mg in 5ml suspension  Weight 20kg: 36ml of 200mg in 5ml suspension  **5 to 7 years:** 30ml to 42ml of 200mg in 5ml suspension or 6 x 250mg capsules or 6 x 250mg tablets  **8 to 10 years:** 45ml to 60ml of 200mg in 5ml suspension  **11 years and those aged 12 and over who are malnourished:** 66ml to 75ml of 200mg in 5ml suspension  Supplies must either be from the manufacturer’s original pack or over-labelled pre-packs, and the individual’s name, the date and additional instructions must be written on the label at the time of supply.  As split packs cannot be supplied, an over-supply might be required. Individuals to be advised to return any remaining product to the Incident Control Team or to a community pharmacy for destruction. |
| **Storage** | Do not store above 25oC. |
| **Disposal** | Any unused product or waste material should be disposed of in accordance with local requirements |
| **Drug interactions** | Individuals taking ergot derivatives listed in the BNF as severe interactions are excluded from this PGD – see [criteria for exclusion](#exclusion)  A detailed list of interactions is available in the [SPC](https://www.medicines.org.uk/emc) |
| **Identification and management of adverse reactions** | Azithromycin is well tolerated with a low incidence of side effects  Very common (≥ 1/10) : nausea, abdominal pain, flatulence, diarrhoea  Other side effects are classified as uncommon to very rare  A detailed list of adverse reactions is available in the [SPC](https://www.medicines.org.uk/emc) |
| **Reporting procedure of adverse reactions** | All suspected adverse reactions in children and severe adverse reactions in adults should be reported using the [Yellow card](https://yellowcard.mhra.gov.uk/) scheme or search for MHRA Yellow Card in the Google Play or Apple App Store.  Any serious adverse reaction to the drug should be documented in the individual’s record.  Alert the supervising doctor promptly in the event of a serious adverse reaction and document in the individual’s record. |
| **Written information to be given** | Supply the marketing authorisation holder's Patient Information leaflet which should be included in the package |
| **Advice /follow up treatment** | Explain why the treatment is necessary and treatment is not fully protective. Close contacts must be alert to symptoms and signs of diphtheria.  Advise the individual or their carer:   * to read the PIL leaflet and to seek medical advice if side effects are experienced * for those taking the suspension, to shake the bottle well before measuring the dose * after taking the suspension a bitter after-taste can be avoided by drinking fruit juice directly after swallowing * to avoid taking simultaneously with antacids * if an over-supply has been required, individuals must be advised to return any remaining product for destruction |
| **Records**  Continued over page  **Records** (continued) | Record:   * whether valid informed consent was given or a decision to supply was made in the individual’s best interests in accordance with the [Mental Capacity Act 2005](https://www.legislation.gov.uk/ukpga/2005/9/contents) * name of individual, address, date of birth and GP with whom the individual is registered or record where an individual is not registered with a GP * name of the member of staff who supplied the product * name and brand of the product * date of supply * dose, formulation and route of administration of the product * quantity supplied * batch number and expiry date * advice given; including advice given if the individual is excluded or declines treatment * details of any adverse drug reactions and actions taken * the product was supplied via PGD * if supplied and an over-supply has been required, record this and that advice to return the remaining product to a community pharmacy for destruction has been given   Records should be signed and dated (or password-controlled on e-records).  All records should be clear, legible and contemporaneous  A record of all individuals receiving treatment under this PGD should also be kept for audit purposes in accordance with local policy |

#### Key references

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| **Key references** | * [Summary of Product Characteristics and Patient Information Leaflet](http://www.medicines.org.uk) * [azithromycin, BNF NICE](https://bnf.nice.org.uk/drugs/azithromycin/) * [Public health control and management of diphtheria, UKHSA (publishing.service.gov.uk)Public health control and management of diphtheria, UKHSA (publishing.service.gov.uk)](https://www.gov.uk/government/publications/diphtheria-public-health-control-and-management-in-england-and-wales) * [WHO Operational protocol for clinical management of diphtheria, WHO Version 10 Dec 2017](https://www.who.int/docs/default-source/documents/publications/operational-protocol-for-clinical-management-of-diphtheria.pdf?sfvrsn=70868342_1) * [diphtheria, MSF medical guidelines](https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fmedicalguidelines.msf.org%2Fen%2Fviewport%2FCG%2Fenglish%2Fdiphtheria-16689456.html&data=05%7C01%7CJackie.Lamberty%40ukhsa.gov.uk%7C224847bc24394f7da50508dabd82a4dd%7Cee4e14994a354b2ead475f3cf9de8666%7C0%7C0%7C638030666046332839%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=25J0LV6EImmqJfkwcmyCqF%2BxddNCf7TzI1e0E1ooTDU%3D&reserved=0) October 2022 * [Health Technical Memorandum 07-01: Safe Management of Healthcare Waste. Department of Health 20 March 2013](https://www.gov.uk/government/publications/guidance-on-the-safe-management-of-healthcare-waste) |

**7.** **Practitioner authorisation sheet**

**Azithromycin\_Diphtheria\_PGDv02.00 Valid from: 21 November 2022 Expiry: 20 November 2024**

**Before signing this PGD, check that the document has had the necessary authorisations in section 2. Without these, this PGD is not lawfully valid.**

**Practitioner**

By signing this PGD you are indicating that you agree to its contents and that you will work within it.

PGDs do not remove inherent professional obligations or accountability.

It is the responsibility of each professional to practise only within the bounds of their own competence and professional code of conduct.

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| I confirm that I have read and understood the content of this PGD and that I am willing and competent to work to it within my professional code of conduct. | | | |
| Name | Designation | Signature | Date |
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**Authorising manager**

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| --- | --- | --- | --- |
| I confirm that the practitioners named above have declared themselves suitably trained and competent to work under this PGD. I give authorisation on behalf of **INSERT NAME OF ORGANISATION** for the above-named health care professionals who have signed the PGD to work under it. | | | |
| Name | Designation | Signature | Date |
|  |  |  |  |

**Note to authorising manager**

Score through unused rows in the list of practitioners to prevent practitioner additions post managerial authorisation.

This authorisation sheet should be retained to serve as a record of those practitioners authorised to work under this PGD.

1. This includes any relevant amendments to legislation [↑](#footnote-ref-2)
2. Exclusion under this PGD does not necessarily mean the medication is contraindicated, but it would be outside it’s remit, and another form of authorisation will be required [↑](#footnote-ref-3)
3. There are differences between the UKHSA, WHO and MSF guidelines regarding dose and duration of treatment with azithromycin. There are no data to support the exact duration required. Guidelines vary between 5 and 14 days. For ease of administration of this PGD, the doses (no loading dose) and duration of 6 days accord with the pack sizes available. [↑](#footnote-ref-4)