BNSSG Shared Care Guidance

Amber Three Months

Section 1: Heading

Trust(s)	University Hospitals Bristol NHS Foundation Trust
	North Bristol NHS Trust
Speciality / Department	Respiratory
Drug	Gentamicin 40mg/ml injection for administration by nebulisation.
Indication	Nebulised Gentamicin for the management of chronic respiratory infections/ colonisation in adults (not including Cystic Fibrosis Patients) on the advice of a respiratory consultant with specialist experience in managing this patient group.

Section 2: Treatment Schedule

Usual dose and frequency of administration	80mg nebulised twice daily May be further diluted with either Sodium Chloride 0.9% or water for injections to 4 - 5ml. No dose adjustments are required in; elderly patients (>65 yrs), patients with renal or hepatic impairment or at extremes of weight. Elderly patients and patients with renal impairment (eGFR <50ml/min) may be at an increased risk of toxicity and this is discussed in the monitoring section.
Route and formulation	Gentamicin 80mg/2ml injection (This is an unlicensed indication). Please Note: The current available brands of gentamicin (i.e. Cidomycin and Genticin are suitable for nebulisation as neither product contains alcohol (which can cause bronchospasm). Patients should be advised to check with their pharmacist if the brand of gentamicin changes.

Duration of treatment	On-going. Initial three month trial (under secondary care) with continuation if tolerated and objective measures of improvement - such as (i) reduced sputum volume / purulence, (ii) reduced frequency of exacerbations, (iii) improvement or stabilisation in rate of FEV1 decline. Secondary care to advise on when it is appropriate to stop treatment.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate

1. FEV1 pre and post-trial dose (initiation only)
2. Assessment of renal function - including U&E's
3. Baseline audiometry in patients at high risk of ototoxicity (organised by secondary care)

Subsequent tests - where appropriate

1. Patients will require periodic assessment of renal function and additional investigations may be required in patients at high risk of nephro- or oto-toxicity. Due to the frequency of regular monitoring this can be carried out during normal follow up by secondary care. Where additional investigations are required these will be organised by secondary care, specifically;
2. For patients with a baseline eGFR >50ml/min, U&E's should be carried out one and three months after initiation and yearly thereafter.
3. For patients with a baseline eGFR <50ml/min, the frequency at which renal function monitoring is required and the requirement for periodic gentamicin therapeutic drug monitoring (TDM) will be determined by the secondary care team.
4. If there is a decline in renal function (> 20% change from baseline and other causes of acute kidney injury are excluded) consider contacting the relevant respiratory team to discuss stopping nebulised gentamicin and referring on-going prescribing of nebulised antibiotics until renal dysfunction resolved.
5. Initial and periodic audiometry in patients at high risk of ototoxicity (if required to be organised by secondary care),
6. Patients may be advised to perform pre- and post-nebulisation FEV1 (forced expiratory volume) assessment and advised to contact the respiratory team if bronchospasm is present despite appropriate use of pre-treatment bronchodilators.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	Although the systemic absorption of aminoglycosides is low the potential for systemic side-effects and interactions should be considered. Bronchospasm can occur following inhalation of medicinal products and has been reported with nebulised gentamicin. The first dose of nebulised gentamicin should be given under

	medical supervision, using a pre-nebulisation bronchodilator if this is already part of the current treatment regimen for the patient. If there is evidence of therapy-induced bronchospasm in a patient not receiving a bronchodilator, the test should be repeated on a separate occasion, using a bronchodilator. Onset of bronchospasm in the presence of bronchodilator therapy may indicate an allergic reaction. Should an allergic reaction be suspected then treatment with nebulised gentamicin should be discontinued. Cough may occur on inhalation of gentamicin. If troublesome or associated with haemoptysis then on-going treatment should be reviewed by an appropriate secondary care specialist. Sore throat or mouth has been reported and may be due to Candida albicans infection (oral thrush) or hypersensitivity. Skin rash may also indicated hypersensitivity. Oropharyngeal candidiasis should be treated if indicated. If hypersensitivity occurs then treatment should be withdrawn. Ototoxicity presenting as; dizziness, vertigo, ataxia, tinnitus, hearing loss or may be associated with nebulised gentamicin, particularly in patient at risk due to concomitant or previous use of ototoxic agents (see Section 5: Drug interactions) for more details. Tinnitus may be transient and resolve without discontinuation of therapy or associated with permanent loss of hearing on audiogram.
Referral back to specialist	The presence of auditory or vestribular toxicity (i.e. manifest as hearing loss, vertigo, ataxia, dizziness or tinnitus which is not transient) should be referred to the respiratory team who will advise.

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions	Concomitant use with; other aminoglycoside antibiotics (such as amikacin and gentamicin), amphotericin, colistimethate, ciclosporin, tacrolimus, polymixin antibiotics (not included topical preparations) and/or platinum compounds (cisplatin / carboplatin) may increase the risk of nephrotoxocity and should be avoided.

	Concomitant use with loop diuretics (such as furosemide and bumetanide) increases the risk of ototoxicity and should be avoided unless strictly indicated. The risk of ototoxicity is also increased by concomitant use of platinumcompounds. Nebulised gentamicin should be used with extreme caution in Myasthenia gravis and may also antagonise the effect of cholinesteraseinhibitors (such as neostigmine or pyridostigmine) used to treat this condition. As an aminoglycoside gentamicin may enhance the effect of non-depolarising muscle relaxants or suxamethonium used during surgery. Gentamicin may increase the effect of botulinum toxin. Nebulised antibiotics should not be given within an hour of dornase-alfa (Pulmozyme®)
Reminder to ask patient about specific problems	Signs or symptoms of auditory or vestibular. Bronchospasm during use despite appropriate use of bronchodilator therapy.

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

1. Hypersensitivity to gentamicin or any of the excipients in the preparation
2. Pregnancy/ lactation - only if benefits outweigh the risks and following appraisal of the potential risks
3. Previous otoxoticity
4. Myasthenia Gravis

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

1. Nebulised antibiotics should be used regularly as prescribed
2. The injection should be further diluted with Sodium Chloride 0.9% or water for injection and poured into the nebuliser
3. The solution is for single use only
4. Usually jet or ultrasonic nebulisers are preferred for antibiotic deliver. The instructions of the manufacturer should be followed for operation and care of the nebuliser and compressor
5. Use your reliever inhaler or nebuliser (salbutamol) at least 20 minutes before inhaling the antibiotic
6. If you are carrying out breathing exercises (i.e. ACBT - Active Cycle of Breathing Technique) this should be done after using the reliever but before nebulising the gentamicin
7. The nebuliser should be used in conjunction with an exhaust filter to prevent others from being exposed to the medication and to prevent a sticky deposit from forming. A new filter should be used for each dose. The procedure should be carried out in a well-ventilated room

8. After drug administration is completed, rinse your mouth, gargle with water and then spit out. This will reduce side-effects such as thrush or mouth ulcers
9. After each use the nebuliser should be cleaned as per nebulisers instructions
10. Do not mix the gentamicin with other nebuliser solutions.

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing the First Three Months of treatment
2. Undertaking the clinical assessment and monitoring for the First Three Months of treatment.
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of DRUG.
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. Arrange for an initial test dose to be administered in hospital under appropriate supervision,
2. Baseline assessments as per section 3,
3. If TDM is indicated this will be organised by secondary care.

Section 9: Responsibilities for Primary Care

Core responsibilities

1. Responsible for taking over prescribing after the first three months of treatment.
2. Responsible for the clinical assessment and monitoring after the first three month of treatment.
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. - no additional responsibilities

Section 10: Contact Details

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Section 11: Document Details

Date prepared	
Prepared by	Helen Charleton - Lead Medicines Information Pharmacist UHBristol Philip Lloyd Mayers - Pharmacist North Bristol NHS Trust
Date of review	June 2015
Document Identification	NEBULISED GENTAMICIN SCP

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. UHBristol Respiratory Dept - including respiratory consultants and specialist nurses
2. UHBristol Pharmacy Dept, including senior members of clinical team
3. NBT Respiratory Dept - including respiratory consultants and specialist nurses
4. NBT Pharmacy Dept, including senior members of clinical team and formulary lead

Section 13: References

Please list references

1. Summary of Product Characteristics: Gentamicin 40mg/ml injection. Hospira. April 2013. Accessed via www.medicines.org.uk last updated 22/08/2011

2. Murray M P A et al. Randomized Controlled Trial of Nebulized Gentamicin in Non–Cystic Fibrosis Bronchiectasiset al, Am J Respir Crit Care Med Vol 183. pp 491–499, 2011