Wrightington, Wigan and Leigh Teaching Hospitals
NHS Foundation Trust

STANDARD OPERATING PROCEDURE	**METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) TREATMENT**
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The WWL Way

AT ALL TIMES, STAFF MUST TREAT EVERY INDIVIDUAL WITH RESPECT AND UPHOLD THEIR RIGHT TO PRIVACY AND DIGNITY

VERSION CONTROL		
Version	**Date**	**Amendment**
9	May 2023	Point 4.2 - updated. Section 5 – Methicillin Resistant Staphylococcus aureus (MRSA) Treatment updated. References – updated.

CONTENTS		PAGE NUMBER

APPENDICES		PAGE NUMBER

1. INTRODUCTION

This Standard Operating Procedure (SOP) is based on "Treatment of Methicillin Resistant *Staphylococcal aureus (*MRSA): updated guidelines from the UK" and takes local antimicrobial sensitivity patterns into account.

2. KEY PRINCIPLES

The aim of this SOP is to encourage rational prescribing based on the best available evidence, and hence improve patient care by:-

2.1 Optimising the treatment of MRSA infections.
2.2 Reducing the risks of drug toxicity.
2.3 Limiting the emergence of resistant strains.
2.4 Reducing unnecessary costs.

3. RESPONSIBILITIES

3.1 It is the responsibility of all Trust Directors to disseminate this SOP to relevant staff, make the SOP available on the Intranet and audit adherence to it on a yearly basis.

3.2 It is the responsibility of staff prescribing antimicrobial therapy to adhere to this SOP. All staff should be aware of the current version and how to access it.

3.3 Consultant Microbiologist is responsible to review the SOP regularly and make it available on the Intranet site.

4. LIMITATIONS

4.1 This SOP is not intended to be comprehensive. Prescribers are advised to consult the British National Formulary (BNF) and the manufacturer's summary of product characteristics for additional information. This is especially relevant for side effects, contraindications, interactions with other drugs and the use of antimicrobials in pregnancy.

4.2 Advice about individual patients with clinical problems may be obtained from the Consultant Microbiologists through switchboard.

5. TREATMENT OF MRSA INFECTIONS

5.1 **Abscesses caused by MRSA:**

5.1.1 Use incision and drainage to treat abscesses caused by MRSA.

5.1.2 Do not use antibiotics routinely in patients with abscesses caused by MRSA that are drained, are less than 5 cm in diameter, and where there is no systemic response (fever and/or cellulitis) and/or immunodeficiency, including neutropenia and defects of cell-mediated immunity.

5.1.3 Use oral clindamycin 450mg QDS or co-trimoxazole 960mg BD for 5 days when oral treatment is warranted, and the MRSA isolate is known to be susceptible.

5.2 **Severe cellulitis caused by MRSA**:

5.2.1 Use intravenous Teicoplanin as first line (dosage guideline in Microguide).

5.2.2 Second line: Daptomycin intravenous 6mg/kg OD or linezolid intravenous or oral 600mg BD.

5.2.3 Oral step down: clindamycin, cotrimoxazole or doxycycline 100mg BD, as indicated by sensitivities.

5.2.4 Duration of course is 5-7 days, or according to clinical response.

5.3 **Mild skin and soft tissue MRSA infections**:

5.3.1 Use oral clindamycin, cotrimoxazole or doxycycline. Check if sensitivities are available. Duration of antibiotic course is 5 days.

5.4 **UTI caused by MRSA** (same consideration should be given to MSSA from a urine sample):

5.4.1 Patient found to have MRSA in a urine sample should undergo a clinical review to ascertain clinical signs and symptoms of UTI and exclude presence of associated MRSA bacteraemia from a deep-seated source.

5.4.2 Presence of MRSA in urine in the absence of urinary symptoms may represent contamination. However, in some patients it may indicate presence of a deep-seated infection elsewhere (e.g. disciitis, abscesses, infective endocarditis, etc).

5.4.3 Exclude associated MRSA bacteraemia or a deep-seated infection before treating a MRSA UTI.

5.4.4 Treat symptomatic **lower UTI** caused by MRSA with an oral agent: doxycycline 100mg BD, trimethoprim 200mg BD, or co-trimoxazole 460mg BD, according to susceptibility. Linezolid is not recommended for the treatment of MRSA UTI because of poor excretion in urinary tract.

5.4.5 **Complicated/ upper UTI**: use intravenous teicoplanin (dose in Microguide) or daptomycin 6mg/kg OD, if teicoplanin is unsuitable. Course duration is 7 days.

5.4.6 **Catheter-associated UTI**: replace urinary catheter with or without a single dose of IV gentamicin (if known sensitive) or teicoplanin if isolate is resistant to gentamicin.

5.5 **MRSA Bone and joint infections**:

5.5.1 Use a multidisciplinary approach for treatment of MRSA bone and joint infections, including surgery or drainage where indicated.

5.5.2 For bone and joint infections caused by MRSA use intravenous teicoplanin 10mg per actual body weight as the first-line choice of treatment (dosage in Microguide).

5.5.3 Consider 2 weeks of intravenous teicoplanin followed by further intravenous or oral antibiotics to complete a total treatment course of a minimum of 4 weeks for septic arthritis or 6 weeks for osteomyelitis.

5.5.4 Use therapeutic drug monitoring to ensure that non-toxic, therapeutic pre-dose serum concentrations of 15–20 mg/L for vancomycin, or 20–40 mg/L for teicoplanin are achieved.

5.5.5 When a glycopeptide is contraindicated consider daptomycin (6-8 mg/kg dose) or linezolid 600mg BD as alternative agents.

5.5.6 Use clindamycin, co-trimoxazole, doxycycline, or linezolid as oral options to complete treatment when the MRSA isolate is known to be susceptible.

5.5.7 Do not use rifampicin, fusidic acid or a quinolone as a single oral agent; use in combination with other agents to which the isolate is susceptible.

5.6 **MRSA bacteraemia**:

5.6.1 Use intravenous vancomycin for uncomplicated bacteraemia caused by MRSA with vancomycin MIC less than 2mg/L) (vancomycin dosage in Microguide).

5.6.2 When vancomycin is contraindicated use linezolid as an alternative first-line choice of treatment.

5.6.3 When first-line agents are contraindicated consider daptomycin 8-10mg/kg OD or teicoplanin.

5.6.4 Do not use co-trimoxazole alone as a first-line agent for MRSA bacteraemia, however, consider using it as an oral step-down when the MRSA isolate is known to be susceptible.

5.6.5 Consider a minimum duration of 14 days of antibiotic therapy for uncomplicated bacteraemia and a minimum duration of 28 days for complicated bacteraemia caused by MRSA.

5.7 **MRSA Infective endocarditis**:

5.7.1 Current BSAC endocarditis guidelines advise the use of vancomycin for vancomycin-susceptible (MIC less than 2mg/L) native or prosthetic valve MRSA endocarditis.

5.7.2 If the patient cannot tolerate vancomycin or if the isolate is not vancomycin

susceptible (MIC is 2mg/L or more) then daptomycin IV 8-10mg/kg OD is recommended as an alternative in combination with a second/ third agent chosen according to antibiotic susceptibility testing.

5.7.3 MRSA native valve endocarditis (vancomycin MIC less than 2mg/L): vancomycin IV (dosage in Microguide) AND rifampicin oral 300mg-600mg BD.

5.7.4 MRSA native valve endocarditis (vancomycin MIC is 2mg/L or more): daptomycin 8-10mg/kg OD AND rifampicin oral 300mg-600mg BD OR gentamicin IV 1mg/kg BD.

5.7.5 MRSA prosthetic valve endocarditis (vancomycin MIC less than 2mg/L): vancomycin IV AND rifampicin oral AND gentamicin IV.

5.7.6 MRSA prosthetic valve endocarditis (vancomycin MIC is 2mg/L or more): daptomycin IV 8-10mg/kg OD AND rifampicin oral AND gentamicin IV.

5.7.7 The guidelines recommend a minimum duration of 4 weeks for patients with native valve endocarditis and 6 weeks for those with prosthetic valve endocarditis.

5.7.8 Use therapeutic drug monitoring to ensure that non-toxic pre-dose serum concentrations (15-20mg/L) of vancomycin and gentamicin (less than 1mg/L) are achieved.

5.8 **MRSA necrotising pneumonia**:

5.8.1 For necrotizing pneumonia caused by MRSA use intravenous vancomycin or linezolid. Course duration is 14 days.

5.8.2 Consider addition of a toxin-inhibiting agent, such as clindamycin or rifampicin, when the MRSA isolate is known to be susceptible.

5.9 **MRSA Hospital-acquired pneumonia**:

5.9.1 First-line therapy: use either intravenous vancomycin or linezolid. Course duration is 7 days.

5.9.2 Do not use daptomycin to treat nosocomial pneumonia caused by MRSA as it is inactivated by lung surfactant.

5.10 **MRSA eye infection**:

5.10.1 For superficial MRSA eye disease consider gentamicin or chloramphenicol eye drops according to isolate susceptibility. Course duration is 5 days.

5.10.2 Consider dissemination secondary to bacteraemia when a patient is diagnosed with endophthalmitis caused by MRSA.

5.10.3 For deep-seated eye infections caused by MRSA consider a multidisciplinary approach comprising specialist ophthalmologists and infection specialists.

5.10.4 For deep-seated eye infections caused by MRSA consider intravitreal vancomycin and systemic quinolones according to susceptibility.

5.10.5 Consider oral linezolid as a treatment option, recognizing that there is limited evidence of efficacy in MRSA infection at this site.

5.11 **Ear, nose, throat or upper respiratory tract infections**:

5.11.1 For severe MRSA-associated ear, nose and throat or upper respiratory tract infections consider intravenous glycopeptide (vancomycin or teicoplanin) or linezolid.

5.11.2 For minor/less-severe infections consider co-trimoxazole or doxycycline as an oral option when the MRSA isolate is known to be susceptible.

5.11.3 Course duration varies depending on severity and clinical response (5-7 days).

5.12 **MRSA intracranial or spinal infection**:

5.12.1 Whenever clinically possible, source control is necessary for intracranial and spinal infections.

5.12.2 Unless surgical intervention is contraindicated use incision and drainage for treatment of intracranial and spinal infections caused by MRSA.

5.12.3 In the absence of neurological deficits consider treating small epidural abscesses with

antibiotics alone. Discuss with a microbiologist.

5.12.4 For treatment of intracranial and spinal infections caused by MRSA consider intravenous vancomycin or linezolid as the first-line choice of treatment.

5.13 **MRSA meningitis**:

5.13.1 Use intravenous vancomycin. For severe infection, consider adding rifampicin according to susceptibility. Course duration to be discussed with microbiologist.

5.13.2 Use therapeutic drug monitoring to ensure that non-toxic, therapeutic pre-dose serum concentrations (15–20 mg/L) of vancomycin are achieved.

5.13.3 In severe cases, or when the patient fails to respond to intravenous vancomycin, patients should be transferred to a neurosurgical centre for instillation of vancomycin directly into the ventricles.

5.13.4 Do not use clindamycin, chloramphenicol or linezolid to treat meningitis caused by MRSA. These drugs are not bactericidal, such activity being a requirement of antibiotics used as therapy of patients with meningitis.

5.13.5 No recommendation can be made for the use of teicoplanin in this clinical setting.

5.14 **MRSA surgical prophylaxis**:

5.14.1 Refer to Surgical Prophylaxis Guidelines.

5.15 **MRSA decolonisation**:

5.15.1 Use mupirocin for nasal decolonisation for those who are colonised or universally (i.e., for all high-risk patients undergoing implant surgery). Five-day course is recommended.

5.15.2 Use chlorhexidine, either selectively or universally, for body decolonisation to reduce MRSA carriage. Five-day course is recommended.

5.15.3 Consider alternatives (e.g. octenidine) where mupirocin and chlorhexidine are not feasible or mupirocin is not available.

5.15.4 Monitor the emergence of resistance, especially to mupirocin and chlorhexidine, if used extensively.

5.15.5 Refer also to Infection Control MRSA TW10-116 SOP 1 for risk assessment and treatment of MRSA colonisation available on Trust Intranet.

6. VANCOMYCIN THERAPEUTIC DRUG MONITORING

6.1 Serum vancomycin levels should be measured after 3 or 4 doses for patients with normal renal function. Those with renal impairment may require earlier measurement of levels and should be discussed with the Microbiologist or Pharmacist.

6.2 'Trough' levels should be taken immediately before the fourth dose and should normally be in the range 10 to 15mg/L. Higher 'trough' levels of 15-20mg/L are desirable when treating MRSA endocarditis. 'Peak' levels are normally unnecessary (except for babies on Special Care Baby Unit) and should not be sent routinely.

7. TEICOPLANIN THERAPEUTIC DRUG MONITORING

7.1 Monitoring of serum Teicoplanin levels is required for patients being treated for endocarditis or serious Staphylococcal infections (for example: prosthetic joint infections, osteomyelitis). Patients in these groups will generally be on the higher dose of 10-12mg per kg body weight per day (normally 800mg).

7.2 Monitoring of 'trough' levels only is performed. A pre-dose teicoplanin level should be measured before the fifth dose for a patient with normal renal function. A trough level of greater than 20mg/L is desirable for good outcome. After achieving a steady serum concentration, teicoplanin levels should be monitored once a week if the renal function remains within normal range.

7.3 Teicoplanin levels are performed by a reference laboratory resulting in a 48 to 72 hour turn around time. Teicoplanin should not be withheld whilst awaiting the result.

7.4 Patients on lower doses of Teicoplanin for less severe infection do not generally require monitoring.

8. HUMAN RIGHTS ACT

Implications of the Human Rights Act have been taken into account in the formulation of this SOP and they have, where appropriate, been fully reflected in its wording.

9. ACCESSIBILITY STATEMENT

This document can be made available in a range of alternative formats for example: large print, Braille and audio cd.

For more details please contact Human Resources Department on 01942 77(3766) or email equalityanddiversity@wwl.nhs.uk.

APPENDIX 1

REFERENCES

Brown NM, Goodman AL, Horner C et al. Treatment of methicillin- resistant Staphylococcus aureus: updated guidelines from the UK. Journal of Antimicrobial Chemotherapy – Antimicrobial resistance, vol 3, issue 1, March 2021.

Gould FK, Denning DW, Elliott TS et al. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. Journal of Antimicrobial Chemotherapy 2012; 67; 269-89.

Coia JE, Wilson JA, Bak A et al. Joint Healthcare Infection Society and Infection prevention Society guidelines for the prevention and control of MRSA in healthcare facilities. Journal of Hospital Infection, December 2021.

Boyce JM. MRSA Patients: proven methods to treat colonisation and infection. Journal of Hospital Infection 2001; 38 (Suppl. A): S9 – 14.

Gemmell CG, Edwards DI, Fraise AP, Gould FK, Ridgeway GL and Warren RE. Guidelines for the prophylaxis and treatment of Methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the UK. Journal of Antimicrobial Chemotherapy (2006); 57: 589-608.

APPENDIX 2

ADULT IV TEICOPLANIN GUIDANCE AND MONITORING

AVOID following this guidance for patients in groups below. Seek specialist advice instead.

- Pregnancy.
- Dialysis patients.
- Paediatrics.
- Surgical prophylaxis (see Antimicrobial Guidelines for doses).

Prescribing guidance

Teicoplanin should be prescribed using an initial loading dose regimen followed by a maintenance dose regimen – see dosing tables below.

All doses should be infused in 100ml sodium chloride 0.9% over 60 minutes.

Loading dose regimen is based on patient's Actual Body Weight and should be prescribed to be given for a total of 5 doses irrespective of renal function	
Actual Body Weight	**Loading regimen**
39kg and under	400mg every 12 hours for 5 doses
40kg to 59kg	600mg every 12 hours for 5 doses
60kg to 79kg	800mg every 12 hours for 5 doses
80kg to 99kg	1000mg every 12 hours for 5 doses
100kg to 119kg	1200mg every 12 hours for 5 doses
120kg to 139kg	1400mg every 12 hours for 5 doses
140kg to 159kg	1600mg every 12 hours for 5 doses
160kg and over	2000mg every 12 hours for 5 doses

Maintenance dose regimen is based on Creatinine Clearance (AVOID using eGFR) and should be prescribed to start 24 hours after the last loading dose is given An online creatinine clearance calculator is available on Microguide to assist you	
Creatinine Clearance (CrCl)	**Maintenance regimen**
CrCl over 90ml/min	1000mg every 24 hours
CrCl 60 to 90ml/min	800mg every 24 hours
CrCl 40 to 59ml/min	600mg every 24 hours
CrCl 20 to 39ml/min	400mg every 24 hours
CrCl less than 20ml/min	200mg every 24 hours

Monitoring

Monitor **Full Blood Count and Urea and Electrolytes** regularly during teicoplanin therapy.

Pre-dose (for example: 'trough') level should be drawn **on day 7** of therapy if treatment is planned to continue. Timing of sample draw must be immediately before the dose is given on that day, **continue to give** the teicoplanin whilst awaiting the result of the level.

Levels are sent away to a reference laboratory and take up to 3 days to process. **Level results are published in the Results section on HIS under the Microbiology header.** The usual target range is **20 to 60mg/L** unless advised otherwise by Microbiology. Ongoing trough levels should be **checked weekly** thereafter.