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சுகாதார, போசணை மற்றும் சுதேச வைத்திய அமைச்சு
Ministry of Health, Nutrition & Indigenous Medicine

To:

All Provincial Directors of Health Services

All Regional Directors of Health Services

Hospital Directors / Medical Superintends,

Heads of Medical Institutions,

Directors of Specialized Campaigns/Programmes/Units,

Director/Private Health Sector Development,

Presidents of Colleges, Associations of Medical Professionals,

District Tuberculosis Control Officers

Guideline on using Rifampicin for indications other than mycobacterial infections

Introduction

- Rifampicin is a potent anti-TB agent with useful antibiotic activity against several pathogenic bacteria other than *Mycobacterium tuberculosis* or other mycobacteria. Most of these other bacteria are sensitive to several other antibiotics which are not used in the treatment of TB whereas Rifampicin is the most effective component of the anti-TB combination therapy.[1]
- However there are a few well recognized microbiological indications for using a short course of rifampicin prophylactically or therapeutically. Some of these indications will require Rifampicin as a part of a combination of antibiotics.
- There may be rare instances in which rifampicin may be used for non-microbiological indications. Justification of such uses will need strong scientific evidence.
- **Use of Rifampicin as a single agent in a patient with TB disease leads to a risk of selection of Rifampicin resistant mutants arising during multiplication of TB bacilli.[1]**
- **Therefore the use of Rifampicin for other indications should be carefully monitored in TB endemic countries to prevent the emergence of Rifampicin resistant forms of TB.**
- **It is equally important to exclude the possibility of any form of active TB before starting Rifampicin for any other indication.**

Mechanism for distribution and maintaining accountability when using Rifampicin for non-mycobacterial infections

The following mechanism is suggested to restrict and monitor the use of Rifampicin for indications other than mycobacterial infections.

Rifampicin as a single agent will be imported only by the Ministry of Health and distributed through the National Programme for TB Control & Chest Diseases (NPTCCD).

The drug will be made available through District Chest Clinics and a small stock will be issued to major hospitals (TH, PGH and DGH level) by the District TB Control Officer (DTCO).

The chief pharmacist of the hospital is accountable for the use of Rifampicin and should maintain a document on stock status. The DTCO should verify the Rifampicin stocks in hospitals on a quarterly basis as well as when replenishing hospital stocks.

A list of recognized indications (Annexure A) will be issued to all the hospitals.

When a clinician decides to use Rifampicin for a recognized indication a properly filled and signed request form (Annexure B) should be sent to the chief pharmacist of the hospital with the signature of the requesting consultant.

Request forms will be issued and received by the chief pharmacist of the hospital (or another pharmacist attached to the hospital and specifically identified to be responsible for this task).

When a request is received at the pharmacy the chief pharmacist should contact the consultant microbiologist (onsite or off-site when services are available). Evidence for microbiological indications (listed in annexure A) should be verified by the consultant microbiologist of the hospital who should complete and sign on the request form (annexure B) and approve the issuance of Rifampicin.

If the stated indication for Rifampicin is outside the NPTCCD Guidelines on using Rifampicin for indications other than mycobacterial infections and the patient's condition is not critical then the consultant microbiologist is advised to request a second opinion from the panel appointed by the NPTCCD for this purpose and inform the hospital chief pharmacist to fax the request form to NPTCCD.

If approval is obtained the chief pharmacist should issue the required quantity of Rifampicin noted on the request form and secure the request forms which should be returned to the DTCO during stock verification.

DTCO should return the requests through director NPTCCD to the Drugs & Therapeutics Committee of the NPTCCD. The committee should review these requests at their meetings.

When Rifampicin is requested for microbiological indications not mentioned in Annexure A or for non-microbiological indications or when the services of a consultant microbiologist are not available the request form should be faxed to the Director NPTCCD.

Director NPTCCD should appoint a panel of experts (comprised of consultants in the Drugs & Therapeutics Committee of the NPTCCD and a representative nominated by the professional college relevant to the clinical specialty from which the request is made) to review the request and advice the relevant pharmacist to issue Rifampicin for a defined duration appropriate for the indication.

Director NPTCCD should send the request to the expert panel for review. Reviewing such requests by the panel can be done through e-mail or telephone communications to expedite the process.

This expert panel should have the authority to decide and advice against the use of Rifampicin when they consider the request to be not justifiable. Director NPTCCD should inform the decision of the panel to the chief pharmacist of the hospital. When the panel does not approve the use of Rifampicin reasons for rejection will be informed to the requesting physician.

Clinicians can decide to use rifampicin from the hospital stock without prior approval as a component of an antibiotic regime in life threatening conditions and in these instances a properly filled and signed request form with adequate evidence should be faxed to the Director NPTCCD by the chief pharmacist of the hospital after issuing rifampicin.

Director General of Health Services

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Annexure A

Indications for using Rifampicin in disease conditions other than mycobacterial infections

I. **Non microbiological indications** - No recognized indications for Rifampicin use with adequate evidence are identified at present. Request forms for these uses should be directed to NPTCCD to be reviewed by an expert panel appointed by NPTCCD

II. **Microbiological indications**

These will be either therapeutic or prophylactic use in non-mycobacterial infections.

A. Therapeutic indications for Rifampicin

Dose and duration for these indications should be decided by the treating clinician and verified by the consultant microbiologist of the hospital (on site/off-site) when reviewing the request. The central committee authorizing the use of Rifampicin should verify the dose and duration when a consultant microbiologist is not available in a hospital.

The use of Rifampicin in following situations should be in combination with other appropriate antibiotics to prevent the emergence of Rifampicin-resistant mutants while on therapy. Culture isolates should ideally be tested for susceptibility to Rifampicin in these instances.

1. **Infective endocarditis**
   - 1.1 Culture proven infection of the prosthetic valves or pacemakers caused by Methicillin Resistant *Staphylococcus aureus* (MRSA) or Methicillin Resistant strains of coagulase negative staphylococci
   - 1.2 Culture proven right sided native valve endocarditis caused by Methicillin Resistant *Staphylococcus aureus* (MRSA)
   - 1.3 Culture negative right sided endocarditis not responding to treatment with adequate doses and durations of regularly used anti staphylococcal agents

2. **Bone and joint infections**
   - 2.1 Culture proven infection of the prosthetic joints caused by Methicillin Resistant *Staphylococcus aureus* (MRSA) or Methicillin Resistant strains of coagulase negative staphylococci

3. **Central nervous system infections**
   - 3.1 Culture proven and refractory shunt associated infections and ventriculitis caused by Methicillin Resistant *Staphylococcus aureus* (MRSA) or Methicillin Resistant strains of coagulase negative staphylococci
   - 3.2 Culture proven meningitis caused by strains of *Streptococcus pneumoniae* resistant to penicillin and cefotaxime/ceftriaxone

4. **Infections caused by *Brucella* species proven by culture or serological tests**

B. Indications for using Rifampicin as post exposure prophylaxis

Presence of organisms in the source should be microbiologically proven and the nature of exposure of recipients should be assessed by the consultant microbiologist before initiating chemoprophylaxis in following instances.

1. Exposure to patients with invasive infections caused by *Neisseria meningitidis*
2. Exposure to patients with invasive infections caused by *Haemophilus influenzae* type b
3. Accidental laboratory exposures to culture isolates of *Brucella* species

Indication	Rifampicin dose & duration	Comments
Exposure to patients with invasive infections caused by *Neisseria meningitides* [2]	***Less than 1 month of age:*** 5 mg/kg, 12 hourly, for 2 days ***≥1 month of age + adults:*** 10 mg/kg – up to maximum 600 mg per dose, 12 hourly, for 2 days	Spread by respiratory droplets, not aerosols. Other alternative antibiotics such as a single dose of oral Ciprofloxacin or IM Ceftriaxone can be used.
Exposure to patients with invasive infections caused by *Haemophilus influenzae* type b (Hib)[3]	***less than 1 month of age:*** 10 mg/kg, once daily, for 4 days ***≥1 month of age + adults:*** 20 mg/kg – up to 600 mg maximum daily dose, once daily, for 4 days	Rifampicin chemoprophylaxis is recommended for index case patients (unless treated with Cefotaxime or Ceftriaxone) and all household contacts only in households with either members aged <4 years who are not fully vaccinated or members aged <18 years who are immunocompromised, regardless of their vaccination status
Accidental laboratory exposures to culture isolates of *Brucella* spp. *Use prophylaxis if risk level is high on assessing exposure.*[4]	600mg once daily for 3 weeks	Rifampicin should be combined with Doxycycline 100mg twice daily for 3 weeks

References

1. Guidelines for Clinical and Operational Management of Drug-Resistant Tuberculosis, 2013, International Union Against Tuberculosis and Lung Disease
2. Centers for Disease Control & Prevention, USA ; Manual for the Surveillance of Vaccine preventable Diseases ; 5th Edition ;2011; Chapter 8; Meningococcal Disease
3. Centers for Disease Control & Prevention, USA ; Manual for the Surveillance of Vaccine preventable Diseases; 2015; Chapter 2: *Haemophilus influenzae* serotype b (Hib)
4. Centers for Disease Control & Prevention, USA ; Brucellosis Homepage; Laboratory Personnel; Assessing laboratory risk level and PEP (page updated 12.12.2012 ; accessed 12.04.2016)

Annexure B

Request form for using Rifampicin for non-mycobacterial indications

Hospital		**District**	
Ward		**BHT No**	
Name of the patient			
Age		**Sex**	
Indication for Rifampicin			
Dose of Rifampicin		**Duration of Rifampicin**	
Requesting Consultant			
Designation			
Signature		**Date**	
Microbiological evidence to justify the request			
Consultant Microbiologist			
Signature		**Date**	
Number of Rifampicin tablets Issued		**Issued Date**	
Signature of hospital chief pharmacist issuing Rifampicin			
Name			

To be filled by DTCO			
Request checked and Rifampicin stock verified & replenished			
Name of DTCO			
Signature		**Date**	

To be filled by NPTCCD	
Decision of NPTCCD committee	
Date	
Panel decision informed to the hospital chief pharmacist & Rifampicin stock at District Chest Clinic drug store verified	
Signature of the chief pharmacist, Central Drug Store of NPTCCD	
Date	

Contact Details	
National Programme for Tuberculosis Control and Chest Diseases (NPTCCD)	**Central Drug Stores of NPTCCD**
Director, **National Programme for Tuberculosis Control and Chest Diseases (NPTCCD)** **No. 555/5, 4th Floor, Public Health Complex, Elvitigala Mawatha, Narahenpita,** **Colombo 05.** **Tel: (94) 0112 368386** **Fax: (94) 0112 368386** **Email: dnptccd@gmail.com**	**Chief Pharmacist,** **Central Drug Stores of NPTCCD,** **National Hospital for Respiratory Diseases Premises,** **Welisara.** **Tel: (94) 0112 956071** **Fax: (94) 0112 956071** **Email: drugstores.nptccd@gmail.com**