GLANDERS and MELIOIDOSIS

General points on treatment

The causative agents of Glanders and Melioidosis are the non-fermenting gram-negative bacilli *Burkholderia mallei* and *Burkholderia pseudomallei,* respectively. Exposure by inhalation is considered most likely in the context of biological warfare and the infective dose is assumed to be low. The probability of transmission from person to person is low.

The incubation period normally ranges from 10 to 14 days but there have been well-documented cases in which the first clinical manifestations of infection have occurred at up to three years after exposure.

Both diseases can present with acute pneumonia or as an overwhelming sepsis. Both diseases may be fatal without treatment.

The antibiotic susceptibility pattern profile of *B. mallei* resembles that of *B. pseudomallei* and both pathogens are usually susceptible *in vitro* to ceftazidime, imipenem, meropenem, doxycycline. (1). There have been reports of high MICs of ciprofloxacin for some strains of *B. pseudomallei* (2).

Although initial treatment with imipenem or meropenem, or with ceftazidime, for 2-3 weeks has been recommended for both infections, there is little experience in treating glanders in humans. In severe cases, combination therapy with doxycycline or cotrimoxazole may be considered (3,4). In mild cases, initial oral therapy with an active agent (such as doxycycline, co-amoxyclav, fluoroquinolones or TMP/SMZ) may be sufficient.

Opinion varies regarding the need for sequential therapy following successful initial treatment and its optimal duration. Regimens that have been proposed include up to 12-24 weeks of doxycycline, co-amoxyclav, fluoroquinolones or TMP/SMX.

The group is currently investigating the evidence regarding the utility of post exposure prophylaxis in humans.

The recommendations below are compiled from references 1 – 6.

RECOMMENDATIONS

In a mass casualty setting parenteral treatment may not be an option and recommendations for oral treatment should be followed.
Otherwise oral therapy should be substituted when the patient's condition improves. In addition, some products show high bioavailability (e.g. ciprofloxacin and doxycycline) making initial oral treatment an option.

Name of active substance **Role in treatment and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases** Duration of initial treatment: 2 to 3 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen**
Imipenem ➢ **First line treatment**	**Posology**	**<u>Adults</u>** 50 mg/kg/day, up to 1 g iv four times daily **<u>Children</u>** >3 years: 15mg/kg, four times daily (up to max 2 g daily). Over 40 kg, use adult dose 3 months – 3 years: 15 – 25 mg/kg, four times daily.	No recommendations can currently be given (see introduction)
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

Name of active substance **Role in treatment and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases** Duration of initial treatment: 2 to 3 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen**
Meropenem ➢ **Alternative to Imipenem**	**Posology**	**<u>Adults</u>** 500 mg – 1g iv, three times daily **<u>Children</u>** >3 months: 10 - 20 mg/kg, three times daily Adult dose for 50 kg and over.	No recommendations can currently be given (see introduction)
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

Name of active substance **Role in treatment and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases** Duration of initial treatment: 2 – 3 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen**
Ceftazidime ➢ **Alternative first line treatment**	**Posology**	**<u>Adults</u>** 2 g iv, three times daily. **<u>Children</u>** > 2 months: 100 mg/kg/day in three divided (maximum dose is 6g) < 2months: 60 mg/kg/day in two divided doses	No recommendations can currently be given (see introduction)
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

Name of active substance **Role in treatment and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases** Duration of initial treatment: 2-3 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen**
Doxycycline ➢ **Combination treatment with imipenem, /meropenem or ceftazidime in severe cases**	**Posology**	**<u>Adults</u>** 100 mg iv twice daily **<u>Children</u>** > 8years and >45 kg: adult dose > 8years and <45 kg: 2.2 mg/kg iv twice daily < 8years 2.2. mg/kg iv twice daily (maximum 200mg per day)	No recommendations can currently be given (see introduction)
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

Name of active substance **Role in treatment and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases** Duration of treatment: 2-3 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen**
TMP-SMX (trimethoprim sulphamethoxazole) ➢ **Combination treatment with imipenem/meropenem or ceftazidime in severe cases**	**Posology**	**<u>Adults</u>** TMP: 6-8 mg/kg/day and SMX: 40mg/kg/day iv in one or two divided doses followed by TMP: 6-8 mg/kg/day and SMX: 40mg/kg/day orally in one or two divided doses.) (Maximum total dose is 1440 mg twice daily. Consideration could be given to reducing the dose after 2 weeks) **<u>Children < 8 years</u>** TMP: 6-8 mg/kg/day and SMX: 30-40mg/kg/day iv in 2 divided doses followed by TMP: 6-8 mg/kg/day and SMX: 30-40mg/kg/day orally in one or two divided doses (Consideration could be given to reducing the dose after 2 weeks).	No recommendations can currently be given (see introduction)
	Contra indications	Should be considered in view of the prescribing information given in the different Member States.	
	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breastfeeding.	

References:

1. Russell P, Elley SM, and Tittball RW. In vitro susceptibilities of *Burkholderia* mallei in comparison to other pathogenic *Burholderia* species.

2. Russell P, Eley SM, Ellis J, et al. Comparison of efficacy of ciprofloxacin and doxycycline against experimental melioidosis and glanders. J Antimicrobial Chemotherapy 2000;45:813—8

3. CDC. Editorial. Laboratory-Acquired Human Glanders --- Maryland, May 2000. MMWR 2000: 49(24); 532-5

4. P. Chetchotisakd, S. Porramatikul, P. Mootsikapun, S. Anunnatsiri and E. Thinkhamrop. Randomized, double-blind, controlled study of cefoperazone-sulbactam plus cotrimoxazole versus Ceftazidime plus cotrimoxazole for the treatment of severe melioidosis. Clinical Infectious Diseases, 2001; 33 : 29-34.

5 Jacobs, in Harrison: Principles of internal medicine. 14th Edition. Melioidosis, p: 969. 1998

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