BRUCELLOSIS

General points on treatment

Four species are pathogenic to man*: B. melitenis* (acquired from goats), *B. suis* (pigs), *B. abortus* (cattle) and *B. canis* (dogs). The bacteria are highly infectious by aerosols. Person to person transmission does not usually occur.

The incubation period varies from 5 days to 6 months. The symptoms can be very diverse (eg. fever, night sweats, malaise cough, joint infections, hepatitis etc. have been described) and vary according to the duration of the infection at the time of clinical presentation.

For most presentations of the disease, combination treatment with doxycycline and rifampicin or an aminoglycoside is recommended as first line treatment (1,2,3,4). Fluoroquinolones can penetrate intracellularly and *in vitro* studies have been encouraging. However, findings in clinical trials with fluoroquinolones have been controversial and high relapse rates have been reported (1,2).

For certain presentations, including endocarditis, joint infections and CNS infections, a more prolonged course of multiple antibiotics is required. In acute neuro-brucellosis, ceftriaxone 2g i.v once a day in combination with another effective drug (such as doxycycline) is the preferred treatment.

This guidance covers treatment regimens of suspected or confirmed clinical cases of brucellosis. Although recommendations are also given for post exposure prophylaxis in case of suspected or confirmed exposure to brucella, there is little evidence to support its utility.

Recommendations are compiled from references 1-4.

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. doxycycline) making initial oral treatment an option.

Name of active substance **Role in therapy and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases** Duration of treatment: 6 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 3-6 weeks
Doxycycline ➢ **First line treatment in combination with rifampicin or streptomycin or with gentamicin in adults and children > 8 years of age** ➢ **First line prophylaxis in combination with rifampicin in adults and children > 8 years of age.**	**Posology**	**<u>Adults</u>** 100mg iv twice daily followed by 100 mg orally twice daily **<u>Children</u>** > 8years and >45 kg: adult dose > 8years and <45 kg: 2.2 mg/kg iv twice daily followed by the same doses orally	**<u>Adults</u>** 100 mg orally twice daily **<u>Children</u>** > 8years and >45 kg: adult dose orally > 8years and <45 kg: 2.2 mg/kg orally twice daily
	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: 6 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 3 – 6 weeks
Rifampicin ➢ **First line treatment in combination with doxycycline in adults and children > 8 years** ➢ **First line prophylaxis in combination with doxycycline in adults and children > 8 years of age** ➢ **First line treatment and prophylaxis in combination with TMP-SMX in children < 8 years of age**	**Posology**	**<u>Adults</u>** 10 – 15 mg/kg/day i.v in one or two doses followed by 600 – 900 mg orally once daily **<u>Children</u>** 10 – 15 mg/kg/day i.v in one or two doses followed by 10 – 15 mg/kg/day orally in one or two doses	**<u>Adults</u>** 600 – 900 mg orally once daily **<u>Children</u>** 10 – 15 mg/kg/day orally in one or two doses
	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 weeks (review the need for further treatment after 2 weeks with aminoglycosides; less for children)	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 3 - 6 weeks
Gentamicin ➢ **Alternative first line treatment in combination with doxycycline in adults and children > 8 years**	**Posology**	**<u>Adults</u>** 3-5 mg/kg iv once daily or 1.5 - 2.5 mg/kg twice daily	**NA**
		<u>Children</u> 1- 2.5 mg/kg iv three times daily.	
	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 weeks (review the need for further treatment after 2 weeks with aminoglycosides; less for children)	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 3 - 6 weeks
Streptomycin ➢ **Alternative first line treatment in combination with doxycycline in adults and children > 8 years**	**Posology**	**<u>Adults</u>** 1 g im once or twice twice daily	NA
		<u>Children</u> 15 mg/kg once or twice daily (maximum dose, 2g per day)	
	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: 6 weeks	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 3 weeks (ref 4)
TMP-SMX (trimethoprim sulphamethoxazole) ➢ **First line treatment and prophylaxis in combination with rifampicin in children < 8 years of age and as an alternative in pregnant women** ➢ **Second line treatment and prophylaxis in combination with rifampicin in adults and children > 8 years**	**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).	**<u>Adults</u>** **<u>There are no official dose recommendations for prophylaxis in adults.</u>** **<u>Children < 8years</u>** TMP: 6-8 mg/kg/day and SMX: 30-40 mg/kg/day orally in one or two divided doses for three weeks.
	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. Jacobs, in Harrison: Principles of internal medicine. 14th Edition. Brucellosis, p: 971. 1998

2. C. Agalar, S Usubutun, R. Turkyilaz. Ciprofloxacin and Rifampicin versus Doxycycline and Rifampicin in the treatment of Brucellosis. Eur J Infect Dis., 1999. 18: 533-538.

3. Drugs and Vaccines against biological weapons. The Medical letter. Vol 41. (Issue 1046). February 12, 1999

4. Anonymous.2001. AFSSAPS homepage. Plan Biotox (www.agmed.sante.gouv.fr/htm/10/indbio.htm), AFSSAPS. France