

Guideline on Antimicrobial Prophylaxis and Empirical Treatment in Patients with Primary Immune Deficiencies (Inborn Errors of Immunity)

Table 1 – Common Microorganisms to cause infections in Primary Immune Deficiencies (PIDs)

Condition	Common sites of infection	Bacteria	Virus	Fungi	Parasites
Combined Immune Deficiencies					
Severe Combined Immune Deficiency (SCID) Complete DiGeorge syndrome Omens syndrome	ENT infection - Otitis media Sinus infection - Sinusitis	<i>Haemophilus influenzae</i> <i>Streptococcus pneumoniae</i>			
	Respiratory tract infection - Pneumonia	<i>Haemophilus influenzae</i> <i>Streptococcus pneumoniae</i>	Influenza A, B Parainfluenza RSV Adenovirus Rhinovirus Human metapneumovirus CMV, other herpesviruses	<i>Pneumocystis jirovecii</i> <i>Candida</i> spp. <i>Aspergillus</i> spp.	<i>Toxoplasma gondii</i>
	Central nervous system Infection - Meningitis - Meningo-encephalitis	<i>Haemophilus influenzae</i> <i>Streptococcus pneumoniae</i> <i>Neisseria meningitidis</i>	Enteroviruses CMV HSV Japanese encephalitis virus	<i>Pneumocystis jirovecii</i> <i>Candida</i> spp <i>Aspergillus</i> spp	<i>Toxoplasma gondii</i>
	Gastroenteritis	<i>Campylobacter</i> <i>Salmonella</i> spp. <i>Shigella</i> spp. <i>Yersinia</i> spp.	Rotavirus Norovirus CMV		<i>Giardia intestinalis</i> <i>Cryptosporidium</i> spp.
	Lymph node - Lymphadenitis	<i>Mycobacterium tuberculosis</i> Atypical Mycobacteria (MOTT)			<i>Toxoplasma gondii</i>
	Skin infection	<i>Staphylococcus aureus</i>	Herpes viruses Human papillomavirus Molluscum contagiosum virus	<i>Candida</i> spp.	
	Blood stream infection	<i>Haemophilus influenzae</i>		<i>Candida</i> spp <i>Aspergillus</i> spp	

		<i>Streptococcus pneumoniae</i> <i>Neisseria meningitides</i>			
Hyper IgE Syndrome (Autosomal Dominant)	Skin infection - Abscess	<i>Staphylococcus aureus</i>		<i>Candida</i> spp.	
	Respiratory tract infection - Pneumonia	<i>Staphylococcus aureus</i> <i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>			
	- Presence of bronchiectasis and pneumatocele	<i>Pseudomonas</i> spp. Atypical Mycobacteria (MOTT)		<i>Aspergillus</i> spp <i>Pneumocystis jirovecii</i> (rare)	
	Internal abscess	<i>Staphylococcus aureus</i> Enterobacteriaceae (Coliforms)			
	CNS - Meningitis/ brain abscess	<i>Staphylococcus aureus</i> <i>Mycobacterium tuberculosis</i> (rare)		<i>Cryptococcus</i> spp. Endemic fungi	
Hyper IgE Syndrome (Autosomal recessive)	Skin infections - Abscess	<i>Staphylococcus aureus</i>	Herpes simplex virus Molluscum contagiosum virus Human papillomavirus Varicella zoster virus		
	Respiratory tract infection - Pneumonia	<i>Staphylococcus aureus</i> <i>Haemophilus influenzae</i> <i>Proteus mirabilis</i> <i>Pseudomonas aeruginosa</i>	Adenovirus, RSV	<i>Pneumocystis jirovecii</i> <i>Histoplasma</i> spp (rare)	
Ataxia telangiectasia	Respiratory tract infection - Pneumonia	<i>Staphylococcus aureus</i> <i>Haemophilus influenzae</i>			

		<i>Streptococcus pneumoniae</i> <i>Pseudomonas aeruginosa</i>			
	Skin infections		Human Papillomavirus		
Wiskott-Aldrich syndrome	Respiratory tract infection - Pneumonia	<i>Haemophilus influenzae</i> <i>Streptococcus pneumoniae</i>		<i>Pneumocystis jirovecii</i>	
	Skin infections		Herpes viruses Papilloma virus Molluscum contagiosum virus	<i>Candida</i> spp	
Neutrophil deficiencies					
Chronic Granulomatous Disease (CGD)	Skin infection - Adenitis - Abscess - Impetigo	<i>Staphylococcus aureus</i> <i>Norcardia</i> spp <i>Actinomycetis</i> spp <i>Mycobacterium</i> spp <i>Salmonella</i> spp <i>Klebsiella</i> spp <i>Serratia</i> spp		<i>Candida</i> spp <i>Aspergillus</i> spp <i>Paecilomyces variotii</i> <i>Inonotus tropicalis</i>	
	Sepsis	Enterobacteriaceae (Coliforms) <i>Burkholderia</i> spp. <i>Pseudomonas</i> spp. <i>Serratia</i> spp. <i>Staphylococcus</i> spp.		<i>Candida</i> spp	
	Internal abscesses	<i>Staphylococcus aureus</i> <i>Serratia</i> spp. <i>Burkholderia</i> spp. <i>Streptococcus</i> spp. <i>Nocardia</i> spp.		<i>Aspergillus</i> spp	
	Gastro-intestinal - Perirectal abscess - Fistulae - Ulcers - Strictures	Enterobacteriaceae (Coliforms) <i>Staphylococcus aureus</i>			

	- Obstruction				
	Central nervous system Infection - Meningitis	<i>Haemophilus influenzae</i> <i>Staphylococcus aureus</i>		<i>Candida</i> spp <i>Aspergillus</i> spp	
	Bone infection -Osteomyelitis	<i>Serratia</i> spp. <i>Staphylococcus aureus</i> <i>Pseudomonas</i> spp. <i>Nocardia</i> spp.		<i>Aspergillus</i> spp	
	Respiratory tract infection - Pneumonia	<i>Streptococcus pneumoniae</i> <i>Nocardia</i> spp. <i>Serratia</i> spp. <i>Pseudomonas</i> spp. <i>Staphylococcus aureus</i> <i>Klebsiella</i> spp.		<i>Candida</i> spp <i>Aspergillus</i> spp	
	Urinary -Pyelonephritis	Enterobacteriaceae (Coliforms)			
Congenital neutropaenia	Skin/ mucosal infection - cellulitis - Subcutaneous abscess - Gingivitis - Stomatitis - Aphthous ulcers	<i>Staphylococcus</i> spp. <i>Serratia</i> spp. <i>Klebsiella</i> spp. Other Coliforms			
	Sepsis	<i>Staphylococcus</i> spp. <i>Serratia</i> spp. <i>Klebsiella</i> spp. Other Coliforms		<i>Candida</i> spp	
	Internal abscess	<i>Staphylococcus</i> spp. <i>Serratia</i> spp. <i>Klebsiella</i> spp. Other Coliforms			
	Respiratory tract infection - Pneumonia	<i>Staphylococcus</i> spp. <i>Streptococcus pneumoniae</i>		<i>Aspergillus</i> spp <i>Candida</i> spp	
	Central			<i>Cryptococcus</i>	

	nervous system Infection - Meningitis			spp	
Leukocyte adhesion deficiency (LAD)	Respiratory tract infection - Pneumonia	<i>Staphylococcus</i> spp. Enterobacteriaceae (Coliforms) <i>Streptococcus</i> spp.		<i>Candida</i> spp	
	Skin/ mucosal infection - Omphalitis - Ulcers - Pyoderma gangrenosum - Gingivitis - Periodontitis	<i>Staphylococcus</i> spp. Enterobacteriaceae (Coliforms)			
	Sepsis	<i>Staphylococcus</i> spp. Enterobacteriaceae (Coliforms)		<i>Candida</i> spp	
Chédiak-Higashi syndrome	Skin/ Periodontal infection -Gingivitis -Oral ulcers - Periodontal infection	<i>Staphylococcus</i> spp. <i>Streptococcus</i> spp.			
Antibody deficiencies					
Bruton's agammaglobulinemia (XLA)	ENT infection - Otitis media Sinus infection - Sinusitis Respiratory tract infection - Pneumonia	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Mycoplasma pneumoniae</i>		<i>Pneumocystis jirovecii</i> (rare)	
	Central nervous system infection - Meningitis - Meningo- encephalitis	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> , <i>Neisseria meningitidis</i>	Enterocytopathic human orphan (ECHO) virus Enteroviruses vaccine strain poliovirus		

	Ecthyma/Pyoderma gangrenosum	<i>Helicobacter</i> spp.			
	Sepsis	<i>Pseudomonas</i> spp. <i>Helicobacter</i> spp. <i>Campylobacter jejuni</i> <i>Mycoplasma</i> <i>Ureoplasma</i>			
	Gastroenteritis	<i>Salmonella</i> spp. <i>Campylobacter</i> spp.	Enteroviruses		<i>Giardia intestinalis</i>
	Septic arthritis	<i>Staphylococcus aureus</i> <i>Mycoplasma</i> <i>Ureoplasma</i>			
Common variable immune deficiency (CVID) Selective IgA deficiency Specific antibody deficiency with normal Ig HIGM without cellular defects (HIGM-2, 4,5) (mutations in AID, UNG, PMS2)	ENT infection - Otitis media Sinus infection - Sinusitis Respiratory tract infection - Pneumonia	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Mycoplasma pneumonia</i>			
	-Presence of bronchiectasis	<i>Pseudomonas aeruginosa</i> <i>Staphylococcus aureus</i>			
	Central nervous system infection - Meningitis	<i>Streptococcus pneumonia</i> <i>Haemophilus influenzae</i> <i>Neisseria meningitides</i>	Enteroviruses		
	Gastroenteritis	<i>Salmonella</i> spp. <i>Campylobacter</i> spp.	Enteroviruses		<i>Giardia intestinalis</i>
	Septic arthritis	<i>Staphylococcus aureus</i> <i>Mycoplasma</i> <i>Ureoplasma</i>			
	If on immune-suppressives for lympho-		Varicella zoster virus (skin)	<i>Pneumocystis jirovecii</i> (lung)	

	proliferative/auto immune diseases				
Hyper IgM syndrome (HIGM) with cellular defects (HIGM-1, HIGM-3) (mutations in CD40, CD40L)	ENT infection - Otitis media Sinus infection - Sinusitis	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>			
	Respiratory tract infection - Pneumonia	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Mycoplasma pneumoniae</i>	CMV HSV	<i>Pneumocystis jirovecii</i> <i>Cryptococcus</i> spp	
	Central nervous system infection - Meningitis	<i>Neisseria meningitidis</i>		<i>Cryptococcus</i> spp	<i>Toxoplasma gondii</i>
	Gastro-intestinal Infection - Gastroenteritis/ sclerosing cholangitis	<i>Campylobacter jejuni</i>			<i>Giardia intestinalis</i> <i>Cryptosporidium</i> spp.
Anhidrotic ectodermal dysplasia with immunodeficiency/ NEMO (defects in the NFκB essential modulator)	Respiratory tract infection - Pneumonia	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Klebsiella</i> <i>Pseudomonas</i> spp. MOTT(Atypical Mycobacteria)	CMV HSV	<i>Pneumocystis jirovecii</i> <i>Candida</i> spp	<i>Toxoplasma gondii</i>
Other Immune deficiencies					
Chronic mucocutaneous candidiasis				<i>Candida albicans</i> Other <i>Candida</i> spp.	
Complement deficiencies C3, Factor H, Factor I MBL	Respiratory tract infection - Pneumonia	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Streptococcus pyogenes</i>			
Terminal Pw	Central nervous	<i>N. meningitidis</i>			

Properdin	system infection - Meningitis				
Mendelian susceptibility to mycobacterial disease (MSMD)		<i>Mycobacteria (MOTT and TB)</i> <i>Salmonella</i> spp. <i>Yersinia</i> spp.	CMV, HSV Varicella zoster virus		

Table 2 – Antimicrobial prophylaxis for patients with PIDs

Condition	Antimicrobial prophylaxis	Alternative prophylaxis	Comment
Combined Immune deficiencies			
Severe Combined Immune Deficiency (SCID) Complete DiGeorge syndrome Omens syndrome	Oral co-trimoxazole Child: 25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) (1,2) + Oral fluconazole Child: 3- 6 mg/kg/ daily (1,2) + Oral acyclovir Child 1 month–2 years: 100–200 mg 4 times daily Child 2–18 years: 200–400 mg 4 times daily (1,2)	Oral dapsone 2mg/kg (max 100mg) once/ day (2) OR Inhaled pentamidine isetionate 300 mg Once every 3 weeks (2) + Oral fluconazole + Oral acyclovir	If BCG is given: add isoniazid + rifampicin until HSCT (2) Child 1 month–12 years: isoniazid 10mg/kg daily (max. 300 mg daily) + rifampicin 15 mg/kg daily (max. 450 mg daily if body-weight less than 50 kg; max. 600 mg daily if body-weight over 50 kg) Child 12–18 years : isoniazid 300 mg daily + rifampicin 600mg daily (rifampicin 450mg daily if body-weight less than 50 kg) Monitor liver enzyme levels in patients receiving fluconazole Prophylaxis is often not necessary for the majority of DiGeorge syndrome patients who are not severely immunodeficient (2).
Hyper IgE Syndrome (Autosomal Dominant)	Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily (Maximum 800 mg/day of	Oral flucloxacillin/ cloxacillin Child:125-250mg twice/day (2) Adult: 2-4 g/day (2)	

	sulfamethoxazole) Adult: 960 mg once daily <u>If bronchiectasis present:</u> Add Oral azithromycin Child < 45kg: 10mg/kg once daily 3 days/week (2) Child >45kg/ Adult: 500mg once daily 3 days/week +/- Inhaled tobramycin/ gentamicin (2) <u>If pneumatocoele present:</u> Add Oral itraconazole Child: 2.5 mg/kg twice daily Adult: 200mg daily (2)	Oral clarithromycin Child: 7.5 mg/kg daily or twice daily Adult: 500 mg daily or twice daily +/- Inhaled amikacin	Refer antibody deficiency for tobramycin/ gentamicin Doses. Tobramycin is not currently available
Hyper IgE Syndrome (Autosomal recessive)	Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily (Maximum 800 mg/day of sulfamethoxazole) Adult: 960 mg once daily + Oral acyclovir Child 1 month–2 years: 100–200 mg 4 times daily Child 2–18 years: 200–400 mg 4 times daily Adult: 200 mg 4 times a day (2)	Oral flucloxacillin/ cloxacillin Child:125-250mg twice/day(2) Adult: 50mg/kg twice/day (maximum 1g)	
Ataxia telangiectasia	If bronchiectasis present: Oral azithromycin Child < 45kg: 10mg/kg once daily 3 days/week (2) Child >45kg/ Adult: 500mg once daily 3 days/week +/- Inhaled tobramycin/ gentamicin	Oral clarithromycin Child: 7.5 mg/kg daily or twice daily Adult: 500 mg daily or twice daily	Prophylaxis is indicated only if bronchiectasis present Refer Antibody deficiency for Tobramycin/ Gentamicin

			Doses.
Wiskott-Aldrich syndrome	Oral co-trimoxazole Child: 25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) Adult: 960 mg once daily 3 days/week (1) + Oral acyclovir Child 1 month–2 years 100–200 mg 4 times daily Child 2–18 years 200–400 mg 4 times daily Adult: 200 mg 4 times a day + Oral fluconazole 3–6 mg/kg once daily (2) <u>If splenectomy done:</u> Add oral penicillin Child < 2 years: 125 mg 12 hourly Child > 2 years and Adults: 250 mg 12 hourly	Oral dapsone 2 mg/kg (max 100 mg) once/day (2) OR Inhaled pentamidine isetionate 300 mg Once every 3 weeks (2) + Oral acyclovir + Oral fluconazole + Add oral amoxicillin Child < 2 years: 20 mg/kg daily Child > 2 years and Adults: 250 mg daily OR Oral erythromycin 250 mg daily for all ages	
Neutrophil deficiencies			
Chronic Granulomatous Disease (CGD)	Oral co-trimoxazole Child: 25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily (Maximum 800 mg/day of sulfamethoxazole) Adult: 960 mg once daily + Oral itraconazole Child: 2.5 mg/kg twice daily	Oral flucloxacillin 25–50 mg/kg daily OR Oral trimethoprim alone 100 mg/day OR Oral cephalexin OR Oral ciprofloxacin (2) + Oral itraconazole Child: 2.5 mg/kg twice	Ciprofloxacin is given only in the presence of sulphonamide or beta-lactam allergy Be aware of visual disturbances due to itraconazole

	Adult: 200mg daily	daily Adult: 200mg daily	
Congenital neutropaenia	Ora flucloxacillin 25-50mg/kg daily	Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole(5 mg/kg/day of TMP) component divided twice daily (Maximum 800 mg/day of sulfamethoxazole) Adult: 960 mg once daily	If profound neutropaenia despite G-CSF add oral itraconazole
Leukocyte adhesion deficiency (LAD)	Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole(5 mg/kg/day of TMP) component divided twice daily (Maximum 800 mg/day of sulfamethoxazole) Adult: 960 mg once daily +/- Oral metronidazole	Oral co- amoxiclav (2) OR Oral ciprofloxacin (2)	
Chédiak-Higashi syndrome		<u>Only if recurrent infections:</u> Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole(5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) Adult: 960 mg once daily 3 days/week OR Ora flucloxacillin 25-50mg/kg daily	Routine prophylaxis is not indicated.
Antibody deficiencies			

Bruton's aggamaglobulinaemia (XLA) Common variable immune deficiency (CVID) Specific antibody deficiency with normal Ig	Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole(5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) (2) Adult: 960 mg once daily 3 days/week(6,7)	Oral azithromycin Child:5mg/kg/day 3 days/week ((alternate days) or 10mg/kg/week(1,2,7) Adult : 250mg 3 days/week or 500mg once/week) (6,7) Or Oral amoxicillin Child:20 mg/kg 1-2 times/day(6,7) Adult: 500mg-1000mg 1-2 times/day) (6,7)	Prophylactic antibiotics are indicated in the setting of recurrent breakthrough infections (more than 3 per year or very severe) or declining lung functions despite IgG replacement(2). Macrolides are preferred in patients with CVID and with chronic cough, bronchiectasis, or other chronic lung disease (1,4). A review has suggested that patients with milder phenotypes presenting with recurrent upper respiratory infections can be managed with antibiotic prophylaxis alone. They are given antibiotics on continuous or intermittent/ seasonal basis. (1,2)
Selective IgA deficiency	Oral co-trimoxazole Child:25 mg/kg/day of sulfamethoxazole(5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) (2) Adult: 960 mg once daily 3 days/week(6,7)	Oral azithromycin Child:5mg/kg/day 3 days/week ((alternate days) or 10mg/kg/week(1,2,7) Adult : 250mg 3 days/week or 500mg once/week) (6,7)	Prophylaxis is only indicated in patients with recurrent infections and/ or with specific antibody deficiency
Antibody deficiency + Presence of bronchiectasis	Oral azithromycin Child < 45kg: 10mg/kg once daily 3 days/week (2) Child >45kg/ Adult: 500mg once daily 3 days/ week +/- Inhaled gentamicin/ tobramycin Inhaled gentamicin: Child Age >6 y: 80 mg twice daily, 28 days on, 28 days off OR: 21 days on, 7 days off Adult: 160 mg twice daily from gentamicin 40 mg/ml solution(2)	Oral clarithromycin Child: 7.5 mg/kg daily or twice daily Adult: 500 mg daily or twice daily +/- Inhaled colistin	Once bronchiectasis has been established, it is informative to document colonization. If colonized by <i>Pseudomonas aeruginosa</i>, long-term inhaled antibiotics can lower the frequency of exacerbations. (2,3). Consideration should be given to patient-held antibiotics for rapid administration at first sign of respiratory symptoms (2)

	Inhaled tobramycin: Age >6 y: 300 mg twice daily, 28 days, on 28 days off (7)		
Hyper IgM syndrome (HIGM) with cellular defects (HIGM-1, HIGM-3) (mutations in CD40, CD40L)	Oral co-trimoxazole Child: 25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) (2) Adult: 960 mg once daily 3 days/week (6,7) +/- Oral azithromycin Child < 45kg: 10mg/kg once daily 3 days/week (2) Child >45kg/ Adult: 500mg once daily 3 days/week		Azithromycin may have a role in prophylaxis against cryptosporidium in hyper-IgM syndromes with cellular defects (1,2,3)
HIGM without cellular defects (HIGM-2, 4,5) (mutations in AID, UNG, PMS2)		Oral co-trimoxazole Child: 25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) (2) Adult: 960 mg once daily 3 days/week (6,7)	Routine prophylaxis is only indicated in patients with recurrent infections.
Anhidrotic ectodermal dysplasia with immunodeficiency/ NEMO (defects in the NFκB essential modulator)	Oral co-trimoxazole Child: 25 mg/kg/day of sulfamethoxazole (5 mg/kg/day of TMP) component divided twice daily 3 days/week (Maximum 800 mg/day of sulfamethoxazole) (2) Adult: 960 mg once daily 3 days/week (6,7) + Oral azithromycin Child < 45kg: 10mg/kg once daily 3 days/week (2) Child >45kg/ Adult: 500mg once daily 3 days/week + Oral acyclovir Child 1 month–2 years		

	100–200 mg 4 times/day daily Child 2–18 years 200–400 mg 4 times/day daily Adult: 200 mg 4 times a day + Oral fluconazole 3- 6 mg/kg/ daily (1)		
Other Immune deficiencies			
Chronic mucocutaneous candidiasis	Oral fuconazole 3 mg/kg/daily		
Complement deficiencies C3, Factor H, Factor I MBL	Oral penicillin Child< 2 years:125mg 12 hourly Child>2 years and Adults: 250mg 12 hourly O R Oral amoxicillin Child<2 years: 20mg/kg daily Child> 2years and Adults: 250mg daily	IM benzathine penicillin Child: 1.2 million units/month Adult: 2.4 million units every 2–3 weeks (3). O R Oral erythromycin 250mg daily for all ages	
Complement deficiencies Terminal Pathway, Properdin	Oral penicillin Child< 2 years:125mg 12 hourly Child>2 years and Adults: 250mg 12 hourly	IM benzathine penicillin Child: 1.2 million units/month Adult: 2.4 million units every 2–3 weeks (3)	Routine prophylaxis is not indicated.
Mendelian susceptibility to mycobacterial disease (MSMD)			Routine prophylaxis is not considered necessary for all subjects or at all times (7,8). In patients with complete IFN- γ R deficiency, treatment doses of antibiotics should be continued indefinitely, after therapy of acute infections. In contrast, in the event of a partial IFN-g receptor deficiency, lifelong azithromycin prophylaxis is extremely successful in preventing recurrence after acute infection (1).

Table 3 - Empirical Antimicrobial Treatment for infections in patients with PIDs

Combined Immune deficiencies (CID)				
PID Condition	Site of Infection	Empirical antibiotic	Alternative antibiotic	Comment
Severe Combined Immune Deficiency (SCID) Complete DiGeorge syndrome Omens syndrome	Respiratory infections			*See notes below
	<u>Otitis media/ Sinusitis</u> Mild	Oral co-amoxiclav	Oral azithromycin or Oral clarythromycin	
	Severe	IV co-amoxiclav	IV cefotaxime or IV ceftriaxone	
	<u>Community acquired pneumonia</u>	IV cefotaxime + IV/Oral clarithromycin	IV levofloxacin or IV moxifloxacin	
	<u>If MRSA is suspected</u>	Add IV vancomycin	Add IV teicoplanin or IV/Oral linezolid	
	<u>With risk factors for Pseudomonas</u> · COPD · Bronchiectasis	IV piperacillin-tazobactam + IV ciprofloxacin / IV levofloxacin	IV meropenem + IV gentamicin In immediate penicillin or cephalosporin hypersensitivity IV ciprofloxacin + IV gentamicin	
	<u>Suspected viral pneumonia</u>	Oral oseltamivir		
	<u>Suspected Pneumocystis pneumonia</u>	Oral co-trimoxazole	IV pentamidine isethionate or dapson PLUS trimethoprim	
	<u>Suspected fungal</u>			

	<u>Suspected viral infections</u>	miconazole or ketoconazole Oral/ IV acyclovir	Oral fluconazole	
	GI infections <u>Diarrhoea</u> <u>Suspected Cryptosporidiosis</u>	Oral/furazolidone +/- Oral metronidazole Oral nitazoxanide + Azithromycin	IV cefotaxime +/- oral metronidazole Oral paromomycin + azithromycin (only partially active)	Add metronidazole if Giardia is suspected Oral nitazoxanide is currently not available in SL.
	Lymphadenitis <u>Suspected TB/BCGitis</u>	Anti-tuberculosis treatment		Consult Microbiologist/chest physician
	Blood stream infection <u>If MRSA is suspected</u>	IV piperacillin-tazobactam + IV amikacin Add IV vancomycin	IV meropenem + IV gentamicin/ IV netilmicin Add IV teicoplanin	If fungaemia is suspected add IV Amphotericin B or IV Caspofungin
Hyper IgE Syndrome	Skin infections	Refer Skin Infections in SCID		
	Respiratory infection <u>Presence of pneumatoceles</u>	Refer respiratory infections in SCID IV piperacillin-tazobactam/ IV meropenem + IV amphotericin B		Pseudomonas and Aspergillus need to be covered
	Internal abscesses	IV ceftriaxone/ cefotaxime + IV metronidazole +/- IV Vancomycin	IV ciprofloxacin + IV metronidazole +/- IV vancomycin	

	<u>Suspected Cryptococcus meningitis</u>	Refer Cryptococcal meningitis in SCID		
Ataxia telangiectasia	Respiratory infection	Refer respiratory infections in CID		
Wiskott-Aldrich syndrome	Respiratory infection	Refer respiratory infections in CID		
	<u>Suspected Pneumocystis pneumonia</u>	Refer Pneumocystis pneumonia in CID		
	CNS	Refer respiratory CNS infections in CID		
	Skin infection			
	<u>Suspected Viral infections</u>	Oral/ IV acyclovir		
	<u>Suspected Candida</u>	Topical clotrimazole/ miconazole/ nystatin	Oral fluconazole	
Neutrophil deficiencies				
Chronic Granulomatous Disease (CGD)	Skin infection			If Mycobacterial infections are suspected, refer to chest physician.
	<u>Impetigo/ abscess</u>	Refer Skin Infections in CID		
Congenital neutropaenia	Mucosal infection			
	<u>Gingivitis/ Periodontitis</u>	Oral co-amoxiclav	Oral doxycycline	
Leukocyte adhesion deficiency (LAD)	Sepsis	IV piperacillin-tazobactam / IV ticarcillin clavulanate +/- IV amikacin	IV meropenem /IV cefepime +/- IV gentamicin / IV netilmicin	
Chédiak-Higashi syndrome	<u>If MRSA suspected</u>	Add IV vancomycin	Add IV teicoplanin	
	Internal organ abscesses	IV piperacillin-tazobactam or IV ceftriaxone + IV ciprofloxacin + IV metronidazole	IV ticarcillin clavulanate + IV metronidazole	
	GI infections			

	<u>Perirectal abscess/ Fistulae/ ulcers/ strictures</u>	IV ceftriaxone + IV ciprofloxacin + IV metronidazole	IV piperacillin- tazobactam/ IV ticarcillin clavulanate + IV metronidazole	
	CNS Infection Bacterial Meningitis Brain abscess	Refer bacterial meningitis in CID IV vancomycin + IV cefotaxime/ceftriaxone + IV metronidazole		Treatment of abscess involves appropriate surgical intervention with parenteral antibiotic therapy
	Bone infections <u>Osteomyelitis</u>	IV flucloxacillin/IV cloxacillin + IV ceftazidme +/- Oral co-trimaxazole	IV vacomycin/ IV clindamycin + IV ticarcillin-clavulanic acid / piperacillin- tazobactam +/- Oral co-trimaxazole	Co-trimaxazole is effective against Norcardia
	Respiratory infections <u>Community acquired pneumonia</u>	IV ticarcillin-clavulanic acid / piperacillin- tazobactam +/- Oral co-trimaxazole	IV levofloxacin +/- Oral co-trimaxazole	Co-trimaxazole is effective against Norcardia
	Lymph node infections <u>Adinitis/ adnopathy</u> <u>Suspected fungal infection</u> (candida/ Aspergillus)	Oral co-trimoxazole Oral itraconazole	Oral ciprofloxin	
	Urinary infections <u>Pyelonephritis</u>	IV co-amoxiclav/ IV cefotaxime +/- IV gentamicin/ netilmicin	IV ciprofloxacin +/-IV gentamicin/ netilmicin	
Antibody deficiencies				

	<u>Cryptococcus infection</u> <u>Suspected Toxoplasmosis</u>	IgE Syndrome Refer Toxoplasmosis in CID		Consult Mycologist/ Parasitologist for treatment of Cryptococcosis /Toxoplasmosis
	GI infections <u>Diarrhoea</u>	Oral/furozolidone +/- Oral metronidazole or Oral/IV ciprofloxacin +/- metronidazole	Oral azithromycin +/- metronidazole	Add metronidazole if Giardia is suspected If cryptosporidium is suspected add nitazoxanide
	Joint Infections <u>Septic arthritis</u>	IV flucloxacillin + IV cefotaxime +/- IV clindamycin	In immediate penicillin/cephalosporine hypersensitivity IV vancomycin + IV ciprofloxacin +/- IV clindamycin	If Gram stain is negative and culture negative add IV clindamycin or tetracycline to cover Mycoplasma.
Anhidrotic ectodermal dysplasia with immunodeficiency/ NEMO (defects in the NFκB essential modulator)	Respiratory infections <u>Pneumonia</u> <u>If MOTT is suspected</u>	Refer respiratory infection in antibody deficiency Anti-tuberculosis treatment		Consult chest physician
Chronic mucocutaneous candidiasis	<u>Mucocutaneous candidiasis</u>	Oral flucanazole		Dose doubled in extensive infections

*Special notes:

1. Patients with PIDs need longer duration of antibiotic treatment for infections than normal immune-competent patients.
2. Consult Microbiologist/ Mycologist/Virologist or Parasitologist for diagnosis and management of opportunistic infections.

Empirical treatment doses for bacterial infections

Antibiotic	Route	Paediatric dose	Adult dose
Amikacin	IV	Neonate: loading dose of 10mg/kg then 7.5mg/kg every 12 hours Child 1month–12 years: 7.5mg/kg every 12 hours	15 mg/kg once daily
Ampicillin -For meningitis	IV	Neonate under 7 days 100 mg/kg every 12 hours; Neonate 7–21 days 100 mg/kg every 8 hours; Neonate 21–28 days 100 mg/kg every 6 hours; Child 1 month–18 years 50 mg/kg every 4–6 hours (max. 2 g every 4 hours)	2 g every 4 hours
Azithromycin	Oral	Child over 6 months 10 mg/kg once daily (max. 500mg once daily)	500 mg once daily
Cefotaxime - For RTI and other infections	IV	Neonate under 7 days 25 mg/kg every 12 hours Neonate 7–21 days 25 mg/kg every 8 hours Neonate 21–28 days 25 mg/kg every 6–8 hours (dose doubled in severe infections) Child 1 month–18 years 50 mg/kg every 8–12 hours; increase to every 6 hours in very severe infections (max. 12 g daily)	1 g every 8 hours
- For CNS infections	IV	Neonate under 7 days 50 mg/kg every 12 hours; Neonate 7–21 days 50 mg/kg every 8 hours; Neonate 21–28 days 50 mg/kg every 6–8 hours; Child 1 month–18 years 50 mg/kg every 6 hours (max. 12 g daily)	2g every 4-6 hourly
Ceftazidime	IV	Neonate under 7 days: 25mg/kg every 24 hours Neonate 7–21 days: 25mg/kg every 12 hours Neonate 21–28 days and Child >1 month: 25mg/kg every 8 hours (doses doubled in severe infection,	1g every 8 hours, doubled in severe infections and meningitis (Elderly >80 years maximum 3 g per day)

		meningitis and febrile neutropenia)	
Ceftriaxone - For RTI and other Infections	IV	Neonate 20–50 mg/kg once daily Child 1 month–12 years Body-weight under 50 kg 50 mg/kg once daily Body-weight 50 kg and over 1 g daily	1-2 g daily
- For CNS infections	IV	Child 1 month–12 years Body-weight under 50 kg 80 mg/kg daily Body-weight 50 kg and over 2–4 g daily	2g every 12 hours
Chloramphenicol - For meningitis	IV	Neonate up to 14 days 12.5 mg/kg twice daily Neonate 14–28 days 12.5 mg/kg 2–4 times daily Child 1 month–18 years 12.5 -25 mg/kg every 6 hours;	12.5-25 mg/kg every 6 hours
Ciprofloxacin	IV	Neonate 10 mg/kg every 12 hours Child 1 month–18 years 10 mg/kg (max. 400 mg) every 8 hours	400 mg every 8–12 hours
Clarithromycin	oral	Neonate 7.5 mg/kg twice daily Child 1 month–12 years Body-weight under 8 kg 7.5 mg/kg twice daily Body-weight 8–11 kg 62.5mg twice daily Body-weight 12–19 kg 125 mg twice daily Body-weight 20–29 kg 187.5mg twice daily Body-weight 30–40 kg 250 mg twice daily	250 mg twice daily increased to 500 mg twice daily, if required in severe infections
	IV	Child 1 month–12 years 7.5 mg/kg (max. 500 mg) every 12 hours	500 mg every 12 hours
Clindamycin	Oral	Neonate < 14 days: 3–6mg/kg 3 times daily Neonate 14–28 days: 3–6mg/kg 4 times daily Child 1 month–18 years: 3–6mg/kg (max. 450mg) 4 times daily	150–300 mg every 6 hours; increased if necessary up to 450mg every 6 hours in severe infection
	IV	Child 1 month–18 years: 3.75–6.25mg/kg 4 times daily; increased up to 10mg/kg (max. 1.2g) 4 times daily in	0.6–2.7 g daily in 2–4 divided doses; increased if necessary up to 4.8 g

		severe infections	daily in life threatening infection
Cloxacillin/Flucloxacillin			
-For skin and subcutaneous infections	Oral/ IV	Neonate under 7 days: 25 mg/kg twice daily Neonate 7–21 days: 25 mg/kg 3 times daily Neonate 21–28 days: 25 mg/kg 4 times daily Child 1 month 2 years(oral): 62.5–125 mg 4 times daily Child 2–12 years (oral): 125–250 mg 4 times daily Child 1 month–18 years (IV): 12.5–25mg/kg every 6 hours (max. 1g every 6 hours); may be doubled in severe infection	500mg every 6 hours (dose doubled in severe infections)
-For Bone and joint infection	IV	Neonate under 7 days: 50–100 mg/kg every 12 hours Neonate 7–21 days: 50–100 mg/kg every 8 hours Neonate 21–28 days: 50–100 mg/kg every 6 hours Child 1 month–18 years: 50 mg/kg (max. 2 g) every 6 hours	2g every 6 hours
Co-amoxiclav	Oral	Neonate and Child 1 month–1 year : 0.25 mL/kg of 125/31 suspension 3 times daily Child 1–6 years: 5mL of 125/31 suspension 3 times daily Child 6–12: years 5mL of 250/62 suspension 3 times daily (dose doubled in severe infection)	co-amoxiclav, one 250/125 strength tablet every 8 hours (dose doubled in severe infection)
	IV	Neonate and Child 1–3 months: 30 mg/kg every 12 hours Child 3 months–12 years : 30 mg/kg (max. 1.2 g) every 8 hours	1.2 g every 8 hours
Doxycycline	Oral		200mg loading dose followed by 100mg daily
Furozolidone	Oral	Child 1 month and over: 1.25 mg/kg four times daily	100mg four times daily
Gentamicin	IV	Neonate less than 7 days: 5 mg/kg every 36 hours Neonate more than 7 days: 5 mg/kg every 24 hours Child 1 month–12 years: initially 7 mg/kg daily	5 mg/kg once daily
Imipenem	IV	Neonate under 7 days: 20mg/kg every	500 mg every 6 hours,

		12 hours Neonate 7–21 days: 20mg/kg every 8 hours Neonate 21–28 days: 20mg/kg every 6 hours Child 1–3 months: 20mg/kg every 6 hours Child 3months–18 years: 15mg/kg (max. 500mg) every 6 hours (infection caused by Pseudomonas, life-threatening infection, or infection in febrile neutropenia 25mg/kg (max. 1g) every 6 hours)	alternatively 1 g every 8 hours In febrile patients with neutropenia: 1 g every 6 hours
Levofloxacin	Oral/IV		500 mg 1–2 times a day
Linezolid	Oral/ IV	Neonate under 7 days: 10 mg/kg every 12 hours, increase to every 8 hours if poor response Neonate over 7 days: 10 mg/kg every 8 hours Child 1 month–12 years: 10 mg/kg (max. 600 mg) every 8 hours	600 mg every 12 hours
Meropenem	IV	Neonate under 7 days: 20 mg/kg every 12 hours Neonate 7–28 days: 20 mg/kg every 8 hours Child 1 month–12 years: Body-weight under 50 kg: 10–20 mg/kg every 8 hours Body-weight over 50 kg: 0.5-1g every 8 hours (Dose doubled in severe infection)	1 g every 8 hours (dose doubled in meningitis)

Metronidazole	oral	Child 1–2 months: 7.5mg/kg every 12 hours Child 2 months–12 years: 7.5mg/kg (max. 400mg) every 8 hours	400 mg every 8 hours, alternatively 500 mg every 8 hours
	IV	Neonate < 26 weeks corrected gestational age: 15mg/kg as a single loading dose followed after 24 hours by 7.5mg/kg daily Neonate 26–34 weeks corrected gestational age: 15mg/kg as a single loading dose followed after 12 hours by 7.5mg/kg every 12 hours Neonate over 34 weeks corrected gestational age and Child 1–2 months: 15mg/kg as a single loading dose followed after 8 hours by 7.5mg/kg every 8 hours Child 2 months–18 years: 7.5mg/kg (max. 500mg) every 8 hours	500 mg every 8 hours
Moxifloxacin	Oral/IV		400 mg once daily
Netilmicin	IV	Premature neonate< 32 weeks: 6mg/kg every 36 hours Premature neonate>32 weeks: 6mg/kg every 24 hours Neonate < 7 days: 3mg/kg every 12 hours Neonate 7-28 days: 2.5-3mg/kg every 8 hours Child 1 month-1 year: 2.5-3mg/kg every 8 hours Child 1 year- 12 years: 2-2.5mg/kg every 8 hour	6.5 mg/kg once daily
Piperacillin-tazobactam	IV	Neonate : 90 mg/kg every 8 hours Child 1 month–12 years: 90 mg/kg every 6–8hours; (max 4.5 g every 6 hours)	4.5 g every 8 hours (Increases to every 6 hours in sever infections and in neutropaenic patient)s
Teicoplanin	IV	Neonate: initially 16 mg/kg for one dose followed 24 hours later by 8 mg/kg once daily Child 1 month–18 years: initially 10 mg/kg (max.400 mg) every 12 hours for 3 doses, then 6 mg/kg(max. 400 mg) once daily	Initially 400 mg every 12 hours for 3 doses, followed by 400 mg once daily
Ticarcillin-clavulinic	IV	Preterm neonate body-weight under	3.2 g every 6–8 hours;

		2kg: 80mg/ kg every 12 hours Preterm neonate body-weight over 2kg and neonate and Child >1 month: 80mg/kg every 8 hours, increased to every 6 hours in more severe infections	increased to every 4 hours in severe infections
Vancomycin	IV (Given over 100 minutes)	Neonate less than 29 weeks corrected gestational age: 15 mg/kg every 24 hours Neonate 29–35 weeks corrected gestational age: 15 mg/kg every 12 hours Neonate over 35 weeks corrected gestational age: 15 mg/kg every 8 hours Child 1 month–18 years: 15 mg/kg every 8 hours (maximum daily dose 2 g) Doses are adjusted according to plasma concentration	1–1.5 g every 12 hours Elderly: 500 mg every 12 hours, alternatively 1 g once daily Doses are adjusted according to plasma concentration

Empirical treatment doses for viral infections

Antiviral	Route	Paediatric dose	Adult dose
Oseltamivir	Oral	Neonate: 2 mg/kg twice daily Child 1–3 months: 2.5 mg/kg twice daily Child 3 months–1 year: 3 mg/kg twice daily Child 1–12 years: Body-weight 10–15 kg 30 mg twice daily Body-weight 15–23 kg 45 mg twice daily Body-weight 23–40 kg 60 mg twice daily Body-weight over 40 kg 75 mg twice daily	75 mg twice daily (dose doubled in severe infection)
Acyclovir -For Herpes simplex	Oral	Child 1 month–2 years 200 mg 5 times daily	Non Genital: 400 mg 5 times a day

-For Chickenpox and herpes zoster infection	Oral	Child 2–18 years 400 mg 5 times daily Child 1 month–2 years 200 mg 4 times daily Child 2–6 years 400 mg 4 times daily Child 6–12 years 800 mg 4 times daily Child 12–18 years 800 mg 5 times daily	Genital herpes: 400 mg 3-5 times a day 800 mg 5 times a day.
	IV	Neonate 20 mg/kg every 8 hours Child 1–3 months 20 mg/kg every 8 hours Child 3 months–12 years 500 mg/m ² every 8 hours Child 12–18 years 10 mg/kg every 8 hours	10 mg/kg every 8 hours

Empirical treatment doses for parasitic infections

Condition	Antiparasitic agent	Route	Paediatric dose	Adult dose
Toxoplasmosis	Combination of Pyrimethamine and sulphadiazine			
	Pyrimethamine	Oral	Neonate: 1 mg/kg twice daily Child 12–18 years: 50mg once daily	200 mg initially, followed by 50-75 mg/day
	Sulphadiazine	Oral	Neonate: 50 mg/kg twice daily Child 12–18 years: 1 g 3 times daily	4-8 g/day
	(Alternatively, trimethoprim-sulfamethoxazole or clindamycin or clarithromycin, or azithromycin can be used).			

Cryptosporidiosis	No agent has proven efficacy for treating cryptosporidiosis and the duration of treatment is uncertain in immunocompromised patients. Nitazoxanide Alternatively Paromomycin or azithromycin (only partially active)	Oral	Nitazoxanide Or Paromomycin Or Azithromycin (please contact Parasitologist for treatment)	
Giardiasis	Metronidazole	Oral	Child 1–3 years: 400 mg once daily Child 3–7 years: 600–800 mg once daily Child 7–10 years: 1 g once daily Child 10–18 years: 2 g once daily for 3 days/ 400mg 3 times daily	400mg 3 times daily or 800mg twice daily
	Tinidazole	Oral	Child 1 month–12 years: single dose of 50–75 mg/kg (max. 2 g) (repeated once if necessary)	2g single dose

Empirical treatment doses for fungal infections

Condition	Antifungal	Route	Paediatric dose	Adult dose
Pneumocystis	Co-trimoxazole	oral	60 mg/kg every 12 hours	960mg twicw daily
Invasive Aspergillus	Voicanazole	Oral	9mg/kg twice daily	300mg twice daily on day 1 and then 200mg twice daily
		IV	9mg/kg 12 hourly for two doses and then 8mg/kg every 12 hours	300mg twice daily on day 1 and then 200mg twice daily
	Amphotericin B - Conventional	IV	Neonate: 1mg/kg once daily Child 1month-18year: 250ug/kg daily	1mg/kg daily
	- Liposomal	IV	Neonate: 1mg/kg once daily Child 1month-18year: 3mg/kg once daily	3-5mg/kg daily

Invasive Candida	Fluconazole	IV	Neonate under 2 weeks: 6–12 mg/kg every 72hours Neonate 2–4 weeks: 6–12 mg/kg every 48 hours Child 1 month–12 years: 6–12 mg/kg (max.800 mg) daily	400mg loading dose and then 200mg twice daily
	Amphotericin B	IV	Refer above for doses	
Skin candida	Clotrimazole Miconazole ketoconazole	Topical Topical Topical	Twice daily application	Twice daily application
	Fluconazole	Oral	3-6mg/kg on day 1 and then 3mg/kg daily	50mg once daily
Extensive Mucocutaneous candida	Fluconazole	Oral	3-6mg/kg on day 1 and then 3mg/kg daily	100mg once daily
Cryptococcus meningitis	Amphotericin B	IV	Refer above	Refer above
	Flucytosine	Oral		100mg/kg daily in 4 divided doses
Fungal lymphadenitis	Itraconazole	Oral	5 mg/kg (max. 200 mg) once daily	200mg twice daily

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