F.10	PYRAZINAMIDE – NEW STRENGTH FORMULATION - TB

Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	Application is to add a 500mg formulation of pyrazinamide, complementing the 400mg formulation that is currently listed Pyrazinamide as a single formulation is required: 1. When Fixed Dose Combinations (FDCs) cannot be given (People living with HIV on a protease inhibitor which precludes use of rifampicin based regimen 2. Drug resistance TB (both complex short course regimen and long all-oral medicines regimen)
Have all important studies and all relevant evidence been included in the application?	☐ Yes ☐ No ☒ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included: Application is to add a new strength of an already listed medicine
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☐ Yes ☐ No ☒ Not applicable Application is to add a new strength of an already listed medicine Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)?
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☐ No ☒ Not applicable Comments: Application is to add a new strength of an already listed medicine

Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments: BUT Application is to add a new strength of an already listed medicine
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Not applicable as application is to add a new strength of an already listed medicine Irrespective of which strength is used, patients will be getting the same dose, hence expecting no change in overall benefit to risk ratio between the new strength (500 mg) and existing strength (400 mg) in EML
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	No evidence is submitted as the application is to add a new strength of an already listed medicine
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: BUT Application is to add a new strength of an already listed medicine: They will be the same for the new strength (500 mg) and existing strength (400 mg) in EML
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments: Pyrazinamide 500 mg is already listed in many National Essential Medicine Lists. I am attaching a Table prepared by a Research Assistant. Information was obtained from the WHO website. Not sure whether the National Lists are the most recent ones.
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable Comments: Medicine (Pyrazinamide) is listed
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Pyrazinamide 500 mg is already listed in many National Essential Medicine Lists. Hence, I assume that these countries would have managed any issues related to access, cost and availability.
Any additional comments	None

Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	I recommend adding the new strength (500 mg Pyrazinamide) 1. TB is an important disease of grave public health concern 2. Since the duration of treatment is long and involve multiple medicines any attempts taken to improve the patient adherence to this multi therapy had to be given importance 3. Lack of adherence not only affect the said patient, but also increase the chance of emergence of DR- TB 4. Pyrazinamide is in the WHO Model list for many years 5. Dose recommendation is 30-35 mg/kg, for an average 60 Kg adult, it will be 1800- 2100 mg: a. With 400 mg tablets- 5 tablets b. With 500 mg tablets - 4 tablets 6. WHO Model EML list (Adults): Both FDCs and single formulation lists pyrazinamide tablet 400 mg + paediatric formulations (150 mg tablet (dispersible & scored) and oral liquid 30 mg/mL) 7. WHO EMLc: FDC has pyrazinamide 150 mg and the paediatric formulations given above 8. BUT Many countries already list 500 mg strength (see Annex) ❖ RECOMMEND ADDING THE 500 MG STRENGTH TO ADULT AND CHILDREN EML To discuss: 1. Whether to keep the 400 mg tablet /space out and remove
References (if required)	1. https://www.who.int/selection_medicines/country_lists/en/ 2. 21st Adult Essential Medicine List 3. 7th EMLc

No	Country	Last edited Year	Available strengths of Pyrazinamide
1	Afghanistan	2007	150mg / 400 mg / 500 mg In fixed dose drug combination: 150mg / 400 mg
2	Algeria	2006	Not mentioned the drug in the list
3	Angola	2008	Not mentioned the drug in the list
4	Argentina	2005	Not given
5	Armenia		
6	Bahrain		
7	Bangladesh	2008	Not given
8	Barbados		
9	Belize	2009-2011	400 mg
10	Bhutan	2012	-
		2011	-
		2009	500 mg In fixed dose drug combination: 400 mg
11	Bolivia (Plurinational State of)	2011-2013	-
		2003	500 mg
12	Botswana		
13	Brazil	2010	500 mg / 1.5 g Suspension: 30 mg/ml In fixed dose drug combination: 400 mg
14	Bulgaria		
15	Burkina Faso		
16	Burundi	2012	400 mg / 500 mg
17	Cambodia	2003	Not mentioned the drug in the list
18	Cameroon	2009	-
		2001	400 mg / 300mg+150mg
19	Cape Verde		
20	Central African Republic	2009	Not given
21	Chad	2007	500 mg In fixed dose drug combination: 150 mg
22	Chile	2005	500 mg
23	China	2011	-
		2010	-
		2009	Not given

24	Colombia		
25	Congo	2013	In fixed dose drug combination: 150 mg / 400 mg
26	Cook Islands	2007	500 mg
27	Côte d'Ivoire		
28	Croatia		
29	Democratic People's Republic of Korea	1999	500 mg
30	Democratic Republic of Congo	2010	-
		2007	400 mg / 500 mg In fixed dose drug combination: 150 mg / 400 mg
31	Djibouti	2007	400 mg
32	Dominican Republic		
33	Ecuador	2009	500 mg In fixed dose drug combination: 300 mg/ 400 mg
34	Egypt	2006	500 mg
35	El Salvador	2011	-
		2009	500 mg In fixed dose drug combination: 400 mg
36	Eritrea	2010	400 mg / 500 mg Tablet (dispersible): 150 mg Tablet (scored): 150 mg Suspension: 30 mg/ ml In fixed dose drug combination: 150 mg / 400 mg
37	Ethiopia	2015	400 mg / 500 mg / 750 mg In fixed dose drug combination: 150 mg / 400 mg
38	Fiji	2006	500 mg
39	Gabon		
40	Georgia		
41	Ghana	2010	-
		2004	500 mg Suspension: 125 mg/ 5 ml
42	Guinea		

43	Guyana	2009-2010	500 mg
44	Haiti	2012	400 mg In fixed dose drug combination: 150 mg/ 400 mg
45	Honduras		
46	India	2011	500 mg / 750 mg / 1000 mg / 1500 mg **Pediatrics:** Tablet: 250 mg/ 500 mg Tablet (dispersible): 150 mg Tablet (scored): 150 mg Suspension: 50 mg/ ml
47	Indonesia	2008	500 mg In fixed dose drug combination: 150 mg / 400 mg/ 500 mg
48	Iran (Islamic Republic of)	2009	500 mg In fixed dose drug combination: 300 mg
49	Iraq	2010	500 mg
50	Jamaica	2008	500 mg
51	Jordan	2011	-
		2009	500 mg
52	Kenya	2010	-
		2008	-
		2003	500mg In fixed dose drug combination: 300 mg / 400 mg
53	Kiribati	2009	150 mg/ 400 mg/ 500 mg In fixed dose drug combination: 150 mg / 400 mg
54	Kyrgyzstan	2009	500 mg / 750 mg In fixed dose drug combination: 75 mg / 750 mg
55	Lebanon		
56	Lesotho	2005	400 mg / 500 mg
57	Madagascar		
58	Malaysia	2008	500 mg In fixed dose drug combination: 400 mg
59	Maldives	2011	-
		2009	-
		2008	Tablet: 400 mg Tablet (dispersible): 150 mg Tablet (scored): 150 mg

			In fixed dose drug combination: 400 mg
60	Mali	2008	300 mg / 500mg In fixed dose drug combination:150 mg / 400 mg
61	Malta	2008	Not mentioned the drug in the list
62	Marshall Islands	2007	500 mg
63	Mauritania		
64	Mexico	2010	-
		2009	500 mg In fixed dose drug combination: 400 mg
65	Mongolia		
66	Montenegro		
67	Morocco	2008	Not mentioned the drug in the list
68	Myanmar	-	500 mg
69	Namibia	2008	500 mg In fixed dose drug combination: 150 mg / 400mg
70	Nauru		
71	Nepal	2009	400 mg In fixed dose drug combination: 150 mg
72	Nicaragua	2011	-
		2009	-
		2001	Not mentioned the drug in the list
73	Nigeria	2010	-
		2003	400 mg
74	Niue	2006	500 mg
75	Oman	2009	500 mg In fixed dose drug combination: 400mg
76	Pakistan	2007	400 mg Tablet (dispersible): 150 mg Tablet (scored): 150 mg In fixed dose drug combination: 150 mg / 400mg / 500 mg
77	Palau	2006	500 mg
78	Papua New Guinea	2002	500 mg
79	Paraguay	2009	400 mg
80	Peru	2010	500 mg

81	Philippines	2008	500 mg Suspensions :250 mg/ 5ml, 60 ml/ 120 ml In fixed dose drug combination: 150 mg/ 300 mg/ 400mg / 500 mg
82	Poland	2009	Not mentioned the drug in the list
83	Republic of Moldova	2009	400 mg / 500 mg In fixed dose drug combination: 150 mg / 400 mg/ 500mg
84	Rwanda	2010	400 mg In fixed dose drug combination: 150 mg / 400 mg
85	Saint Vincent and the Grenadines		
86	Senegal	2008	400 mg In fixed dose drug combination: 150 mg
87	Serbia	2010	Not mentioned the drug in the list
88	Seychelles		
89	Slovakia	2010	Not mentioned the drug in the list
90	Slovenia	2010	Not mentioned the drug in the list
91	Solomon Islands	2010	500 mg In fixed dose drug combination: 400mg
92	Somalia	2007	400 mg / 500 mg In fixed dose drug combination: 400mg / 300- 400mg
93	South Africa	2008	In fixed dose drug combination: 400mg – adult/ 150 mg - children
94	Sri Lanka	2009	500 mg In fixed dose drug combination: 400 mg
95	Sudan	2007	400 mg
96	Suriname	2014	500 mg In fixed dose drug combination: 400 mg
97	Sweden	2016	Not mentioned the drug in the list
98	Syrian Arab Republic	2008	Not given
99	Tajikistan	2009	400 mg In fixed dose drug combination: 400 mg /500 mg
100	Thailand	2012	In fixed dose drug combination: 400 mg

101	The former Yugoslav Republic of Macedonia	2010	500mg
102	Timor-Leste	2004	400 mg In fixed dose drug combination: 400 mg
103	Togo		
104	Tonga	2007	500 mg
105	Trinidad and Tobago	2010	500 mg
106	Tunisia	2008	Not given
107	Tuvalu	2010	4/ 500 mg / 1500mg Tablet (dispersible): 150 mg
108	Uganda	2007	500 mg
109	Ukraine	2010	In fixed dose drug combination: 400 mg /800 mg/ 1200mg / 1600 mg
110	United Republic of Tanzania	2013	In fixed dose drug combination: 275 mg / 400 mg
111	Uruguay	2011	-
		2008	Not given
112	Vanuatu	2007	400 mg
113	Venezuela (Bolivarian Republic of)	2004	400 mg
114	Viet Nam		
115	Yemen	2007	500 mg In fixed dose drug combination: 400 mg
116	Zambia		
117	Zimbabwe	2006	500

1. Documents from some countries were not accessible {those countries are highlighted in green colour]
2. For some countries, recently updated NEMLs was not accessible – Only what is listed in the last available version is given {those countries are highlighted in yellow colour]

May 25th, 2021