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StopTB Partnership's Global Drug Facility FAQs on pretomanid

US FDA approval-related questions

1. What is pretomanid?

Pretomanid is the third new medicine for drug-resistant tuberculosis (DR-TB) to be approved by a stringent regulatory authority in the past decades and the second drug in a class of medicines called nitroimidazoles. Pretomanid was developed by the TB Alliance and is supplied by Mylan. It was approved by the US FDA in August 2019.

2. What are the US FDA approved indications for pretomanid use?

Pretomanid is indicated, as part of a combination regimen with bedaquiline and linezolid (e.g., BPaL), for the treatment of adults with pulmonary TB that is:

- extensively drug resistant (XDR),
- multidrug-resistant (MDR) and intolerant to treatment, or
- MDR-TB that is nonresponsive to treatment

3. Can pretomanid be combined with other TB medicines?

Pretomanid is only approved for use with bedaquiline and linezolid as part of the BPaL regimen. The safety and effectiveness of pretomanid tablets have not been established for its use in combination with other medicines.

4. Where to find full pretomanid prescribing information?

For more information about pretomanid, please refer to the prescribing information:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212862s000lbl.pdf

WHO Rapid Communication on Drug-Resistant TB December 2019 related questions

1. What information is available from WHO on the use of pretomanid?

WHO published a Rapid Communication on key changes to the treatment of drug-resistant tuberculosis in December 2019. This was accompanied by a FAQ document that covers questions related to implementation, procurement, funding and advocacy related to the Rapid Communication. The documents are available here:

- Rapid Communication: https://www.who.int/tb/publications/2019/WHO_RapidCommunicationMDR_TB2019.pdf?ua=1
- FAQ: <https://www.who.int/tb/areas-of-work/drug-resistant-tb/faqs-updated-final-version.pdf?ua=1>

WHO's Rapid Communication states that *"The BPaL regimen may be used under operational research conditions in patients with XDR-TB who have not had previous exposure to bedaquiline and linezolid. This regimen may not be considered for programmatic use worldwide until additional evidence on efficacy and safety has been generated. However, in individual patients for who design of an effective*

regimen based on existing recommendations is not possible, BPaL regimen may be considered as a last resort under prevailing ethical standards."

GDF supply-related questions

1. Is GDF able to supply pretomanid, as part of the BPaL regimen, in alignment with the WHO Rapid Communication?

Yes - GDF can supply pretomanid as part of the BPaL regimen. Programmes procuring pretomanid will be requested to complete a one-page form confirming pretomanid will be implemented in alignment with the WHO Rapid Communication (e.g., only as part of the BPaL regimen and under an operational research protocol or named-patient basis). This form is very similar to the form that was used during the launch of bedaquiline and delamanid.

2. Will GDF be able to supply pretomanid for small orders such as for 1 or 2 treatment courses?

Yes - The manufacturer Mylan has confirmed that small orders, even those for just 1 treatment course, can be procured.

3. Will GDF be able to supply pretomanid for other types of research (e.g., for other regimens besides BPaL)?

Yes - GDF will be able to supply pretomanid for other types of research, such as randomized controlled trials. GDF will work closely with Mylan on any requests to procure pretomanid for use outside of the WHO Rapid Communication. Please contact GDF at gdf@stoptb.org for more information on how to order and what documents need to be provided (e.g., protocol, ethics review, clinical trial registry number, etc.).

4. What is the access price of pretomanid via GDF?

The GDF access price is 2 USD per pretomanid tablet. The total cost of pretomanid for one, six-month treatment course is 364 USD

5. How will pretomanid be supplied?

Pretomanid will initially be available in bottles of 26 tablets, with a shelf-life of 24 months. Seven bottles will be required for one, six-month treatment course.

6. What is the estimated cost of the BPaL regimen via GDF?

The treatment costs for one BPaL regimen, consisting of pretomanid, bedaquiline and linezolid combined, is calculated in Table 1 below. GDF has multiple suppliers of linezolid and the price may vary depending on the supplier quoted with each order.

Table 1 BPaL treatment regimen estimated costs:

<i>Medicine</i>	<i>Cost per medicine in the regimen (USD)</i>
Bedaquiline	425
Linezolid	251
Pretomanid	364
Treatment cost (USD)	1040

*- based on GDF weighted average tablet price

7. The BPAL regimen requires both bedaquiline and linezolid in addition to pretomanid. Can StopTB's GDF provide all the medications?

Yes - all of the medications are available from GDF.

- More information on planning orders with GDF, including lead-times, is available here: <http://stoptb.org/gdf/placeOrder.asp>
- More information on products supplied by GDF is available in the product catalogue here: http://stoptb.org/gdf/drugsupply/drugs_diagnostics.asp
- Please note that the duration of bedaquiline use in the BPAL regimen is 26 weeks and a total of 200 tablets. Bedaquiline is currently available in bottles of 188 tablets. Programmes may need to consider ordering two bottles of bedaquiline per treatment course of BPAL.

8. Is there a pretomanid donation program?

No. There is no donation programme available from the GDF.

9. Will the Global Fund support introduction of pretomanid?

Yes - Global Fund will support introduction of pretomanid once there is a WHO recommendation on pretomanid and the BPAL regimen. If a Principal Recipient would like to access pretomanid, please contact the Fund Portfolio Manager.

10. What is the list of countries eligible to procure pretomanid via GDF at the access price?

There are 150 countries and territories eligible for the access price when procuring via GDF. Please refer to the Table 2 below.

Table 2. 150 countries and territories eligible for the access price when procuring via GDF

1	Afghanistan
2	Albania
3	Algeria
4	American Samoa
5	Angola
6	Argentina
7	Armenia
8	Azerbaijan
9	Bangladesh
10	Belarus
11	Belize
12	Benin
13	Bhutan
14	Bolivia
15	Bosnia and Herzegovina
16	Botswana
17	Brazil
18	British Virgin Islands
19	Bulgaria
20	Burkina Faso
21	Burundi
22	Cabo Verde
23	Cambodia
24	Cameroon
25	Central African Republic
26	Chad
27	Chile
28	Colombia
29	Comoros
30	Congo, Dem. Rep.
31	Congo, Rep.
32	Costa Rica
33	Côte d'Ivoire
34	Cuba
35	Djibouti
36	Dominica
37	Dominican Republic
38	Ecuador
39	Egypt, Arab Rep.
40	El Salvador
41	Equatorial Guinea
42	Eritrea

43	Estonia
44	Ethiopia
45	Fiji
46	Gabon
47	Gambia, The
48	Georgia
49	Ghana
50	Gibraltar
51	Grenada
52	Guatemala
53	Guinea
54	Guinea-Bissau
55	Guyana
56	Haiti
57	Honduras
58	Hungary
59	India
60	Indonesia
61	Iran, Islamic Rep.
62	Iraq
63	Jamaica
64	Jordan
65	Kazakhstan
66	Kenya
67	Kiribati
68	Korea, Dem. People's Rep.
69	Kosovo
70	Kyrgyz Republic
71	Lao PDR
72	Latvia
73	Lebanon
74	Lesotho
75	Liberia
76	Libya
77	Lithuania
78	Macedonia, FYR
79	Madagascar
80	Malawi
81	Malaysia
82	Maldives
83	Mali
84	Marshall Islands
85	Mauritania

86	Mauritius
87	Mexico
88	Micronesia, Fed. Sts.
89	Moldova
90	Mongolia
91	Montenegro
92	Morocco
93	Mozambique
94	Myanmar
95	Namibia
96	Nauru
97	Nepal
98	Nicaragua
99	Niger
100	Nigeria
101	Northern Mariana Islands
102	Oman
103	Pakistan
104	Palau
105	Panama
106	Papua New Guinea
107	Paraguay
108	Peru
109	Philippines
110	Romania
111	Rwanda
112	Samoa
113	São Tomé and Príncipe
114	Saudi Arabia
115	Senegal
116	Serbia
117	Seychelles
118	Sierra Leone
119	Solomon Islands
120	Somalia
121	South Africa
122	South Sudan
123	Sri Lanka
124	St. Lucia
125	St. Vincent and the Grenadines
126	Sudan
127	Suriname
128	Swaziland

129	Syrian Arab Republic
130	Tajikistan
131	Tanzania
132	Thailand
133	Timor-Leste
134	Togo
135	Tonga
136	Tunisia
137	Turkey
138	Turkmenistan
139	Tuvalu
140	Uganda
141	Ukraine
142	United Arab Emirates
143	Uzbekistan
144	Vanuatu
145	Venezuela, RB
146	Vietnam
147	West Bank and Gaza
148	Yemen, Rep.
149	Zambia
150	Zimbabwe