31 March 2023

Secretary of the Expert Committee on the Selection and Use of Essential Medicines
Department of Essential Medicines and Health Products
World Health Organization
20 Avenue Appia
CH-1211, Geneva 27, Switzerland

Re. Statement in support of including Pretomanid, 200mg tablet, in the World Health Organization Model List of Essential Medicines
关于支持将 Pretomanid，200mg tables，加入世界卫生组织《基本药物标准清单》的声明

Dear Expert Committee:
尊敬的专家委员会:

Shenyang Hongqi Pharmaceutical Co., Ltd （Hongqi）submits this letter in support of adding a 200 mg tablet formulation of pretomanid to the World Health Organization (WHO) Model List of Essential Medicines (EML) for the treatment of tuberculosis (TB). Shenyang Hongqi Pharmaceutical Co., Ltd. was founded in 1964. Since the 1980s, it has focused on the R&D, production, sales and service of tuberculosis drugs. After more than three decades of unremitting efforts, it has become the largest R&D and production base of anti tuberculosis drugs in China, providing high-quality drugs and services for more than 13 million tuberculosis patients.
沈阳红旗制药有限公司提交此信支持将 Pretomanid tables 200mg 配方添加到世界卫生组织(WHO)用于治疗结核病的基本药物标准清单(EML)中。红旗成立于 1964 年，从 80 年代起专注于抗结核药物的研发、生产、销售与服务，经过三十余年不懈努力已成为中国最大的抗结核药品研发和生产基地，为超过 1300 万例结核病患者提供了优质的药品与服务。

The new tuberculosis drug PA-824 developed by the non-profit organization TB Alliance passed the FDA review and came into the market in 2019, and formed the BPaL regimen with bedaquiline and linezolid for the treatment of adults with what was then defined as pulmonary extensively drug-resistant (XDR-TB), treatment- intolerant or nonresponsive multidrug resistant tuberculosis (MDR-TB). Pretomanid has currently been approved by the European Drug Administration, South Korea, India, South Africa, Tajikistan, and more than 10 countries, and has been pre approved by WHO. It has started to be supplied to more than 35 countries worldwide.
由非营利组织 TB Alliance 研发的新型结核药物 PA-824 于 2019 年通过 FDA 审评上市，与贝达喹啉和利奈唑胺组成 BPaL 方案治疗当时被定义为广泛耐药结核病(XDR-TB)或无法耐受治疗/疗效欠佳的耐多药结核病(MDR-TB)患者。 Pretomanid 目前已通过欧洲药品管理局、韩国、印度、南非、塔吉克斯坦等 10 多个国家审批，并通过了 WHO 的预认可，开始在全球超过 35 个国家供应。

Nix-TB is an open label phase III single arm clinical trial conducted in South Africa, mainly to

evaluate the safety and effectiveness of the BPaL regimen in refractory drug-resistant pulmonary tuberculosis. The Nix-TB results show that the BPaL regimen has a good therapeutic effect on refractory drug-resistant pulmonary tuberculosis. Of the 109 patients treated with the BPaL regimen (71 cases of extensive drug resistance and 38 cases of refractory multidrug resistance), 98 patients were cured and did not relapse after 2 years of follow-up, The cure rate was 90% (95% CI: 83%～95%). ZeNix (NC007) is a partially blind randomized clinical trial designed to evaluate the safety and effectiveness of bedaquiline, pretomanid, and different doses of linezolid (BPaL) in patients with refractory drug-resistant pulmonary tuberculosis. After adjusting the dose of linezolid, the treatment success rate was similar to that of Nix-TB research. The treatment success rates of 1200mg for 6 months, 1200mg for 2 months, 600mg for 6 months, and 600mg for 2 months were 93%, 89% ,91% and 84%, but the group treated with 1200 mg for 6 months experienced more peripheral neuropathy and anemia, with the incidence rates of 38% and 22%, respectively. The other three groups experienced 24% and 17%, 24% and 2%, 13% and 7%, respectively, indicating that the 6-month regimen of linezolid 600 mg has better therapeutic efficacy and better safety.

Nix-TB 是在南非进行的一个开放标签的III期单臂临床试验，主要是在难治性耐药肺结核中评估 BPaL 方案的安全性和有效性，Nix-TB 结果表明，BPaL 方案对于难治性耐药肺结核具有很好的治愈效果，在接受 BPaL 方案治疗的 109 例受试者（广泛耐药 71 例、难治性耐多药 38 例）中，98 例患者被治愈并在随访 2 年后未复发，治愈率达 90%（95%CI：83%～95%）。ZeNix（NC007）是一个部分盲法的随机临床试验，主要是在难治性耐药肺结核患者中评估贝达喹啉、Pretomanid 和不同剂量的利奈唑胺（BPaL）的安全性和有效性，调整利奈唑胺剂量后得到了与 Nix-TB 研究相似的治疗成功率，1200mg 治疗 6 个月、1200mg 治疗 2 个月、600mg 治疗 6 个月和 600mg 治疗 2 个月治疗成功率为 93%、89%、91%和 84%，但 1200mg 治疗 6 个月组出现了更多的外周神经病变和贫血，发生比例分别为 38% 和 22%，其余三组发生外周神经病变和贫血的比例依次为 24%和 17%、24%和 2%、13%和 7%，说明利奈唑胺 600mg 应用 6 个月的方案具有更好的治疗效果和更好的安全性。

TB-PACTECAL is a multicenter, open label, multi group, randomized, controlled, multi-stage, 2-3 phase trial, which evaluated the short-term treatment regimen containing bedaquiline and pretomanid in combination with existing and reused anti tuberculosis drugs (such as linezolid and clofazimine) to treat microbial confirmed MDR/RR-TB patients, and the 6-month BPaLM regimen consisting of bedaquiline, pretomanid, linezolid (600mg) and moxifloxacin, It is possible to replace the 9-month or long-term (>18 months) regimen in MDR/RR-TB patients ≥ 15 years of age who have no previous exposure to bedaquiline, pretomanid, and linezolid (defined as drug exposure>1 month).

TB-PACTECAL 是一项多中心、开放标签、多组、随机、对照、多阶段、2-3 期试验，评估了含有贝达奎林和 Pretomanid 的短期治疗方案与现有和重新利用的抗结核病药物（如利奈唑胺和氯法齐明）联合治疗微生物证实的 MDR/RR-TB 患者，由贝达喹啉、Pretomanid、利奈唑胺（600mg）和莫西沙星组成的 6 个月 BPaLM 方案，可以在≥15 周岁既往无贝达喹啉、Pretomanid 和利奈唑胺暴露史（定义为药物暴露＞1 月）的 MDR/RR-TB 患者中替代 9 个月或长程（＞18 个月）方案。

The low detection rate and treatment success rate of multidrug-resistant tuberculosis are the biggest obstacles to tuberculosis control. The course of treatment for multidrug-resistant

tuberculosis lasted for 9 to 24 months, with serious adverse drug reactions and poor patient treatment compliance. Some patients could not choose effective treatment schemes with second-line anti tuberculosis drugs due to their extensive drug resistance spectrum, resulting in high mortality. The BPaL regimen has been recommended by WHO and BPaLM regimen in the 2022 update. The regimen is the last life-saving method for MDR/RR-TB pulmonary tuberculosis patients who cannot construct an effective treatment regimen and whose lives are seriously threatened, demonstrating the extreme importance of this regimen.
耐多药结核病发现率低、治疗成功率低，是结核病控制的最大障碍。耐多药结核病治疗疗程长达 9~24 个月、药物不良反应重、患者治疗依从性差，部分患者因耐药谱广泛，不能选择二线抗结核药物组成有效的治疗方案，导致死亡率高。BPaL 方案已被 WHO 推荐，并在 2022 年 update 中升级为 BPaLM 方案，方案对于那些无法构建有效治疗方案且生命受到严重威胁的 MDR/RR-TB 肺结核患者是最后挽救生命的办法，说明了该方案的极其重要性。

Thank you for the opportunity to share our views on the importance of adding the Pretomanid 200 mg tablet to the WHO EML. If you need additional information on our support of this application, please contact Frank Liu,frank.liu@hongqipharma.com.
感谢有机会分享我们对将 Pretomanid 加入世卫组织 EMLc 的重要性的看法。如果您需要更多关于我们支持这一申请的信息，请联系刘亚洲，frank.liu@hongqipharma.com.

Respectfully submitted,
此致,

Bo Yang
杨波
Chairman of the Board
董事长
Shenyang Hongqi Pharmaceutical Co., Ltd
沈阳红旗制药有限公司