



theAlfred

12 March 2025

**WHO Essential Medicines List
EML Secretariat
emlsecretariat@who.int**

Dear WHO Essential Medicines List Committee,

I write to support the listing of zanubrutinib on the WHO EML list for treatment of CLL/SLL both in the frontline and a relapsed/ refractory setting.

I am a Haematologist and a Specialist treating CLL/SLL ("CLL") based in Australia, with a leadership position in the use of novel therapies for CLL, I have extensive links with colleagues treating this disease internationally including Singapore, Taiwan, China, Thailand, as well as Philippines and Saudi Arabia. I have also personally seen the transition of CLL treatment from chemo-immunotherapy to the age of BTK inhibitors for the treatment of CLL. We have seen at least in western countries a marked improvement in the patients with CLL with the introduction of ibrutinib. Zanubrutinib is a next generation BTKi that I have extensive personal experience with, having developed the drug in the phase 1 setting, and having led several phase 3 studies. The purpose of the zanubrutinib development program was to provide a safer alternative to ibrutinib, and this improved safety is now confirmed across 2 Phase 3 studies (one in Waldenström's macroglobulinaemia and one in CLL) demonstrating improved cardiovascular safety, in particular a greatly reduced risk of atrial fibrillation (a troublesome and treatment limiting side effect of ibrutinib). Additionally, ibrutinib is associated with a risk of fatal ventricular arrhythmias and there is accumulated evidence to suggest that zanubrutinib may be less likely to cause this devastating complication. In terms of efficacy, zanubrutinib has been shown in head to head studies against ibrutinib to be more effective in the relapsed refractory CLL setting. In the frontline setting zanubrutinib has been compared against the best standard of care chemotherapy, and it has been shown to be superior.

In conclusion, zanubrutinib is an improved version of ibrutinib with greater efficacy and reduced side effects. I strongly support its inclusion in the WHO EML List.

Yours sincerely,

Electronically checked & authorised

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