Ziihera

Procedural steps taken and scientific information after the authorisation*

*Due to the Agency`s update of its procedure management systems, an additional document, reflecting the historical lifecycle may be available in the 'Assessment history' section. For the complete product lifecycle procedures, you may need to also refer to **EPAR - Procedural steps taken and scientific information after authorisation (archive)**.

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
Variation type II / EMA/VR/0000316398	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the	21/05/2026		SmPC	Section 5.1 Pharmacodynamic properties of the SmPC Immunogenicity […] ADA were rarely detected. Zanidatamab is categorised as a low-risk

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of sections 5.1, and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from study ZW25-ZW1-101 and PopPK analysis. Study 101 is a phase 1 trial of ZW25 in patients with locally advanced (unresectable) and/or metastatic HER2-expressing cancers. In addition, the MAH took the opportunity to introduce editorial changes to the PI.				molecule to elicit an immune response on the basis of assessment of the immunogenicity risk factors and the low incidence of ADA observed in Study 203 (1.2% [1 of 85 evaluable participants]). No evidence of ADA impact on pharmacokinetics, efficacy or safety was observed, however, data are limited. Section 5.2 Pharmacokinetic properties of the SmPC Zanidatamab PK exhibited non-linear kinetics with more rapid clearance (CL) at low doses ranging from 5 to 30 mg/kg. Following the first dose, the geometric mean zanidatamab Cmax was dose proportional with increasing doses, while total systemic exposure (AUC0-∞) was greater than dose proportional with increasing doses. The geometric mean Ctrough accumulation ratio of zanidatamab is approximately 2.4. The observed zanidatamab exposure and PK parameters following the first administration in the first cycle and steady state, based on the available sampling scheme, are described in Table 7. The pharmacokinetics of zanidatamab following intravenous infusion in participants with HER2 expressing cancers was evaluated in a population pharmacokinetic (PopPK) model analysis from 279 participants. From the PopPK analysis, participants with BTC were predicted to have a typical CL of 0.0110 L/h, a typical volume of distribution of the central compartment (Vc) of 3.22 L, a typical volume of distribution of the peripheral compartment (Vp) of 3.20 L, and an estimated t½ of approximately 19 days. Based on the estimated t½, it would take approximately 3.2 months (i.e., 5 half-lives) to

					reach steady state following multiple dose administration of zanidatamab. […] Distribution Following intravenous dosing, zanidatamab undergoes biphasic elimination from the circulation. Based on population pharmacokinetic analysis, participants with HER2 amplified BTC were predicted to have a typical Vc of 3.22 L and a typical Vp of 3.20 L. Elimination Based on population pharmacokinetic analysis, participants with BTC were predicted to have a typical CL of 0.0110 L/h and an estimated t1/2 of approximately 19 days for zanidatamab administered at 20 mg/kg every 2 weeks at steady-state. For more information, please refer to the Summary of Product Characteristics.
Variation type IB / EMA/VR/0000315901	Outcome: B. QUALITY CHANGES - B.z Other variation - Accepted	06/01/2026			
Variation type IB / EMA/VR/0000314733	Outcome: This was an application for a group of variations. B.I.d.1.a Re-test period/storage period - B.I.d.1.a.4 Extension or introduction of a re-test period/storage period supported by real time data - Accepted B.II.f.1.b Extension of the shelf life of the finished product - B.II.f.1.b.1 As packaged for sale (supported by real time data) -	17/12/2025		SmPC and PL	

	Accepted				
Variation type IB / EMA/VR/0000308496	Outcome: B.I ACTIVE SUBSTANCE - B.I.z Other variation - Accepted	17/11/2025			
Variation type IB / EMA/VR/0000283742	Outcome: B.I.a.2 Changes in the manufacturing process of the active substance - B.I.a.2.z Other variation - Accepted	11/07/2025			