

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
July 12, 2016**

Page #	Section/Item	Edits (Changes in Bold , Deletion in Strikeout)	Rationale
7	Last Paragraph	The ABP 501 drug product was developed as a single-use pre-filled syringe (PFS) and a single-use autoinjector (AI) in a strength approved for US-licensed Humira (i.e. 20 mg/0.4 mL and 40 mg/0.8mL for the PFS, and 40 mg/0.8 mL for the AI); it also has the same dosage form and route of administration as those approved for US-licensed Humira.	Clarification for completeness. Three presentations were developed for ABP 501: <ul style="list-style-type: none"> • 20 mg/0.4 mL PFS • 40 mg/0.8mL PFS • 40 mg/0.8 mL AI
10	Executive Summary (3 rd bullet point)	A comparative clinical study (Study 262) between ABP 501 and EU-approved US-licensed Humira in patients with RA to support a demonstration of no clinically meaningful differences in terms of safety, purity, and potency.	Typographical error. Study 262 used ABP 501 and US-licensed Humira in the study.
11	2 nd paragraph	Review of an extensive battery of test results provided by Amgen confirmed the adequacy of the scientific bridge and hence the relevance of comparative clinical and non-clinical data with EU-approved Humira to support a demonstration of biosimilarity to US-licensed Humira.	Typographical error. EU-approved Humira was not used in ABP 501 nonclinical studies.
11	3 rd paragraph	Specifically, the results from the comparative clinical efficacy, safety, and PK studies, which included a spectrum of chronic dosing regimens of ABP 501 and EU-approved US-licensed Humira (40 mg Q2W SC on the background of methotrexate,) for Study 262 and EU-approved Humira with a loading dose of 80 mg on Day 1,	Typographical error. US-licensed Humira was used in Study 262 and EU-approved Humira was used in Study 263.

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
July 12, 2016**

		followed by 40 mg Q2W SC starting one week later as monotherapy) for Study 263.	
13	Executive Summary	Secondly, a comparison of US licensed Humira, EU-approved Humira and ABP 501 was needed to establish the analytical component of the scientific bridge to justify the relevance of data generated using EU-approved Humira as the comparator in some clinical and nonclinical studies.	Clarification that EU-approved Humira was not used in ABP 501 nonclinical studies.
16	ABP 501 Manufacturing: 2 nd paragraph	The ABP 501 drug product was developed as a single-use pre-filled syringe or a single use autoinjector in some of the same strengths approved for US-licensed Humira (i.e. 20 mg/0.4 mL and 40 mg/0.8mL for the PFS, and 40 mg/0.8 mL for the AI);	Clarification that three presentations were developed for ABP 501: <ul style="list-style-type: none"> • 20 mg/0.4 mL PFS • 40 mg/0.8mL PFS • 40 mg/0.8 mL AI
18	2 nd paragraph	Pairwise comparisons of ABP 501, US-licensed Humira, and EU-approved Humira were used to support the analytical portion of the scientific bridge between the three products to justify the relevance of the comparative data generated using EU-approved Humira from some clinical and nonclinical studies.	Clarification that EU-approved Humira was not used in ABP 501 nonclinical studies.
19	Table 3	Quality Attribute: Bioassay/ mechanism of action Exploration Delete the bullet point that states: Induction of regulatory macrophages	Clarification as macrophage induction is inferred from T-cell proliferation already listed.

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
July 12, 2016**

19	Table 3	Microflow Fluid Imaging	Typographical error
27	1 st paragraph	Further, these analyses support the analytical component of the scientific bridge between US-licensed Humira, EU-approved Humira and ABP 501 to justify the relevance of comparative data generated from clinical and non-clinical studies that used EU-approved Humira.	Clarification that EU-approved Humira was not used in ABP 501 nonclinical studies.
29	1 st paragraph	Further, these analyses support the analytical component of the scientific bridge between US-licensed Humira, EU-approved Humira and ABP 501 to justify the relevance of comparative data generated from clinical and non-clinical studies that used EU-approved Humira.	Clarification that EU-approved Humira was not used in ABP 501 nonclinical studies.
31	3 rd paragraph	To evaluate binding to FcγRIIIa (158V), the high affinity FcγRIIIa receptor, 10 lots of ABP 501, 40 17 lots of US-Approved Humira, and 40 15 lots of EU-licensed Humira were used.	Typographical error
31	Table 8	Binding (SPR) (AlphaLISA)	Error in description
31	3 rd paragraph	Summarized d in Peak et al., 2013	Typographical error

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
July 12, 2016**

35	Figure 9	<p style="text-align: center;">◆ US-Licensed Humira ● ABP 501 ▲ EU-Approved Humira</p>	Figure 9 was a duplicate of as Figure 8. Corrected figure attached.
37	Caption Figure 11	Figure 11. Comparison of Binding Affinity to mTNF-α Inhibition of Proliferation in a Mixed Lymphocyte Reaction for ABP 501, US-licensed Humira, and EU-approved Humira	Figure 11 caption was a duplicate of Figure 10
38	2 nd paragraph	Microflow imaging (MFI) and light obscuration (HAIG) (HIAC)	Typographical error
38	2 nd paragraph	The Applicant pooled-drug substance used a pooling approach to create 5 additional lots of drug product to supplement the 10 drug product lots generated from unique drug substance lots. to create additional lots of drug product in order to generate additional lots of material. drug product to supplement the 10 drug product lots generated from unique drug substance lots.	Clarification for how drug product lots were created.
38	2 nd paragraph	Similar results were observed for all products based on a quality range analysis.	Clarification that Subvisible particles were assigned to Tier 3 for testing and did not have a quality range with the exception

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
July 12, 2016**

			of $\geq 5 \mu\text{m}$ non-spherical particles.
39	Last paragraph	Amgen provided a sufficiently robust analysis for the purposes of establishing the analytical component of the scientific bridge among the three products to justify the relevance of comparative data generated from clinical and nonclinical -studies that used EU-approved Humira, to support a demonstration of biosimilarity of ABP 501 to US-licensed Humira.	EU-approved Humira was not used in ABP 501 nonclinical studies.
41	1 st bullet point for Description of Relevant Clinical Pharmacology Studies	Study 217 was a randomized, double-blind single-blind , three-arm, parallel-group study following a single 40-mg/0.8 mL SC injection via 1-mL PFS to compare the PK, safety, tolerability, and immunogenicity of ABP 501, EU-approved Humira, and US-licensed Humira in healthy subjects (N=67-69/arm).	Typographical error. Study 217 was a single-blind study.
42	3 rd bullet point for Study 263	Trough serum concentrations were assessed for comparison between ABP 501 and EU-approved Humira in PSsO patients.	Typographical error. PS changed to PsO.
50	1 st paragraph (discussion on the Similarity Margin)	The Applicant pre-specified a similarity margin of (0.74 38 , 1/0.74 38) with respect to the risk ratio and provided a justification for the margin based on historical data from one randomized clinical trial of adalimumab (Keystone 2004) ²⁶ and the goal of preserving at least 50% of the effect size of US-licensed Humira. The Agency does not agree with the Applicant's selection of historical studies,	Typographical error. Edits to correct for typographical errors in the margins. The pre-specified margin for Study 262 is (0.738, 1/0.738).

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
July 12, 2016**

		<p>as three important studies were not included in the meta-analysis. The Agency also does not agree with the proposed 0.7438, 1/0.7438) margin. Instead, FDA recommends the use of the absolute difference scale, as this scale is considered important from a clinical perspective for an evaluation of benefit risk in clinical trials in RA. The Agency also recommends a margin of $\pm 12\%$.</p>	
55	1 st paragraph	<p>One notable difference was the allowance of anti-TNF experience. The historical placebo-controlled trials did not allow anti-TNF experience while the comparative clinical study allowed it (although the proportion was relatively small at 28%). Estimated treatment effects with respect to ACR20 for the four historical trials were displayed earlier in Table 4-11. The estimated effects ranged from 21% to 53% on the absolute difference scale, with an overall estimated effect size of 35%. Thus, the information in Tables 4-11 and 8 18 (on page 56) indicates that...</p>	<p>Table 1 changed to Table 11 to refer to the correct table. Table 8 changed to Table 18 (on page 56) refer to the correct table. Tables were not adequately captioned.</p>
65	1 st paragraph under Overall Conclusion on Efficacy	<p>In summary, the Applicant has provided statistically robust comparative clinical data demonstrating similar efficacy between ABP 501 and EU-approved US-licensed Humira in patients with moderate-to-severe RA despite methotrexate, using 40 mg Q2W SC dosing on background methotrexate, and between ABP 501 and EU-approved Humira in patients with moderate-to-severe PsO, using a loading dose of 80 mg on Day 1, followed a week later by 40 mg</p>	<p>Typographical error. Study 262 used US-licensed Humira in the trial. Study 263 used EU-approved Humira in the study.</p>

**Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
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Q2W SC dosing as a monotherapy.			
67	Table 27, Study 263 columns	USEU -ADA	Typographical error. Study 263 used EU-approved Humira in the study.
74	Table 29, Study 263, Through Week 16 Column	USEU -ADA	Typographical error. Study 263 used EU-approved Humira in the study.