From: [redacted]
To: [redacted]
Cc: [redacted]
Subject: RE: Request for clinical comment - BRALTUS - tiotropium bromide inhalation PM-2017-03103-1-5 [DLM=For-Official-Use-Only]
Date: Thursday, 9 August 2018 4:23:36 PM
Attachments: image001.png

Hi [redacted]

As mentioned, I have discussed with [redacted] re: Braltus submission. Below are our suggestions:

- Vcaps: Since it has been clarified that the product comes with Vcaps as the only option, we suggest that in the PI, it needs to be stated as "Braltus Vcaps", instead of "Braltus capsules" at all places that it has been mentioned; particularly in the Presentation and storage section, under the heading Braltus powder for inhalation in capsules. This will enable prescribers to have a clearer impression that Braltus is available only in Vcaps.
- As per the information on National Asthma Council of Australia website, the LAMA medications are presented with a green coloured device. In that aspect green colour for the device: "Zonda inhaler" is considered reasonable. No other inhalers were found with identical presentation/shape. https://assets.nationalasthma.org.au/resources/MSC1551-NAC-Asthma-COPD-Medications-Chart-2018_HR_Internal.pdf
- From a clinical perspective, the sponsor's response to justify the use of two capsules of test and reference products in pivotal study seems adequate. The initial studies CLL 11002 and CLL 12003 were with the primary objective of estimating the bioavailability of tiotropium. Both these studies utilised Tiotropium 13mcg and 18 mcg one capsule as the dose. There was greater variability in the PK parameters as a greater proportion of the measured values were below the LLOQ for sensitivity of the assay. In this aspect, utilising two capsules of each test and reference products to achieve a measurable systemic level of tiotropium is considered acceptable.

Best Regards

[redacted]

From: [redacted]
Sent: Friday, 3 August 2018 4:07 PM
To: [redacted]
Subject: Request for clinical comment - BRALTUS - tiotropium bromide inhalation PM-2017-03103-1-5 [DLM=For-Official-Use-Only]

Good afternoon,

[redacted] is the PCS delegate for this submission and while [redacted] is on leave I am acting for [redacted]

I have been reviewing the responses received for the above submission and would like to get your opinion on the following issues:

Labelling
I note that in your second round report that you share PCS' concerns that dosing confusion

might result as a consequence of the presentation of the product strength on the labels compared to the innovator product.
PCS will be recommending that the BRALTUS labels should also include the delivered dose of tiotropium. For example, "Each capsule contains 13 micrograms of tiotropium (as bromide) and will deliver 10 micrograms of tiotropium".

1. Do you think that any further statements are warranted on the BRALTUS labels? (e.g. Braltus and Spiriva deliver the same dose (10 micrograms))

I note that the company provides quite a justification for the proposed labelling in their response to Q.2 of the S31. Additionally, this justification states that 'educational material for HCPs will be aimed at providing information related to the BE between Braltus and Spiriva; in spite of the difference in the quantity of API.' A DHCP letter has been included in the response, which appears to be the version for distribution in Ireland. The company does note that a similar one will be distributed in Australia prior to launch.

2. I will be asking for the proposed AU version to be provided, is there any objection to a similar DCHP letter being supplied in Australia? Should any further information be included?

Product Information

I note your comments made in your Rd 2 report under PI considerations.

3. The company has proposed to use only one type of capsule (vegetarian Vcaps capsules) and so I am unclear how best to address your concerns numbered 3 & 4. Could you please clarify?

Device

For you information, I consider that the in vitro information provided is satisfactory to demonstrate that the EU and AU reference products are the same.
The sponsor was asked to provide a justification for using different colours on the proposed delivery device compared to the AU reference product.

4. Are the company's responses acceptable from a clinical perspective (Q.23)?

Bioequivalence study

The bioequivalence study CLL13002 involved a single dose of two capsules. It was unclear why two capsules were used as the PI recommends a single capsule once per day. The sponsor has provided a justification for why the results of this bioequivalence study can be relied upon.

5. Do you have any concerns relating to the company's response (Q.27)?

For your information the Round 1 and 2 (draft) PCS reports are: D18-10408790 and D18-10785551.

Thank you in advance,

[redacted]
[redacted] Pharmaceutical Chemistry Section
Scientific Evaluation Branch | Medicines Regulation Division

Health Products Regulation Group
Australian Government Department of Health

[redacted]

PO Box 100, Canberra ACT 2601, Australia

The Department of Health acknowledges the traditional owners of country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and their cultures, and to elders both past and present.