Braltus
Response to File Note:
19 September 2018

BRALTUS
Tiotropium (as bromide) Powder for Inhalation
13 microgram

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RMP Evaluation (TRIM D18-10969662)

Recommendation 1

To ensure adequate counselling for patients, it is recommended that the following advice is added to the DHPC:

> *Each box of BRALTUS contains a new ZONDA inhaler and inhalation capsules. Patients being switched from SPIRIVA must use the ZONDA inhaler with BRALTUS to deliver the intended dose. The ZONDA inhaler should be discarded after 30 uses.*

Response:

The advice has been added to the *Direct Healthcare Professional Communication* letter (dated 25 September 2018).

Recommendation 2

The proposed [redacted] *the distribution list.*

Response:

The sponsor accepts the recommendation to include [redacted] on the distribution list.

Recommendation 3

The sponsor should provide its implementation plan for the DHPC. The following aspects should be included:

a. *Planned delivery time frame;*
b. *How will the list of individual recipients be obtained to ensure the intended recipients are included;*
c. *How will the DHPC be delivered electronically? If the DHPC is to be delivered by email, delivery and read receipts should be requested.*

Response:

[redacted]

timing will align with the effective PBS listing date. [redacted]

In the event that there is a need to substantially revise the distribution method between now and the planned launch date, we are agreeable to resuming this discussion with the RMP section if required.

Recommendation 4

It is noted that unlike the instructions for use provided in the CMI for SPIRIVA, no instructions on cleaning with water have been provided for BRALTUS. It is unclear whether this is because the ZONDA device is not expected to be reused for more than 30 times and therefore, does not require water cleaning. The sponsor should provide clarification as to whether the ZONDA device can be cleaned and rinsed with water. Advice on/against water cleaning should be provided in both 'Information for the patient' and the CMI to ensure adequate maintenance of the device

Response:

In-vitro studies have shown that the product is robust throughout the use of 30 capsules; the device should then be discarded and not reused. Therefore, there are no cleaning requirements associated to this product.

The 'Information to the patient' and CMI has been amended to state that the device should not be cleaned with water see Module 1.3.1 and Module 1.3.2.

Recommendation 5
The delegate has made a specific request for advice from the RMP evaluator on the following matter:

We (PCS) would prefer that the delivered dose was displayed in a more prominent location in addition to the metered dose. See below for an example:

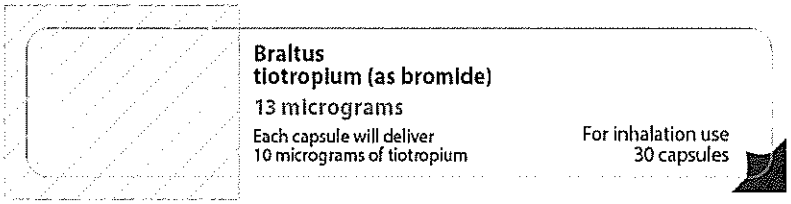
'Braltus

Tiotropium (as bromide) 13 microgram metered dose

Tiotropium (as bromide) 10 microgram delivered dose'

The RMP evaluator supports the proposed label change to show the delivered dose in addition to the metered dose to avoid confusion. However, it has been noted that the DHPC states '13 microgram' as 'pre-metered dose' whilst the label states '13 microgram' as 'metered dose'. It is recommended that the term is used consistently to avoid confusion.

Label

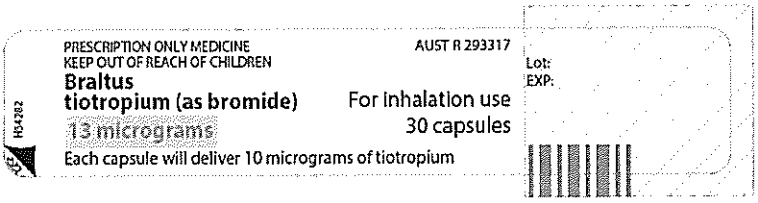


In relation to the bottle, it is unclear how each of the three labels will be displayed. Could the sponsor please clarify this.

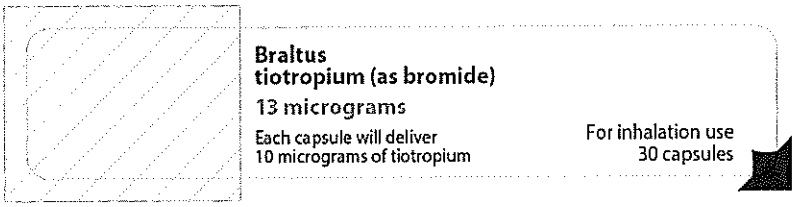
Response
The artwork has been amended so that the delivered dose is displayed in a more prominent location in addition to the metered dose, see Module 1.3.3.

In relation to the bottles, please find an explanation on how the labels will be displayed. The three labels are superimposed, most similar to a little book. This is the position:

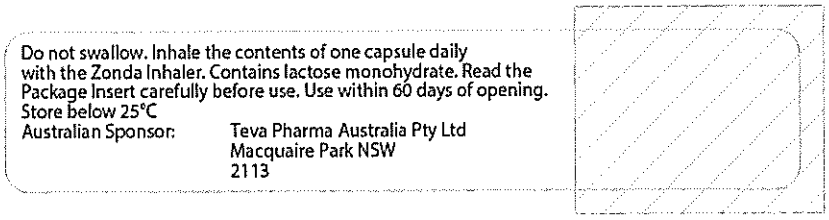
The first position



The second position
If you remove it, you will see the second label.



The third position
If you remove it, you will see the third label.



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page 4, BRALTUS pharmacokinetic profile:

For inhaled products, the amount of drug delivered is dependent upon the formulation and the device used. Please include the trade name and the name of the delivery device for the reference product.

page 19 and 1 NAME

Please include the statement: 'BRALTUS is a generic version of SPIRIVA' and relocate the statement "BRALTUS and SPIRIVA both deliver 10 micrograms of tiotropium bromide" from the Dosage and administration section to the NAME OF

MEDICINE section. I acknowledge that this is not a usual requirement for a generic. However, BRALTUS has a number of features not typical of a generic.

Page 1 and 20

The description of the Vcap under presentation and description remains confusing. It reads as the Vcaps are an excipient. Please clarify that the outer capsule is known as a Vcap and describe what it is made of. Please clarify if the capsule shell is inhaled or remains in the device.

Response

The PI has been updated with the above recommendation, See Module 1.3.1 (version 0.4).

The amendments have also been made to the PI presented in the TGA's preferred new format.

Health care provider letter

Please use metered dose rather than pre-metered dose for consistency.

Please respond to the RMP evaluator's recommendations.

Response
The *Direct Healthcare Professional Communication* letter has been updated to use metered dose rather than pre-metered dose.

The Sponsor had accepted all of the recommendations from the RMP evaluator.

CMI

Please respond to the RMP evaluator's recommendations

Response
The Sponsor has accepted the recommendations from the RMP evaluator. The 'Information to the patient' and CMI and has been amended to state that the device should not be cleaned with water see Module 1.3.1 and Module 1.3.2.

Date: TBC (aproximate to launch)

DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

BRALTUS® tiotropium (as bromide) powder for inhalation, hard capsule, 13 micrograms

Delivered dose is 10 micrograms of tiotropium per capsule

Dosing guidance for BRALTUS® (bioequivalent to SPIRIVA®) –

Advice to minimise the risk of medication error between the two medicines

Dear Healthcare Professional,

The above referenced product, BRALTUS® tiotropium (as bromide) powder for inhalation, hard capsule 13 microgram has been registered in Australia based on established bioequivalence to the innovator product, Spiriva® (tiotropium) capsules.

The indication for BRALTUS is the same as that of SPIRIVA, for the long term maintenance treatment of bronchospasm and dyspnoea associated with chronic obstructive pulmonary disease (COPD) and for the prevention of COPD exacerbations

In agreement with the Therapeutic Goods Administration, Teva Pharma Australia Pty Ltd is sending this communication in order to highlight differences in how the active ingredient content is presented on the BRALTUS (tiotropium) label and Product Information compared to that of Spiriva (tiotropium) capsules.

- Should prescribers make a decision to switch patients between the originator product (SPIRIVA® - tiotropium bromide) and BRALTUS, it is important that the dosing instructions are correctly understood. This letter highlights the correct use of the new product.
- Each box of BRALTUS contains a new ZONDA inhaler and inhalation capsules. Patients being switched from SPIRIVA must use the ZONDA inhaler with BRALTUS to deliver the intended dose. The ZONDA inhaler should be discarded after 30 uses.
- The metered dose of tiotropium in BRALTUS (13 microgram) is lower than the metered dose of SPIRIVA® (18 microgram), however the 'delivered doses' (i.e. dose delivered to the patient) of both products are the same (10 microgram).
- The BRALTUS outer carton includes information on both the metered and delivered doses of tiotropium (13 microgram and 10 microgram respectively) whereas the SPIRIVA® carton states only the pre-metered dose of tiotropium (18 microgram).

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- It is important to note that **both products provide the same delivered dose of tiotropium to the patient and the dosing regimen of one capsule, once daily, is the same with both products.**

Further information

The recommended dose in adults (18 years and older) is one capsule taken once daily with the Zonda inhaler.

BRALTUS contains a smaller amount of tiotropium bromide in its capsules than the originator product SPIRIVA®, **but provides an equivalent amount of tiotropium (the delivered dose).**

The table below illustrates how the description of the products differ:

Variable	BRALTUS	SPIRIVA®
Active capsule contents*	16 microgram tiotropium bromide	22.5 microgram tiotropium bromide monohydrate
Tiotropium equivalent (metered dose)	13 microgram tiotropium	18 microgram tiotropium
Delivered dose	10 microgram tiotropium	10 microgram tiotropium
Dosing regimen	One capsule, once daily	One capsule, once daily

*Please note that not all of this information in included in the package insert and the CMI.

It is important to note that if patients are being switched between SPIRIVA and BRALTUS, the dosing schedule of **one capsule, once daily remains the same and does not change.**

For further inquiries concerning this information, please contact Teva's Medical Information Department as follows: Email: Medinfo.Australia@tevapharm.com; Tel: 1800 288 382

Call for reporting

You are reminded to report any suspected adverse reactions directly to the TGA (Tel: 1800 020 653) or to Teva Pharma Australia via Email: safety.australia@tevapharm.com; Tel: 1800 288 382.

Yours faithfully,
Teva Pharma Australia Pty Ltd
Senior Medical Director

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