

ינואר 2019

רופא/ה נכבד/ה
רוקח/ת נכבד/ה שלום רב,

פרסום עדכון בעלון התכשיר : Duaklir Genuair 340 /12 mcg

הרכב:

Each delivered dose (the dose leaving the mouthpiece) contains 396 micrograms of aclidinium bromide (equivalent to 340 micrograms of aclidinium) and 11.8 micrograms of formoterol fumarate dihydrate. This corresponds to a metered dose of 400 micrograms of aclidinium bromide (equivalent to 343 micrograms of aclidinium) and a metered dose of 12 micrograms of formoterol fumarate dihydrate.

התוויה:

Duaklir Genuair is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).

חברת אסטרהזניקה ישראל מבקשת להודיע על עדכון עלון בהתאם להוראות משרד הבריאות בתאריך **בדצמבר 2018**.

העדכון העיקרי בעלון לרופא הוא:

תוספת טקסט או טקסט בעל שינוי משמעותי מסומן בצבע. מחיקת טקסט מסומנת בקו חוצה.

4. Clinical particulars

4.2 Posology and method of administration

Method of administration

For inhalation use.

Patients should be instructed on how to administer the product correctly as the Genuair inhaler may work differently from inhalers the patients may have used previously. It is important to instruct the patients to read the instructions for use in the Package Leaflet, which is packed together with each inhaler.

4.8 Undesirable effects

Summary of the safety profile

The safety experience with Duaklir Genuair comprised exposure in clinical trials at the recommended therapeutic dose for up to 12 months, and in post-marketing experience.

Tabulated summary of adverse reactions

Immune system disorders	Hypersensitivity ⁴	Rare
	Angioedema ⁴ Anaphylactic reaction ²	Not known
Cardiac disorders	Tachycardia ² Electrocardiogram QTc prolonged ² Palpitations ³ Angina pectoris ³	Uncommon
Gastrointestinal disorders	Diarrhoea ³ Nausea ³ Dry mouth ²	Common
	Stomatitis ³	Uncommon

5. Pharmacological properties

5.1 Pharmacodynamic properties

Lung volumes, exercise endurance and physical activity

The effect of Duaklir Genuair on lung volumes, exercise endurance and physical activity was investigated in an 8-week parallel, randomised, placebo-controlled clinical study in COPD patients with hyperinflation (functional residual capacity [FRC] >120%).

After 4 weeks of treatment Duaklir Genuair implied improvement versus placebo in change from baseline in morning pre-dose (trough) FRC, the primary endpoint, but the difference was not statistically significant (-0.125 L; 95% CI=(-0.259, 0.010); p=0.069*).

Duaklir Genuair showed improvements compared to placebo in lung volumes at 2-3h post dose (FRC=-0.366 L [95% CI=-0.515, -0.216; p<0.0001]; residual volume [RV]=-0.465 L [95% CI=-0.648, -0.281; p<0.0001] and inspiratory capacity [IC]= 0.293 L [95% CI=0.208, 0.378; p<0.0001]).

Duaklir Genuair also showed improvements in exercise endurance time compared to placebo after 8 weeks of treatment (55 seconds [95% CI=5.6, 104.8; p=0.0292]; baseline value: 456 seconds).

After 4 weeks of treatment, Duaklir Genuair improved the number of steps per day compared to placebo (731 steps/day; 95% CI=279, 1181; p=0.0016) and reduced the percentage of inactive patients (<6000 steps per day) [40.8% compared to 54.5%; p<0.0001]. Improvements in the PROactive total score were observed in patients treated with Duaklir Genuair compared with placebo (p=0.0002).

A behavioural intervention program was added to both treatment groups for an additional 4 weeks. The number of steps/day in the Duaklir Genuair treatment group was maintained resulting in a treatment effect compared to placebo of 510 steps/day (p=0.1588) and a reduction versus placebo in the percentage of inactive patients (<6000 steps per day) (41.5% compared to 50.4%; p=0.1134).

*As the primary endpoint did not achieve statistical significance, all p-values for secondary endpoints are tested at a nominal significance level of 0.05, and no formal statistical inference can be drawn.

5.2 Pharmacokinetic properties

Elimination

Following inhalation of Duaklir Genuair 340/12 micrograms, with plasma sampling up to 24 hours post-dose, the terminal elimination half-life observed for acclidinium bromide ranged from 11-33 hours and for formoterol from 12-18 hours

Mean effective half-lives* observed for both acclidinium and formoterol (based on the accumulation ratio) are approximately 10 hours.

*Half-life consistent with product accumulation based on a known dose regimen.

Race

Following repeated inhalations of Duaklir Genuair 340/12 micrograms, the systemic exposure of acclidinium and formoterol, as measured by AUC, is similar in Japanese and Caucasian patients

Instructions for Use

Getting Started

Read these Instructions for Use before you start using the medicine.

Become familiar with the parts of Genuair inhaler.

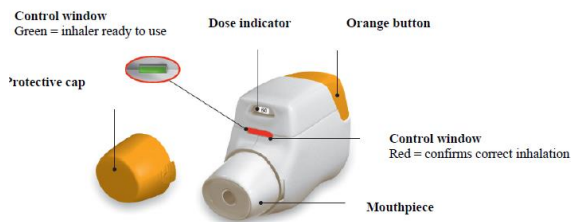


Figure A

Before use:

a) Before first use, tear open the sealed bag and remove the inhaler. Throw away the bag and the desiccant.

b) Do not press the orange button until you are ready to take a dose.

c) Pull off the cap by lightly squeezing the arrows marked on each side (Figure B).

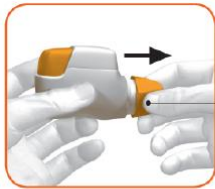


Figure B

STEP 1: Prepare your dose

1.1 Look in the opening of the mouthpiece and make sure nothing is blocking it (Figure C).

1.2 Look at the control window (should be red, Figure C).

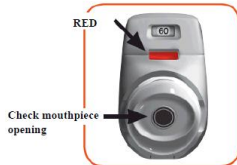


Figure C

1.3 Hold the inhaler horizontally with the mouthpiece facing you and the orange button on top (Figure D).



Figure D

1.4 Press the orange button all the way down to load your dose (Figure E).

When you press the button all the way down, the control window changes from red to green.

Make sure the orange button is on top. Do not tilt.

1.5 Release the orange button (Figure F).

Make sure you release the button, so the inhaler can work correctly.



Figure E

Figure F

Stop and Check:

1.6 Make sure the control window is now green (Figure G).

Your medicine is ready to be inhaled.

Go to 'STEP 2: Inhale your medicine'.



Figure G

What to do if the control window is still red after pressing the button (Figure H).



Figure H

The dose is not prepared. **Go back to ‘STEP 1 Prepare your dose’ and repeat steps 1.1 to 1.6.**

STEP 2: Inhale your medicine

Read steps 2.1 to 2.7 fully before use. **Do not tilt.**

2.1 Hold the inhaler away from your mouth, and breathe out completely. Never breathe out into the inhaler (Figure I).



Figure I

2.2 Hold your head upright, put the mouthpiece between your lips, and close your lips tightly around it (Figure J).

Do not hold the orange button down while inhaling.



Figure J

2.3 Take a strong, deep breath through your mouth. Keep breathing in for as long as possible.

A ‘click’ will let you know that you are inhaling correctly. Keep breathing in as long as possible after you hear the “click”. Some patients may not hear the “click”. Use the control window to ensure you have inhaled correctly.

2.4 Take the inhaler out of your mouth.

2.5 Hold your breath for as long as possible.

2.6 Slowly breathe out.

Some patients may experience a grainy sensation in their mouth, or a slightly sweet or bitter taste. Do not take an extra dose if you do not taste or feel anything after inhaling.

Stop and Check:

2.7 Make sure the control window is now red (Figure K). This means you have inhaled your medicine correctly.



Figure K

What to do if the control window is still green after inhalation (Figure L).



Figure L

This means you have not inhaled your medicine correctly. Go back to ‘STEP 2 Inhale your medicine’ and repeat steps 2.1 to 2.7.

If the control window still does not change to red, you may have forgotten to release the orange button before inhaling, or you may not have strongly enough. If that happens, try again. Make sure you have released the orange button, and you have breathed out completely. Then take a strong, deep breath through the mouthpiece.

Please contact your doctor if control window is still green after repeated attempts.

Push the protective cap back onto the mouthpiece after each use (Figure M), to prevent contamination of the inhaler with dust and other materials. You should discard your inhaler if you lose the cap.



Figure M

Additional information

What should you do if you accidentally prepare a dose?

Store your inhaler with the protective cap in place until it is time to inhale your medicine, then remove the cap and start at Step 1.6.

How does the dose indicator work?

- The dose indicator shows the total number of doses left in the inhaler (Figure N).
- On first use, every inhaler contains at least 60 doses, or at least 30 doses, depending on the pack size.
- Each time you load a dose by pressing the orange button, the dose indicator moves by a small amount towards the next number (50, 40, 30, 20, 10, or 0).

When should you get a new inhaler?

You should get a new inhaler:

- If your inhaler appears to be damaged or if you lose the cap, or
- When a red band appears in the dose indicator, this means you are nearing your last dose (Figure N), or
- If your inhaler is empty (Figure O).

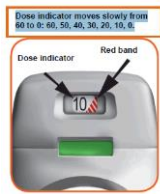


Figure N

How do you know that your inhaler is empty?

When the orange button will not return to its full upper position and is locked in a middle position, you have reached the last dose (Figure O). Even though the orange button is locked, your last dose may still be inhaled. After that, the inhaler cannot be used again and you should start using a new inhaler.



Figure O

How should you clean the inhaler?

NEVER use water to clean the inhaler, as this may damage your medicine.

If you wish to clean your inhaler, just wipe the outside of the mouthpiece with a dry tissue or paper towel.

העדכון העיקרי בעלון לצרכן הוא:

קבוצה תרפויטית:

התרופה מכילה שני מרכיבים פעילים מקבוצת מרחיבי סימפונות.

תופעות לוואי שאינן שכיחות (משפיעות לכל היותר על 1:10 מטופלים):

-טכיקרדיה (דופק מהיר)

כאבים או לחץ בחזה (אנגינה פקטוריס)

-טשטוש ראיה

דיספנויה (-שינויים בקול

-אצירת שתן (שבין תסמיניה: קושי במתן שתן או תחושה שהשלפוחית לא מתרוקנת לחלוטין)

(QT-הפרעת קצב לבבית (הארכת מקטע

-שינויים בתחושת הטעם

-גירוי בגרון

- דלקת בחלל הפה (סטומאטיטיס)

-עליה בלחץ הדם

-אי שקט

-פריחה

-גרד בעור

הוראות השימוש בעלון לצרכן התעדכנו בהתאם למידע שהתעדכן בעלון לרופא.

העלוניים מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בכבוד רב,

קארין קנבל דובסון

רוקחת ממונה

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