J-C Health Care Ltd.

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Johnson&Johnson

אוקטובר 2025

רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

הנדון: **Tracleer® 62.5mg film-coated tablets**
Tracleer® 125mg film-coated tablets

בעל הרישום J-C Health Care Ltd. מבקש להודיעכם כי העלונים לרופא ולצרכן של התכשירים שבנדון עודכנו באוקטובר 2025.

פרטי העדכון העיקריים מופיעים בהמשך *(טקסט שנוסף מסומן ב*אדום*, טקסט שהושמט מסומן כטקסט כחול עם קו חוצה)*, אך קיימים עדכונים נוספים.

מרכיב פעיל:

BOSENTAN as monohydrate 62.5mg
BOSENTAN as monohydrate 125mg

ההתוויות המאושרות לתכשיר בישראל:

Treatment of pulmonary arterial hypertension (PAH) in patients of WHO functional class II-IV. Reduction in the number of new digital ulcers in patients with systemic sclerosis with active digital ulcer disease.

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות: https://israeldrugs.health.gov.il/#!/byDrug.

כמו כן, מצורפים לפרסום זה וניתן לקבל העתק מודפס שלהם באמצעות פנייה לבעל הרישום: J-C Health Care Ltd , קיבוץ שפיים, 6099000, טל': 09-9591111.

בברכה,
שרון כץ
רוקחת ממונה

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בהודעה זו כלולים העדכונים המהותיים בלבד.

עלון לצרכן

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4. תופעות לוואי

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תופעות לוואי נדירות – (rare) עלולות להופיע בעד משתמש אחד מתוך 1,000

- הלם אנפילקטי (תגובה אלרגית כללית), אנגיואדמה (נפיחות, בדרך כלל מסביב לעיניים, לשפתיים, ללשון או לגרון)
- שחמת הכבד, אי-ספיקת כבד (הפרעה חמורה בתפקודי כבד), הפטיטיס אוטואימונית (דלקת בכבד הנגרמת על ידי מערכת ההגנה של הגוף התוקפת את תאי הכבד) שיכולה להתרחש גם כמה חודשים עד שנים לאחר תחילת הטיפול.

עלון לרופא

4.4 Special warnings and precautions for use

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Liver function

Elevations in liver aminotransferases, i.e., aspartate and alanine aminotransferases (AST and/or ALT), associated with bosentan are dose dependent. Liver enzyme changes typically occur within the first 26 weeks of treatment but may also occur late in treatment (see section 4.8). These increases may be partly due to competitive inhibition of the elimination of bile salts from hepatocytes but other mechanisms, which have not been clearly established, are probably also involved in the occurrence of liver dysfunction. The accumulation of bosentan in hepatocytes leading to cytolysis with potentially severe damage of the liver, or an immunological mechanism, are not excluded. Rare cases of autoimmune hepatitis with a latency of few months to years have been reported. Liver dysfunction risk may also be increased when medicinal products that are inhibitors of the bile salt export pump, e.g., rifampicin, glibenclamide and cyclosporine A (see sections 4.3 and 4.5), are co-administered with bosentan, but limited data are available.

Liver aminotransferase levels must be measured prior to initiation of treatment and subsequently at monthly intervals for the duration of treatment with Tracleer. In addition, liver aminotransferase levels must be measured 2 weeks after any dose increase.

Recommendations in the event of ALT/AST elevations

ALT/AST levels	**Treatment and monitoring recommendations**
> 3 and ≤ 5 × ULN	The result should be confirmed by a second liver test; if confirmed, a decision should be made on an individual basis to continue Tracleer, possibly at a reduced dose, or to stop Tracleer administration (see section 4.2). Monitoring of aminotransferase levels should be continued at least every 2 weeks. If the aminotransferase levels return to pre-treatment values continuing or re-introducing Tracleer according to the conditions described below should be considered.

> 5 and ≤ 8 × ULN	The result should be confirmed by a second liver test; if confirmed, treatment should be stopped and aminotransferase levels monitored at least every 2 weeks. If the aminotransferase levels return to pre-treatment values re-introducing Tracleer according to the conditions described below should be considered.
> 8 × ULN	Treatment must be stopped and re-introduction of Tracleer is not to be considered.

In the event of associated clinical symptoms of liver injury or autoimmune hepatitis, i.e., nausea, vomiting, fever, abdominal pain, jaundice, unusual lethargy or fatigue, flu-like syndrome (arthralgia, myalgia, fever)**, treatment must be stopped and re-introduction of Tracleer is not to be considered.**

Re-introduction of treatment
Re-introduction of treatment with Tracleer should only be considered if the potential benefits of treatment with Tracleer outweigh the potential risks and when liver aminotransferase levels are within pre-treatment values. The advice of a hepatologist is recommended. Re-introduction must follow the guidelines detailed in section 4.2. **Aminotransferase levels must then be checked within 3 days after re-introduction, then again after a further 2 weeks, and thereafter according to the recommendations above.**

ULN=upper limit of normal

4.8 Undesirable effects

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System organ class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Common	Anaemia, haemoglobin decrease, (see section 4.4)
	Not known	Anaemia or haemoglobin decreases requiring red blood cell transfusion[1]
	Uncommon	Thrombocytopenia[1]
	Uncommon	Neutropenia, leukopenia[1]
Immune system disorders	Common	Hypersensitivity reactions (including dermatitis, pruritus and rash)[2]
	Rare	Anaphylaxis and/or angioedema[1]
Nervous system disorders	Very common	Headache[3]
	Common	Syncope[1,4]
Eye disorders	Not known	Blurred vision[1]
Cardiac disorders	Common	Palpitations[1,4]
Vascular disorders	Common	Flushing
	Common	Hypotension[1,4]
Respiratory, thoracic and mediastinal disorders	Common	Nasal congestion[1]
Gastrointestinal disorders	Common	Gastrooesophageal reflux disease Diarrhoea
Hepatobiliary disorders	Very common	Abnormal liver function test, (see section 4.4)
	Uncommon	Aminotransferase elevations associated with hepatitis (including possible exacerbation of underlying

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		hepatitis) and/or jaundice1 (see section 4.4)
	Rare	Liver cirrhosis, liver failure[1] Autoimmune hepatitis
Skin and subcutaneous disorders	Common	Erythema
General disorders and administration site conditions	Very common	Oedema, fluid retention[5]

[1] Data derived from post-marketing experience, frequencies based on statistical modelling of placebo-controlled clinical trial data.
[2] Hypersensitivity reactions were reported in 9.9% of patients on bosentan and 9.1% of patients on placebo.
[3] Headache was reported in 11.5% of patients on bosentan and 9.8% of patients on placebo.
[4] These types of reactions can also be related to the underlying disease.
[5] Oedema or fluid retention was reported in 13.2% of patients on bosentan and 10.9% of patients on placebo.

In the post-marketing period rare cases of unexplained hepatic cirrhosis were reported after prolonged therapy with Tracleer in patients with multiple co-morbidities and therapies with medicinal products. There have also been rare reports of liver failure and autoimmune hepatitis with a latency of few months to years. These cases reinforce the importance of strict adherence to the monthly schedule for monitoring of liver function for the duration of treatment with Tracleer (see section 4.4).