December 2023

Vabysmo® (faricimab) **120 mg/mL solution for injection**

ואביסמו

צוות רפואי נכבד,

<u>הנדון: סיכון לדלקת של כלי דם ברשתית ו/או חסימה של כלי דם ברשתית בשימוש ב- Vabysmo® (faricimab)</u>

חברת רוש פרמצבטיקה (ישראל) בע"מ, בשיתוף משרד הבריאות, מעוניינת להביא לידיעתך את המידע הבא הנוגע לבטיחות השימוש בתרופה Vabysmo

להלן עיקרי הדברים:

- דלקת כלי דם ברשתית **(Retinal Vasculitis)** ו/או חסימה של כלי דם ברשתית **(Retinal Vascular Occlusion)** דווחו בחולים שטופלו ב-Vabysmo.
- דלקת כלי דם ברשתית עם או ללא חסימה הינה תופעת לוואי חמורה שיכולה לגרום לאובדן ראיה בלתי הפיך.
- הדיווחים התקבלו לאחר תחילת השיווק של התכשיר ונכון לאוגוסט 2023 שיעור הדיווח מוערך ב- 0.17 ל-10,000 זריקות עבור דלקת כלי דם ברשתית עם וללא חסימה מתוכם שיעור הדיווח של דלקת כלי דם ברשתית עם חסימה מוערך ב-0.06 ל-10,000 זריקות.

<u>הנחיות לצוות הרפואי</u>:

  - יש ליידע את המטופל אודות היתרונות והחסרונות של הטיפול ב-Vabysmo, כולל הסיכון להופעת דלקת של כלי דם ברשתית עם או ללא חסימה של כלי הדם.
  - יש להדריך את המטופל לדווח על כל שינוי בראייה ללא דיחוי, ולפנות מייד לרופא עיניים במקרה של הופעת אדמומיות בעין, רגישות לאור, כאב או שינויים בראייה.
  - יש להפסיק את הטיפול ב-Vabysmo במטופל שפיתח תופעות אלה.
- המידע לעיל עודכן בעלון בפרק אזהרות ופרק תופעות הלוואי.
- למידע נוסף אודות התכשיר יש לפנות לעלון.

Roche Pharmaceuticals (Israel) Ltd.
Drugs Regulatory Affairs

6 Hacharash St.
P.O.B. 6391
Hod Hasharon 4524079

Tel. + 972-9-9737777
Fax + 972-9-9737850

December 2023

Subject: VABYSMO® (faricimab), New Warnings and Precautions: Retinal Vasculitis and/or Retinal Vascular Occlusion

Dear Health Care Provider:

The purpose of this letter is to inform you of the updated safety information for VABYSMO. VABYSMO is a vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2) inhibitor indicated for the treatment of patients with:

● Neovascular (Wet) Age-Related Macular Degeneration (nAMD)

● Diabetic Macular Edema (DME)

Risk of Retinal Vasculitis and/or Retinal Vascular Occlusion

An update to the Warnings and Precautions (section 5.4) and Adverse Reactions (section 6) - Postmarketing Experience (section 6.2) sections of the physician leaflet has been made following spontaneous post-marketing reports of retinal vasculitis with or without occlusion in patients treated with VABYSMO. Patient leaflet have been updated accordingly in section 4, "Adverse Reactions". Retinal vasculitis with or without occlusion is a serious event that can cause permanent vision loss.

As of the end of August 2023, with 1.5 million vials dosed globally, the estimated reporting rate of retinal vasculitis with occlusion is 0.06/10,000 injections (for retinal vasculitis with or without occlusion: 0.17/10,000 injections).

Please also refer to section 6.2 in the physician leaflet:

The following adverse reactions have been identified during postapproval use of VABYSMO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Eye disorders: retinal vasculitis with or without retinal vascular occlusion.

The benefit-risk profile of VABYSMO for all its approved indications continues to be favorable.

Prescriber Action

● Counsel patients about the benefits and risks of VABYSMO, including the risk of retinal vasculitis with or without retinal vascular occlusion.

● Patients treated with VABYSMO should be instructed to report any changes in vision without delay to permit prompt and appropriate management [see Patient leaflet]. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise the patient to seek immediate care from an ophthalmologist.

● VABYSMO should be discontinued in patients who develop these events.

● Prescribers should refer to the Warnings and Precautions Section 5.4 of the physician leaflet.

Roche Pharmaceuticals (Israel) Ltd.
Drugs Regulatory Affairs
6 Hacharash St.
P.O.B. 6391
Hod Hasharon 4524079
Tel. + 972-9-9737777
Fax + 972-9-9737850

Call for reporting

Healthcare professionals should report any adverse events, which are suspected to be associated with the use of Vabysmo, to the Israeli Ministry of Health by using an online form:
https://sideeffects.health.gov.il
It could also be reported to Roche Israel drug safety department at 09-9737722 or israel.drugsafety@roche.com.

Company contact point

Should you have any questions regarding the use of Vabysmo, please feel free to contact us at:

Roche Pharmaceuticals (Israel) Ltd.,
Israel.drugsafety@roche.com
09-9737777.

Yours sincerely,

DocuSigned by:
Tamar Birenboim-Gal
Signer Name: Tamar Birenboim-Gal
Signing Reason: I approve this document
Signing Time: 14-Mar-2024 | 2:26:34 PM CET
C6405CA2ED31419684C0FD05D3E92F57

DocuSigned by:
Siyona Kolatkar
Signer Name: Siyona Kolatkar
Signing Reason: I approve this document
Signing Time: 14-Mar-2024 | 2:15:59 PM CET
D23B49E51173443A8434DC9507B12CA8

Dr. Tamar Birenboim-Gal
Medical Director

Siyona Kolatkar
Qualified Person for Pharmacovigilance

Roche Pharmaceuticals (Israel) Ltd.
Drugs Regulatory Affairs

6 Hacharash St.
P.O.B. 6391
Hod Hasharon 4524079

Tel. + 972-9-9737777
Fax + 972-9-9737850

DocuSign

Certificate Of Completion

Envelope Id: 38DB27A5F1AA4AFDB87877882648BF56
Status: Completed
Subject: Complete with DocuSign: 5. Vabysmo DHPC_ Dec 2023_Final_Clean.docx
Source Envelope:
Document Pages: 3
Signatures: 2
Envelope Originator:
Certificate Pages: 4
Initials: 0
Siyona Kolatkar
AutoNav: Enabled
Grenzachstrasse 124
EnvelopeId Stamping: Disabled
Basel, Basel-Stadt 4070
Time Zone: (UTC+01:00) Amsterdam, Berlin, Bern, Rome, Stockholm, Vienna
siyona.kolatkar@roche.com
IP Address: 194.120.84.9

Record Tracking

Status: Original
3/14/2024 2:14:20 PM
Holder: Siyona Kolatkar
siyona.kolatkar@roche.com
Location: DocuSign

Signer Events	Signature	Timestamp
Siyona Kolatkar siyona.kolatkar@roche.com CFR Part 11 - Joint - Sub Account_310 Security Level: Email, Account Authentication (Required)	Siyona Kolatkar Signature Adoption: Pre-selected Style Signature ID: D23B49E5-1173-443A-8434-DC9507B12CA8 Using IP Address: 194.120.84.9 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 3/14/2024 2:15:27 PM Viewed: 3/14/2024 2:15:41 PM Signed: 3/14/2024 2:16:03 PM
Electronic Record and Signature Disclosure: Accepted: 11/24/2019 12:46:15 PM ID: 52a083ad-7405-4ca2-a04a-622f6154f8c2 Company Name: F.Hoffmann-La Roche Ltd. - CFR Part 11 - Sub 3		
Tamar Birenboim-Gal tamar.birenboim-gal@roche.com Country Medical Director Tamar Birenboim-Gal Security Level: Email, Account Authentication (Required), Login with SSO	Tamar Birenboim-Gal Signature Adoption: Pre-selected Style Signature ID: C6405CA2-ED31-4196-84C0-FD05D3E92F57 Using IP Address: 196.3.50.247 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 3/14/2024 2:16:05 PM Viewed: 3/14/2024 2:24:23 PM Signed: 3/14/2024 2:26:44 PM
Electronic Record and Signature Disclosure: Accepted: 4/30/2020 6:11:09 PM ID: bc59b108-4883-4415-8101-29ef4b999f83 Company Name: F.Hoffmann-La Roche Ltd. - CFR Part 11 - Sub 3		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	3/14/2024 2:15:27 PM
Certified Delivered	Security Checked	3/14/2024 2:24:23 PM
Signing Complete	Security Checked	3/14/2024 2:26:44 PM
Completed	Security Checked	3/14/2024 2:26:44 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

Guidelines for the use of the DocuSign electronic signing system within F. Hoffmann-La Roche and companies of the Roche Group

LEGAL DISCLOSURE

By placing my electronic signature on this document, I expressly consent to use and rely on Electronic and Digital Signatures and I understand my signature will have the same binding effect as if I was providing a handwritten signature.

I also confirm the email address that I am using as a valid one to be notified and identified electronically, for example through the DocuSign System, and/or to identify me as the signer of the document. I should inform Roche in the case that the email address changes.

CONSUMER DISCLOSURE

From time to time, F. Hoffmann-La Roche and companies of the Roche Group (hereinafter referred to as we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign, Inc. (DocuSign) electronic signing system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to these terms and conditions, please confirm your consent by clicking the 'I agree' button at the bottom of this document.

Consequences of changing your mind

To indicate to us that you are changing your mind, you must withdraw your consent using the DocuSign 'Withdraw Consent' form on the signing page of a DocuSign envelope instead of signing it. This will indicate to us that you have withdrawn your consent to receive required notices and disclosures electronically from us and you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

All notices and disclosures will be sent to you electronically

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact us

You may contact us to let us know of your changes as to how we may contact you electronically, to request certain information from us and to withdraw your prior consent to receive notices and disclosures electronically. To do so contact the sender of the envelope.

To advise us of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to the sender of the envelope and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address. In addition, you must notify DocuSign, Inc. to arrange for your new email address to be reflected in your DocuSign account by following the process for changing email in the DocuSign system.

To withdraw your consent

To inform us that you no longer want to receive future notices and disclosures in electronic format you may decline to sign a document from within your DocuSign session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent.

Acknowledging your access and consent to receive materials electronically

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please verify that you were able to read this electronic disclosure and that you also were able to print on paper or electronically save this page for your future reference and access or that you were able to email this disclosure and consent to an address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format on the terms and conditions described above, please let us know by clicking the 'I agree' button below.

By checking the 'I agree' box, I confirm that:

- I can access and read this Electronic CONSENT TO ELECTRONIC RECEIPT OF ELECTRONIC CONSUMER DISCLOSURES document; and
- I can print on paper the disclosure or save or send the disclosure to a place where I can print it, for future reference and access; and
- Until or unless I notify the account owner as described above, I consent to receive from exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to me by the account owner during the course of my relationship with you.
- I acknowledge the information included in the DocuSign Privacy Policy