DPS
DEPARTMENT OF PHARMACEUTICAL SERVICES
MINISTRY OF HEALTH
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Rujukan Kami:
Our Reference: (02)PRS/ADMIN/2022

25th July 2022
26 Zulhijjah 1443

Dear Product Licence Holders and Importers,

DIRECTIVE FOR WARFARIN CONTAINING PRODUCTS IN BRUNEI DARUSSALAM: UPDATE ON PACKAGE INSERT ON RISK OF ANTI-COAGULANT-RELATED NEPHROPATHY (ARN)

The Brunei Darussalam Medicines Control Authority in its 41st meeting held on 21st July 2022 has determined for information on all warfarin containing products registered and marketed in Brunei Darussalam to be updated on the risk of anti-coagulant-related nephropathy (ARN) to ensure that healthcare professionals are aware and promptly manage ARN to prevent potential serious complications[1]. This update was based on safety information from the National Pharmaceutical Regulatory Agency (NPRA) Malaysia[1] and directive from NPRA[2] to Product Registration Holders in Malaysia.

2. Therefore, all product licence holders and importers are required to update the package insert of all warfarin containing products to include the following information:

a) Under 'Warnings and Precautions'[2]:

Anticoagulant-related nephropathy[2]
In patients with altered glomerular integrity or with a history of kidney disease, acute kidney injury may occur, possibly in relation to episodes of excessive anticoagulation and hematuria[2]. A few cases have been reported in patients with no pre-existing kidney disease[2]. Close monitoring including renal function evaluation is advised in patients with a supratherapeutic INR and hematuria (including microscopic)[2].

b) Under 'Adverse Effects/ Undesirable Effects'[2]:

Renal and urinary disorders[2]
Frequency 'not known': Anticoagulant-related nephropathy[2]

3. The implementation date on the requirement is as follows:

i) New applications and applications which are still in process of registration: **1 August 2022**

ii) Registered products: **1 February 2023**

4. Update on package insert for registered products is required to be submitted as a variation application prior to the implementation date.

Thank you for your kind cooperation in the matter.

Yours Sincerely

(Dyg Rosmah Hj Mohamad Shah)
Acting Director of Pharmaceutical Services
For Chair of BDMCA

References:

1) National Pharmaceutical Regulatory Agency (NPRA) Malaysia. *Warfarin and risk of Anticoagulant-Related Nephropathy (ARN)* dated 6th May 2022. Available from: https://www.npra.gov.my/index.php/en/component/content/article/435-english/safety-alerts-main/safety-alerts-2022/1527345-warfarin-risk-of-anticoagulant-related-nephropathy-arn.html?Itemid=1391 [Accessed 18th June 2022]
2) National Pharmaceutical Regulatory Agency (NPRA) Malaysia. *Peraturan-Peraturan Kawalan Dadah dan Kosmetik 1984 Arahan Pengarah Perkhidmatan Farmasi bilangan 4 tahun 2022: Direktif untuk semua produk yang mengandungi warfarin: Pengemaskinian sisip bungkusan dan risalah maklumat ubat untuk pengguna (RiMUP) dengan maklumat keselamatan berkaitan risiko Anticoagulant-related nephropathy (ARN).* Reference NPRA.600-1/9/13 (4) Jld.1 dated 11th April 2022. Available from: Ruj. Kami: NPRA.600-1/9/13 (4) Jld.1 [Accessed 18th June 2022]