Not so swell:

Leg cellulitis and oedema after unintended double dosing of trametinib

Emma Booth and Sarah Smith
Pharmacy Department, Calvary Public Hospital Bruce ACT
emma.booth@calvary-act.com.au

Case Report

Clinical details:

An independent 72-year-old female (MW) presented from home with infected bilateral foot ulcers with surrounding cellulitis and severe bilateral leg oedema. Excessive leg swelling and fluid seepage appeared over two to three weeks prior to admission.

MW had a history of metastatic melanoma, BCC, SCC, COPD, depression, lymphoedema and was a current smoker (60 pack year history).

Medications on admission are shown below:

Medication	Dose	Reason/Duration
Trametinib	2mg twice daily	Metastatic melanoma Six weeks
Dabrafenib	150mg twice daily	Metastatic melanoma Six weeks
Frusemide	40mg mane	Leg Oedema 2 weeks
Cephalexin	500mg tds	Cellulitis 2 days

Pharmacist Intervention:

Medication reconciliation on admission revealed MW had been inadvertently taking a double dose of trametinib - 2mg twice daily rather than 2mg daily for six weeks due to unclear labelling.

Case Progress:

On admission, MW was treated with intravenous flucloxacillin, an increased dose of frusemide and her dose of trametinib was decreased to the intended dose of 2mg daily.

Over the course of 10 days the cellulitis and oedema resolved and she was moved to the rehabilitation ward.

Oncologist review noted an excellent response to melanoma treatment, with complete resolution of brain metastases and those in the chest. MW was able to tolerate the corrected dose of trametinib during admission and she was counselled about ongoing correct medication administration.

After a 2 month hospital stay MW was unable to recover her full mobility and function and was discharged to a nursing home.

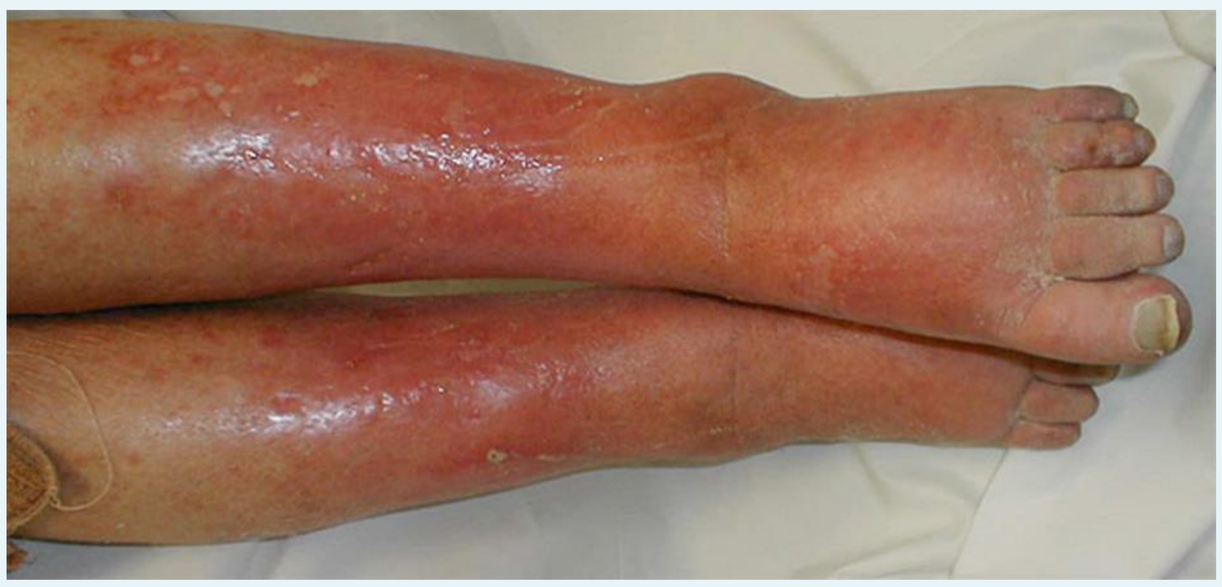
Discussion

Combination of Trametinib and Dabrafenib for melanoma:

Dabrafenib acts as a BRAF inhibitor and trametinib a MEK inhibitor. BRAF and MEK are key components of the pathway which regulates normal growth and death of cells, including skin cells[1].

Adverse cutaneous adverse reactions are common with these medicines (although they are less frequent when BRAF inhibitors are used in combination with a MEK inhibitor rather than alone) and at times require a dose interruption and/or reduction. Pooled data from the COMBI-d and COMBI-v clinical trials of trametinib administered in combination with dabrafenib, found cellulitis occurred in <10% of patients and peripheral oedema in 21%[1]. A double dose of trametinib would be expected to increase this risk.

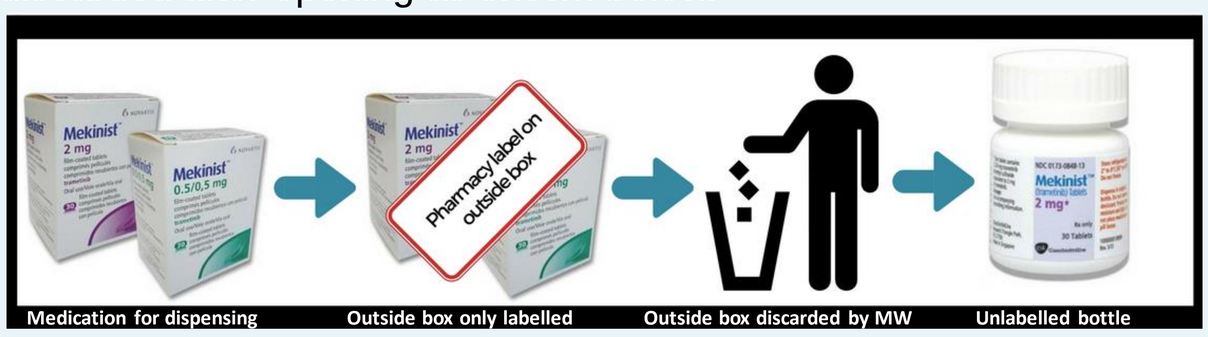
Image of leg cellulitis. Courtesy of *woundcareadvisor.com*



Role of the pharmacist:

Medication reconciliation completed by a pharmacist aims to ensure patients receive all intended medicines and to avoid errors. It is particularly important at transition of care points which are prone to error[2].

On completion of a medication reconciliation it was found that MW had been taking a double dose of trametinib due to confusion about the frequency and lack of directions on the medication's bottle. The instruction label had been placed on the outside box rather than the original container which was subsequently discarded after opening as shown below.



Conclusion:

This case highlights that unintended medication nonadherence can be a hidden problem. It is important that a new high risk medicine is safely dispensed and clearly labelled to enhance compliance, improve the patient's understanding of treatment and prevent adverse effects.

The Pharmacy Board of Australia states in its *Guidelines for Dispensing of Medicines* that a label is to be attached to the immediate container and that patients have the right to receive counselling about their medicine[3].

References:.

1. Mekinist. US Approved Product Information; Revised June 2017
2. Australian Commission on Safety and Quality in Healthcare; National Medication Management Plan User Guide; Nov 2013
3. Pharmacy Board of Australia; Guidelines for Dispensing of Medicines; Dec 2015

Calvary Public Hospital Bruce