

## Warfarin + Ifosfamide/Etoposide (Final)

Ifosfamide/etoposide, as a combination<sup>1,2</sup> and individually<sup>2-4</sup>, may potentiate the effects of warfarin resulting in increased risk of bleeding. The mechanism of effect is unknown. Alteration of CYP2C9 metabolism of warfarin by ifosfamide has been proposed as a potential mechanism<sup>1,2</sup>. The evidence previously cited supporting inhibition of CYP2C9 by ifosfamide is not strong<sup>5,6</sup>.

INR available w/in last 30 days	No	Yes	
INR is suprathereapeutic		Yes	No
Daily INR monitoring and management is available		Yes	No
Risk of bleeding is increased		◆	
Risk of bleeding may be increased	■ <sup>7</sup>		■ <sup>1-4,7</sup> ◆

○ = No special precautions. ■ = Assess risk and take action if necessary. ◆ = Use only if benefit outweighs risk

### Footnotes:

1. Okada N, Watanabe H, Kagami S, Ishizawa K. Ifosfamide and etoposide chemotherapy may interact with warfarin, enhancing the warfarin induced anticoagulant response. *Int J Clin Pharmacol Ther.* 2016;54(1):58-61.
2. Hall G, Lind MJ, Huang M, et al. Intravenous infusions of ifosfamide/mesna and perturbation of warfarin anticoagulant control. *Postgrad Med J.* 1990;66(780):860-861.
3. Le AT, Hasson NK, Lum BL. Enhancement of warfarin response in a patient receiving etoposide and carboplatin chemotherapy. *Ann Pharmacother.* 1997;31(9):1006-1008.
4. Ward K, Bitran JD. Warfarin, etoposide, and vindesine interactions. *Cancer Treat Rep.* 1984;68(5):817-818.
5. Donelli MG, Franchi G, Rosso R. The effect of cytotoxic agents on drug metabolism. *Eur J Cancer.* 1970;6(2):125-126.
6. Lind MJ, Margison JM, Cerny T, Thatcher N, Wilkinson PM. Comparative pharmacokinetics and alkylating activity of fractionated intravenous and oral ifosfamide in patients with bronchogenic carcinoma. *Cancer Res.* 1989;49(3):753-757.
7. Manage warfarin through monitoring INR .