**Warfarin + Ifosfamide/Etoposide (Final)**

Ifosfamide/etoposide, as a combination1,2 and individually2-4, 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 mechanism1,2. The evidence previously cited supporting inhibition of CYP2C9 by ifosfamide is not strong5,6.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| INR available w/in last 30 days | No | Yes | | |
| INR is supratherapeutic |  | Yes | No | |
| Daily INR monitoring and management is available |  |  | Yes | No |
| Risk of bleeding is increased |  |  |  |  |
| Risk of bleeding may be increased | 7 |  | 1-4,7 |  |

 = 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 .