of pulmonary embolism, 5 of which were fatal. In addition, there are press reports of four cases, including one death from the United Kingdom.

In some of these one or more of the usually accepted inciting causes of thrombophlebitis were evident; in some they were not.

Reports to the manufacturer do not reflect the accurate incidence of reactions and the available statistics are not adequate to determine whether or not there is a causal relationship, but caution requires consideration of this possibility.

It must be remembered that pulmonary embolism can occur without discernible inciting cause and without preceding peripheral thrombophlebitis. Nevertheless, careful studies by investigators experienced in the measurement of the extremely complex factors involved in the clotting mechanism are continuing, including an evaluation of the role of fluid accumulation sometimes seen after Enovid administration. This will be reported in a technical bulletin at an early date. At the present time the available laboratory data neither prove nor disprove a causal relationship between Enovid administration and the occurrence of thrombophlebitis.

The cases of thrombophlebitis reported to us have usually occurred early in the course of Enovid administration and at the lower dosage level. Experience based on patients taking Enovid at higher doses has not demonstrated any dose response relationship.

Physicians should be as alert to the possible occurrence of thrombophlebitis in patients to whom Enovid is prescribed as they are in patients taking other medication.

The above facts should be given particular attention if Enovid is considered for administration to patients with thrombotic disease or a history of thrombophlebitis.

We request that any thromboembolic occurrence in women receiving Enovid be reported to us and to the Food and Drug Administration.

Sincerely yours,

(S) Irwin C. Winter,

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