WHAT WE LEARNED FROM THE RECENT EU REFERRAL PROCEDURE
CONCERNING COMBINED HORMONAL CONTRACEPTIVES -
CONCLUSIONS FOR CMA/EE

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The 1995 pill scare over the allegedly lower risk of venous thromboembolism (VTE) in users of levonorgestrel-ethinylestradiol (LNG/EE) containing combined oral contraceptives (COC's) ended in a hefty debate of the quality of observational research and the appropriateness of early 'warnings' by the authorities.

The EU-wide review included all of the known progestin - estrogen combinations and concluded as the benefits of COCs in preventing unwanted pregnancies continue to outweigh their risks, and that the well-known risk of VTE with all CHCs is small. Moreover, there is no reason for any woman to stop using her current contraceptive. Even today, there is no consensus as prospective studies consistently find no differential risk among COCs.

In the its recent referral procedure, the European Medicines CommissionAgency (EMA) choose to disqualify prospective studies (postmarketing, active surveillance) as 'not trustworthy' ('sponsored by the industry') and non-contraceptive benefits and their impact on compliance as 'unproven'. LNG-EE combination is regarded as a reference product for all comparisons and EMA's is now requesting proof from each of the Marketing Authority Holders (MAH) that users of their products carry no higher risk of VTE than users of LNG-COCs. This remarkable change of its policy has done considerable damage to small companies and is likely to reduce the variety of different COC preparations significantly. Particularly CMA/EE-containing -COCs have never been suspected to carry higher risks of VTE than LNG-COCs according to the results coming from the long and documented clinical experience. Body of evidences for CMA/EE has included as high exposure as it was evaluated by large-scale post-authorization safety studies, eg. EURAS. Their safety and Anti-androgenic benefits of CMA/EE and its consequent positive contribution to the high satisfaction among women have been proven in the past are appreciated in the market for several decades clearly indicating the need for CMA/EE in our COC portfolio more than 30 years now. The collateral damage done to CMA containing COCs is not justified.