The term progesterone should only be used for the natural hormone produced by the ovaries or in-clude in a registered drug. The modern history of progesterone begins with the first book d-scription of the female reproductive system including the corpus luteum and later with the Nobel aWARDS for hormone research. It is a versatile molecule with many biologic activi-TIES, including antagonistic and agonistic actions at the progesterone receptor (PR). PR is present in the cytosol of various cells and in the nucleus, where it regulates gene expression. The PR forms a heterodimer with the retinoid X receptor (RXR) in hormone target cells, making it an important regulator of gene expression in the human body.

Selective progesterone receptor modulators (SPRMs) are steroid progesterone receptor ligands able to induce agonistic or antagonistic activities. Mifepristone, the class leader, was primarily used for pregnancy termination from the 1980s. Emergency contraception with extended activity was the preferred method of control. However, with the advent of non-steroidal options such as progesterone, other choices became available. Progesterone is an alternative method for prevention of pregnancy in women of childbearing age, and it is also widely used as an adjunc-tive therapy in the treatment of symptoms associated with the perimenopausal and postmenopausal periods. Me-thods for the systemic administration of progesterone include oral, rectal, and transdermal routes. Transdermal therapy is preferred over oral and rectal therapy because the use of progesterone does not cause an additional increase in estrogen levels. However, the systemic administration of progesterone is associated with higher levels of estrogen, and this must be considered when evaluating the potential risks and benefits.

When menstrual cycles are normal length and normally ovulatory, E2 and P4 are balanced and the risk of venous thromboembolism and breast cancer does not appear to increase with use of combined with progesterone and support the current evidence based recommendations on HT, es-pecially in women at high VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (MPA) (RR 1.58; RR 0.97, 95% CI 0.87-1.09, respectively). Norpregnane derivatives (norethisterone/edroxyprogesterone acetate) did not show a significant increase in VTE risk. In women using opposed estrogen, results were highly heterogeneous due to important differences related to VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among wome