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## **Diethylstilbestrol (DES)**

Overview DES was first synthesized in early 1938 by Leon Golberg, then a graduate student of Sir Robert Robinson at the Dyson Perrins Laboratory at the University of Oxford. DES (in tablets up to 5 mg) was approved by the United States Food and Drug Administration on September 19, 1941 for four indications: gonorrheal vaginitis, atrophic vaginitis, menopausal symptoms, and postpartum lactation suppression to prevent breast engorgement. It was first prescribed by physicians to prevent miscarriages (in women who had had previous miscarriages) in the 1940s as an off-label use. On July 1, 1947, the FDA approved the first supplemental new drug application (by Squibb) adding prevention of miscarriage as an indication and approved 25 mg (and later 100 mg) tablets of DES for this indication, and approved applications of several other pharmaceutical companies in the second half of 1947. On April 15, 1971, the New England Journal of Medicine published a report by three physicians at Massachusetts General Hospital on the association of DES therapy started during the first trimester of pregnancy by mothers of 7 of 8 girls and young women ages 14 to 22 diagnosed with adenocarcinoma of the vagina. In November 1971, the FDA sent a FDA Drug Bulletin to all U.S. physicians advising them to stop prescribing DES to pregnant women because it was linked to a rare vaginal cancer in female offspring, and on November 10, 1971 ordered that prevention of miscarriage be removed from indications and pregnancy be added to contraindications in the physician prescribing information for DES.