CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-090

PHARMACOLOGY REVIEW(S)

HFD-580: DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS

REVIEW AND EVALUATION OF PHARMCOLOGY AND TOXICOLOGY DATA

Original submission

NDA No. 21-090 **Submission dated:** 5-7-1999

Reviewer: Krishan L. Raheja **Review completed:** 5-27-1999

Information to be conveyed to sponsor: Yes ( ) No (*)

Sponsor: Organon Inc. JUN 2 1999

Drug name: Desogestrel (DSG) and ethinyl estradiol (EE)

Drug class: Progestin and estrogen (steroids)

Indication: [redacted]

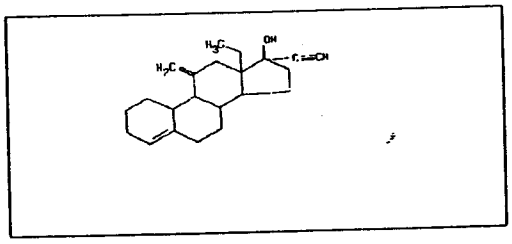
Desogestrel

Code name: CTR 77 **CAS Registry Number:** 54024-22-5 **Laboratory code name:** ORG 2969

Chemical names: 1. (17a)-13-ethyl-11-methylene-18,-19-dinor-pregn-4-en-20-yn-17-ol
2. 17a-ethynyl-18-methyl-11-methylene-Δ^4-estren-17B-ol.

Molecular formula: $C_{22}H_{30}O$ **Molecular mass:** 310.48

Structural formula:



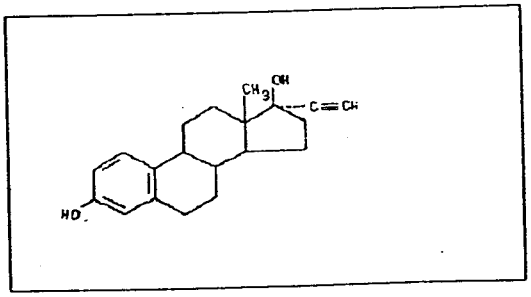
Ethinyl estradiol

CAS Registry Number: 57-63-6

Chemical names: 1. (17a)-19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol
2. 17a-ethynyl-1,3,5(10)-estratriene-3,17B-diol

Molecular formula: $C_{20}H_{24}O_2$ **Molecular mass:** 296.4

Structural formula:



Dosage form: Tablets **Route of administration:** Oral

Dosage strength and dosing regimen: CTR tablets provide 28-day oral contraception in a triphasic regimen as shown below:

100 ug DSG/25 ug EE (yellow tablets, days 1-7)
125 ug DSG/25 ug EE (orange tablets, days 8-14)
150 ug DSG/25 ugEE (red tablets, days 15-21)
Placebo (green tablets, days 22-28)

Related INDs and NDAs:

INDs 32,483 CTR 04 (DSG & EE) tablets

IND43,289 CTR 25 (DSG & EE) tablets

NDA 20-071 Desogen (DSG & EE) tablets

Previous clinical experience: The combination of 150 ug desogestrel with 30 ug ethinyl estradiol as an oral monophasic contraceptive is FDA approved product under sponsor's NDA 20-071 as CTR 04 (Desogen) and as Ortho-cept 21 and 28.

Labeling: Labeling is similar to that for the approved NDA 20-071 for the monophasic contraceptive product containing desogestrel and ethinyl estradiol. It is in accordance with Combination OC Class Labeling (Revised August 1994) and modified to reflect FDA approved text included in Mircette (desogestrel/ethinyl estradiol and ethinyl estradiol) tablets Package Insert dated 4/98 (NDA 20-713).

Note: It should be pointed out that in the labeling, product safety is based on human epidemiological observations and clinical literature citations. No preclinical toxicology findings have been described. The usual subtitle Carcinogenesis, mutagenesis, impairment of fertility (CFR 201-571, April 1, 1997) is stated only as Carcinogenesis and referred to Warning section. As such neither animal carcingenicity, mutagenicity or teratogenicity studies results are included in the labeling nor considered in human risk assessment.

Recommendations and regulatory action: Since all preclinical toxicology is cross-referred to NDA 20-071 and as the dose levels of both the desogestrel and ethinyl estradiol in the proposed formulation under consideration are equal or lower than those in the sponsor's approved monophasic formulation, Pharmacology recommends approval of the NDA 21-090 for the triphasic formulation.

/S/ 5/25/99

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/S/ 5/28

Original NDA 21-090
HFD-345
HFD-580
HFD-580/A.Jordan/D.davis/J.Mercier
HFD-580/K.Raheja, 5-27-1999, N21090.ori