Pack Insert
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Malaysia Export
Revised

Size : L- 310 x H-210 mm

Medical Examination
A complete medical history should be taken and a physical and gynecological examination should be performed prior to the initiation or reinstitution of the use of dienogest, guided by the contraindications and warnings, and these should be repeated regularly during the use of dienogest. The frequency and nature of these assessments should be adapted to the individual woman but should generally include special reference to blood pressure, breasts, abdomen and pelvic organs, and should also include cervical cytology.

INTERACTIONS WITH OTHER MEDICAMENTS
Note: The prescribing information of concomitant medication should be consulted to identify potential interactions.

Effects of other medicinal products on dienogest
Progestogens including dienogest are metabolized mainly by the cytochrome P450 3A4 system (CYP3A4) located both in the intestinal mucosa and in the liver. Therefore, inducers or inhibitors of CYP3A4 may affect the progestogen drug metabolism.

An increased clearance of sex hormones due to enzyme induction may reduce the therapeutic effect of dienogest and may result in undesirable effects e.g., changes in the uterine bleeding profile.

A reduced clearance of sex hormones due to enzyme inhibition may increase the exposure to dienogest and may result in undesirable effects.

- Substances increasing the clearance of sex hormones (diminished efficacy by enzyme-induction), e.g.:

phenytoin, barbiturates, primidone, carbamazepine, rifampicin, and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin and products containing St. John's wort (Hypericum perforatum)

Enzyme induction can already be observed after a few days of treatment. Maximum enzyme induction is generally seen within a few weeks. After cessation of drug therapy enzyme induction may be sustained for about 4 weeks.

The effect of the CYP 3A4 inducer rifampicin was studied in healthy postmenopausal women. Coadministration of rifampicin with estradiol valerate/dienogest tablets led to significant decreases in steady state concentrations and systemic exposures of dienogest and estradiol. The systemic exposure of dienogest and estradiol at steady state, measured by AUC(0-24h), were decreased by 83% and 44%, respectively.

- Substances with variable effects on the clearance of sex hormones:

When co-administered with sex hormones, many combinations of HIV protease inhibitors and nonnucleoside reverse transcriptase inhibitors, including combinations with HCV inhibitors can increase or decrease plasma concentrations of the progestin. The net effect of these changes may be clinically relevant in some cases.

- Substances decreasing the clearance of sex hormones (enzyme inhibitors)

Dienogest is a substrate of cytochrome P450 (CYP) 3A4.

The clinical relevance of potential interactions with enzyme inhibitors remains

Concomitant administration of strong CYP3A4 inhibitors can increase plasma concentrations of dienogest.

Coadministration with the strong CYP3A4 enzyme inhibitor ketoconazole resulted in a 2.9-fold increase of AUC (0-24h) at steady state for dienogest. Concomitant administration of the moderate inhibitor erythromycin increased the AUC (0-24h) of dienogest at steady state by 1.6-fold.

Effects of dienogest on other medicinal products
Based on in vitro inhibition studies, a clinically relevant interaction of dienogest with the cytochrome P450 enzyme mediated metabolism of other medication is unlikely.

Interaction with food
A standardized high fat meal did not affect the bioavailability of dienogest.

Laboratory tests
The use of progestogens may influence the results of certain laboratory tests, including biochemical parameters of liver, thyroid, adrenal and renal function, plasma levels of (carrier) proteins (e.g., corticosteroid binding globulin and lipid/lipoprotein fractions), parameters of carbohydrate metabolism and parameters of coagulation and fibrinolysis. Changes generally remain within the normal laboratory range.

PREGNANCY AND LACTATION
Pregnancy
There is limited data from the use of dienogest in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Dienogest must not be administered to pregnant women because there is no need to treat endometriosis during pregnancy.

Lactation
Treatment with dienogest during lactation is not recommended.

It is unknown whether dienogest is excreted in human milk. Data in animals have shown excretion of dienogest in rat milk.

A decision must be made whether to discontinue breast-feeding or to abstain from dienogest therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
Based on the available data, ovulation is inhibited in the majority of patients during treatment with dienogest. However, dienogest is not a contraceptive.

If contraception is required a non-hormonal method should be used

Based on available data, the menstrual cycle returns to normal within 2 months after cessation of treatment with dienogest.

SIDE EFFECTS
Presentation of undesirable effects is based on MedDRA.

The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions.

Undesirable effects are more common during the first months after the start of treatment with dienogest, and subside with continued treatment. There may be changes in bleeding pattern, such as spotting, irregular bleeding or amenorrhea. The following undesirable effects have been reported in users of dienogest. The most frequently reported undesirable effects under treatment with dienogest are headache (9.0%), breast discomfort (5.4%), depressed mood (5.1 %) and acne (5.1 %).

In addition, the majority of patients treated with dienogest experience changes in their menstrual bleeding pattern. Menstrual bleeding patterns were assessed systematically using patient diaries and were analyzed using the WHO 90 days reference period method. During the first 90 days of treatment with dienogest the following bleeding patterns were observed (n=290; 100%): Amenorrhea (1.7%), infrequent bleeding (27.2%), frequent bleeding (13.4%), irregular bleeding (35.2%), prolonged bleeding (38.3%), normal bleeding, i.e., none of the previous categories (19.7%). During the fourth reference period the following bleeding patterns were observed (n=149; 100%): Amenorrhea (28.2%), infrequent bleeding (24.2%), frequent bleeding (2.7%), irregular bleeding (21.5%), prolonged bleeding (4.0%), normal bleeding, i.e., none of the previous categories (22.8%). Changes in menstrual bleeding patterns were only occasionally reported as adverse event by the patients (See adverse event table).

The frequencies of adverse drug reactions (ADRs) by MedDRA system organ classes (MedDRA SOCs) reported with dienogest are summarized in the table below. Within each frequency grouping, undesirable effects are presented in order of decreasing frequency.

Table 1, Adverse reactions table.

System Organ Class (MedDRA)	Common	Uncommon
Blood and lymphatic system disorders		anemia
Metabolism and nutrition disorders	weight increase	weight decrease increased appetite
Psychiatric disorders	depressed mood sleep disorder nervousness loss of libido altered mood	anxiety depression mood swings
Nervous system disorders	headache migraine	autonomic nervous system imbalance disturbance in attention
Eye disorders		dry eye
Ear and labyrinth disorders		tinnitus
Cardiac disorders		unspecific circulatory systemv disorder palpitations
Vascular disorders		hypotension
Respiratory, thoracic and mediastinal disorders		dyspnoea
Gastrointestinal disorders	nausea abdominal pain flatulence abdominal distension vomiting	diarrhoea constipation abdominal discomfort gastrointestinal inflammation gingivitis
Skin and subcutaneous tissue disorders	acne alopecia	dry skin hyperhidrosis pruritus hirsutism onychoclasis dandruff dermatitis abnormal hair growth photosensitivity reaction pigmentation disorder
Musculoskeletal and connective tissue disorders	back pain	bone pain muscle spasms pain in extremity heaviness in extremities
Renal and urinary disorders		urinary tract infection
Reproductive system and breast disorders	breast discomfort ovarian cyst, hot flushes uterine / vaginal bleeding including spotting	vaginal candidiasis vulvovaginal dryness genital discharge pelvic pain atrophic vulvovaginitis breast mass fibrocystic breast disease breast induration
General disorders and administration site conditions	asthenic conditions irritability	Oedema

Decrease of bone mineral density
In an uncontrolled clinical trial with 111 adolescent women (12 to <18 years) who were treated with dienogest, 103 had BMD measurements. Approximately 72% of these study participants experienced a decrease in BMD of the lumbar spine (L2-L4) after 12 months of use.

OVERDOSAGE AND TREATMENT
Acute toxicity studies performed with dienogest did not indicate a risk of acute adverse effects in case of inadvertent intake of a multiple of the daily therapeutic dose. There is no specific antidote. A daily intake of 20 - 30 mg dienogest (10 to 15 times higher dose than in Evafact) over 24 weeks of use was very well tolerated.

EFFECTS ON ABILITY TO DRIVE AND OPERATE MACHINARY
No effects on the ability to drive and use machines have been observed in users of products containing dienogest.

STORAGE
Store below 30°C. Store in the original packaging to protect from light.

PACKAGING AVAILABLE
14 tablets are packed into a blister strip comprising of printed aluminum foil and green rigid PVC-PVDC. 2 blister strips are packed into an outer box with a product leaflet.

Pack size: 2 x 14's tablets.

BSV

PRODUCT OWNER
Bharat Serums and Vaccines Limited
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MANUFACTURER
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LEAFLET REVISION DATE
SEPTEMBER 2026.

IN234TE1MY

Black Colour

Paper : 40 gsm, ITC Print Paper
Outline & Cutting marks not to print
Artwork Code No. : IN234TE1MY
Back to Back Printing
2 Vertical & 3 Horizontal Folds
Final Fold Size : 77.5 x 26.25 mm.

Font size: 7 pt
Font name: Times New Roman