Package Leaflet: Information for the user

DERMESTRIL-Septem 25 micrograms/24hours
DERMESTRIL-Septem 50 micrograms/24hours
DERMESTRIL-Septem 75 micrograms/24hours

Estradiol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What DERMESTRIL-Septem is and what it is used for
2. What you need to know before you use DERMESTRIL-Septem
3. How to use DERMESTRIL-Septem
4. Possible side effects
5. How to store DERMESTRIL-Septem
6. Contents of the pack and other information

1. What DERMESTRIL-Septem is and what it is used for

DERMESTRIL-Septem is a Hormone Replacement Therapy (HRT). It contains 17-β estradiol. DERMESTRIL-Septem is used in postmenopausal women with at least 6 months since their last natural period.

DERMESTRIL-Septem is used for:

Relief of symptoms occurring after menopause

During the menopause, the amount of oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"). DERMESTRIL-Septem alleviates these symptoms after menopause. You will only be prescribed DERMESTRIL-Septem if your symptoms seriously hinder your daily life.

2. What you need to know before you use DERMESTRIL-Septem

Medical history and regular check-ups

The use of HRT carries risks which need to be considered when deciding whether to start taking it, or whether to carry on taking it.

The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited. If you have a premature menopause the risks of using HRT may be different. Please talk to your doctor.

Before you start (or restart) HRT, your doctor will ask about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or internal examination, if necessary.
Once you have started on DERMESTRIL-Septem you should see your doctor for regular check-ups (at least once a year). At these check-ups, discuss with your doctor the benefits and risks of continuing with DERMESTRIL-Septem.

Go for regular breast screening, as recommended by your doctor.

Do not take DERMESTRIL-Septem

if any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before taking DERMESTRIL-Septem,

Do not take DERMESTRIL-Septem

- If you have or have ever had **breast cancer**, or if you are suspected of having it
- If you have **cancer which is sensitive to oestrogens**, such as cancer of the womb lining (endometrium), or if you are suspected of having it
- If you have any **unexplained vaginal bleeding**
- If you have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated.
- If you have or have ever had a **blood clot in a vein** (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism)
- If you have a **blood clotting disorder** (such as protein C, protein S, or antithrombin deficiency)
- If you have or recently have had a disease caused by blood clots in the arteries, such as a **heart attack**, **stroke** or **angina**
- If you have or have ever had a **liver disease** and your liver function tests have not returned to normal
- If you have a rare blood problem called "porphyria" which is passed down in families (inherited)
- If you are **allergic** (hypersensitive) to Estradiol or any of the other ingredients of DERMESTRIL-Septem (listed in section 6 Further information)

If any of the above conditions appear for the first time while taking DERMESTRIL-Septem, stop taking it at once and consult your doctor immediately.

When to take special care with DERMESTRIL-Septem

Tell your doctor if you have ever had any of the following problems, before you start treatment, as these may return or become worse during treatment with DERMESTRIL-Septem. If so, you should see your doctor more often for check-ups:

- fibroids inside your womb
- growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia)
- increased risk of developing blood clots (see "Blood clots in a vein (thrombosis)")

- increased risk of getting a oestrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer)
- high blood pressure
- a liver disorder, such as a benign liver tumour
- diabetes
- gallstones
- migraine or severe headaches
- a disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE)
- epilepsy
- asthma
- a disease affecting the eardrum and hearing (otosclerosis)
- a very high level of fat in your blood (triglycerides)
- fluid retention due to cardiac or kidney problems

Stop taking DERMESTRIL-Septem and see a doctor immediately

If you notice any of the following when taking HRT:

- any of the conditions mentioned in the 'DO NOT take DERMESTRIL-Septem' section
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease
- a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness).
- migraine-like headaches which happen for the first time.
- if you become pregnant
- if you notice signs of a blood clot, such as:
  - painful swelling and redness of the legs
  - sudden chest pain
  - difficulty in breathing

For more information, see 'Blood clots in a vein (thrombosis)'

Note: DERMESTRIL-Septem is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.

HRT and cancer

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)

Taking oestrogen-only HRT will increase the risk of excessive thickness of the lining of the womb (endometrial hyperplasia) and cancer of the womb lining (endometrial cancer).

Taking a progestogen in addition to the oestrogen for at least 12 days of each 28 day cycle protects you from this extra risk. So your doctor will prescribe a progestogen separately if you still have your womb. If you have had your womb removed (a hysterectomy), discuss with your doctor whether you can safely take this product without a progestogen.

In women who still have a womb and who are not taking HRT, on average, 5 in 1000 will be diagnosed with endometrial cancer between the ages of 50 and 65.
For women aged 50 to 65 who still have a womb and who take oestrogen-only HRT, between 10 and 60 women in 1000 will be diagnosed with endometrial cancer (i.e. between 5 and 55 extra cases), depending on the dose and for how long it is taken.

DERMESTRIL-Septem 75 contains a higher dose of oestrogens than other oestrogen-only HRT products. The risk of endometrium cancer when using DERMESTRIL-Septem 75 together with a progestogen is not known.

Unexpected bleeding
You will have a bleed once a month (so-called withdrawal bleed) while taking DERMESTRIL-Septem. But, if you have unexpected bleeding or drops of blood (spotting) besides your monthly bleeding, which:

- carries on for more than the first 6 months
- starts after you have been taking DERMESTRIL-Septem more than 6 months
- carries on after you have stopped taking DERMESTRIL-Septem

see your doctor as soon as possible

Breast cancer
Evidence shows that taking combined oestrogen-progestogen or oestrogen-only hormone replacement therapy (HRT) increases the risk of breast cancer. The extra risk depends on how long you use HRT. The additional risk becomes clear within 3 years of use. After stopping HRT the extra risk will decrease with time, but the risk may persist for 10 years or more if you have used HRT for more than 5 years.

Compare
Women aged 50 to 54 who are not taking HRT, on average, 13 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period.
For women aged 50 who start taking oestrogen-only HRT for 5 years, there will be 16-17 cases in 1000 users (i.e. an extra 0 to 3 cases)
For women aged 50 who start taking oestrogen-progestogen HRT for 5 years, there will be 21 cases in 1000 users (i.e. an extra 4 to 8 cases).
Women aged 50 to 59 who are not taking HRT, on average, 27 in 1000 will be diagnosed with breast cancer over a 10-year period.
For women aged 50 who start taking oestrogen-only HRT for 10 years, there will be 34 cases in 1000 users (i.e. an extra 7 cases)
For women aged 50 who start taking oestrogen-progestogen HRT for 10 years, there will be 48 cases in 1000 users (i.e. an extra 21 cases).

- **Regularly check your breasts. See your doctor if you notice any changes such as:**
  - dimpling of the skin
  - changes in the nipple
  - any lumps you can see or feel

Additionally, you are advised to join mammography screening programs when offered to you. For mammogram screening, it is important that you inform the nurse/healthcare

Professional who is actually taking the x-ray that you use HRT, as this medication may increase the density of your breasts which may affect the outcome of the mammogram. Where the density of the breast is increased, mammography may not detect all lumps.

Ovarian cancer
Ovarian cancer is rare- much rarer than breast cancer. The use of oestrogen-only or combined oestrogen-progestagen HRT has been associated with a slightly increased risk of ovarian cancer.
The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).

Effect of HRT on heart and circulation

Blood clots in a vein (thrombosis)

The risk of **blood clots in the veins** is about 1.3 to 3-times higher in HRT users than in non-users, especially during the first year of taking it.

Blood clots can be serious, and if one travels to the lungs**,** it can cause chest pain, breathlessness, fainting or even death.

You are more likely to get a blood clot in your veins as you get older and if any of the following applies to you. Inform your doctor if any of these situations applies to you:
- you are unable to walk for a long time because of major surgery, injury or illness (see also section 3, If you need to have surgery)
- you are seriously overweight (BMI >30 kg/m2)
- you have any blood clotting problem that needs long-term treatment with a medicine used to prevent blood clots
- if any of your close relatives has ever had a blood clot in the leg, lung or another organ
- you have systemic lupus erythematosus (SLE)
- you have cancer.

For signs of a blood clot, see "Stop taking DERMESTRIL-Septem and see a doctor immediately".

Compare
Looking at women in their 50s who are not taking HRT, on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein.
For women in their 50s who have been taking oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).
For women in their 50s who have had their womb removed and have been taking oestrogen-only HRT for over 5 years, there will be 5 to 8 cases in 1000 users (i.e. 1 extra case).

Heart disease (heart attack)

There is no evidence that HRT will prevent a heart attack.

Women over the age of 60 years who use oestrogen-progestogen HRT are slightly more likely to develop heart disease than those not taking any HRT.

For women who have had their womb removed and are taking oestrogen-only therapy there is no increased risk of developing a heart disease.

Stroke

The risk of getting stroke is about 1.5-times higher in HRT users than in non-users. The number of extra cases of stroke due to use of HRT will increase with age.

Compare
Looking at women in their 50s who are not taking HRT, on average, 8 in 1000 would be expected to have a stroke over a 5-year period. For women in their 50s who are taking HRT, there will be 11 cases in 1000 users, over 5 years (i.e. an extra 3 cases).

Other conditions

- HRT will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using HRT after the age of 65. Speak to your doctor for advice.

Using other medicines
Some medicines may interfere with the effect of DERMESTRIL-Septem. This might lead to irregular bleeding. This applies to the following medicines:

- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepin)
- Medicines for **tuberculosis** (such as rifampicin, rifabutin)
- Medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir and nelfinavir)
- Herbal remedies containing **St John's Wort** (Hypericum perforatum).

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without a prescription, herbal medicines or other natural products.

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are taking DERMESTRIL-Septem, because this medicine can affect the results of some tests.

Pregnancy and breast-feeding
DERMESTRIL-Septem is for use in postmenopausal women only. If you become pregnant, stop taking DERMESTRIL-Septem and contact your doctor.

Driving and using machines
DERMESTRIL-Septem is not expected to influence the ability to drive or to use machines.

3. How to use DERMESTRIL-Septem

Always use DERMESTRIL-Septem exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Three strengths of DERMESTRIL-Septem are available, DERMESTRIL-Septem 25, 50, 75. The choice of which DERMESTRIL-Septem patch will suit you best will be made by your doctor, although most women start with the DERMESTRIL-Septem 25 patch. During treatment your doctor will adjust the dose of patch to your individual need and this will depend on how effective the treatment is and if you are suffering from side effects. For initiation and continuation of therapy, your

doctor will aim to prescribe the lowest dose of patch to treat your symptoms for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.
Bleeding and drops of blood (spotting) may occur during the first months of treatment. If break-through bleeding or spotting appears after some time on therapy, or continues after treatment has been discontinued please contact your doctor.

How to apply the patch
You should apply the patch to clean, dry skin, but not on top of cuts, spots or blemishes or to an area where you have just applied cream, moisturiser or talc.

You **MUST NOT** apply DERMESTRIL-Septem patches on or near the breasts.

Your DERMESTRIL-Septem patch should be applied to the hip, buttock or abdomen (see Figure 1).

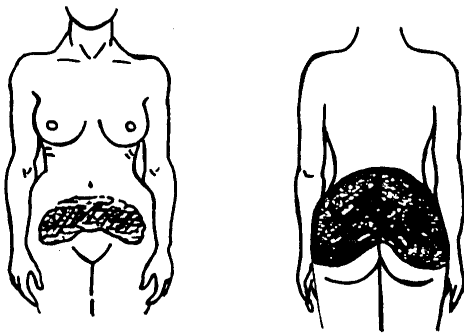

Figure 1
Shaded areas are the correct places to apply your patch.

Do not apply a patch to a part of the body that folds during movement or where your clothing (eg. elasticated waistbands) may make the patch fall off.
Do not apply patches one after the other to the same place.
A DERMESTRIL-Septem patch should be applied to the skin as soon as it is removed from its sachet, as follows:

(i) Tear open the sachet at the indentation.
Do not use scissors (see Figure 2).

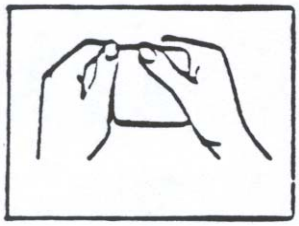

Figure 2

(ii) Hold the patch between your thumb and index finger at the pull-off tag (see Figure 3).

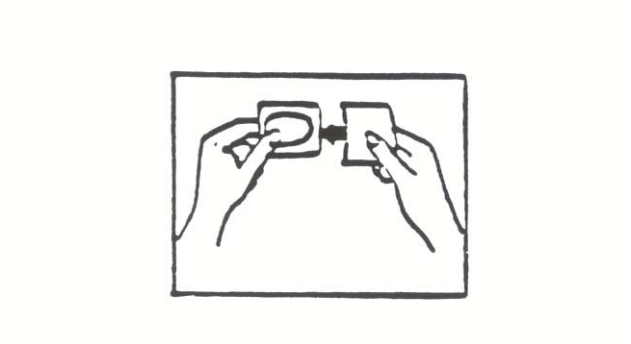

Figure 3

(iii) Peel off the protective liner with your other hand (see Figure 4). Do not touch the sticky side of the patch or it will not stick properly.

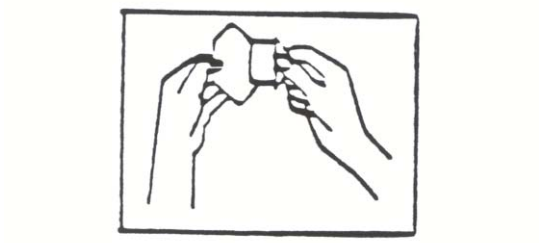

Figure 4

(iv) Apply the open part of the patch to your skin and remove the remaining part of the protective liner. Press firmly for about 10 seconds on the whole surface of the patch. Run your finger along the edges to make sure it is firmly stuck down.

How often you should change the patch

There is enough hormone in each patch to last for several days. In order to ensure a steady supply of hormone, the patch must be changed at one-week intervals; thus each used patch has to be removed after seven days and replaced by a new one. The patch may be applied at any time of the day.

What to do if a patch comes off

If DERMESTRIL-Septem is applied correctly, it is most unlikely that the patch will fall off. However if the patch does fall off, replace it with a new one and then change the patch again as usual on your next regular day.

Your patch should stay on in the shower or bath, but may fall off if you have a sauna or a particularly hot bath.

How to remove the patch

To remove a patch, just peel away at the edge and pull the patch smoothly until it comes off. After use, fold the patch in half, sticky side inwards and throw in a dustbin where children cannot reach it.

When to start the treatment

You can initiate the treatment with DERMESTRIL-Septem at any convenient time if you are not currently on any estrogen therapy.

If you are currently using cyclic or sequential estrogen-progestogen therapy, you should complete the on-going treatment cycle before beginning treatment with DERMESTRIL-Septem; the appropriate time to begin treatment with DERMESTRIL-Septem would be the first day of a withdrawal bleeding. If you are already using a continuous combined estrogen/progestogen therapy you may switch to DERMESTRIL-Septem directly.

How to take progestogen with DERMESTRIL-Septem
If you have a uterus i.e. have not had a hysterectomy, your doctor may prescribe a progestogen for you with DERMESTRIL-Septem patch to prevent any problems due to a build up of the lining of the womb, i.e. endometrial hyperplasia (see special warning on endometrial cancer). Your doctor will prescribe the progestogen usually for 12-14 days every months of the 28 day cycle. You may experience a "withdrawal bleed" (like a period) during the last few days of, or after stopping, the progestogen treatment.

If you use more DERMESTRIL-Septem patches than you should
If you accidentally put too many patches on, you may find that you suffer from breast tenderness and/or vaginal bleeding, irritability, anxiety, nausea, vomiting, sleepiness, dizziness, swelling of the abdomen or pelvis, flatulence, fluid retention and a feeling of heaviness in the legs. The effects of using too many patches may be reversed simply by removing them.
Aforementioned information is also applicable for overdosing in children.

If you forget to change DERMESTRIL-Septem patch
If you forget to change the patch at the right time, you should replace it as soon as possible, and then follow your original regular schedule for applying the next patch. If you forget a dose you may increase the likelihood of break-through bleeding and spotting.

If you stop using DERMESTRIL-Septem
When stopping the treatment with DERMESTRIL-Septem, you may experience a recurrence of postmenopausal symptoms.

If you need to have surgery
If you are going to have surgery, tell the surgeon that you are taking DERMESTRIL-Septem. You may need to stop taking DERMESTRIL-Septem about 4 to 6 weeks before the operation to reduce the risk of a blood clot (see section 2, Blood clots in a vein). Ask your doctor when you can start taking DERMESTRIL-Septem again.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines**,** DERMESTRIL-Septem can cause side-effects, although not everybody gets them.

The following diseases are reported more often in women using HRT compared to women not using HRT:

- breast cancer
- abnormal growth or cancer of the lining of the womb (endometrial hyperplasia or cancer)
- ovarian cancer
- blood clots in the veins of the legs or lungs (venous thromboembolism)
- heart disease
- stroke

- probable memory loss if HRT is started over the age of 65

For more information about these side effects, see Section 2.

The following side-effects may occur with HRT**:**

Common side effects: may affect up to 1 in 10 people
- headache
- nausea
- abdominal pain
- Disturbed menstruation period (metrorrhagia), uterine/vaginal bleeding including spotting
- weight changes
- rash (red and inflammed skin)
- pruritus (itching).

Uncommon side effects: may affect up to 1 in 100 people
- vaginal thrush
- dizziness
- hypersensitivity reactions
- depressed mood
- visual disturbances (disturbed vision)
- palpitations (irregular heartbeat)
- dyspepsia (difficult or disturbed digestion)
- gall bladder disorder
- erythma nodosum (painful reddish skin nodules)
- urticaria (hives)
- breast pain, breast tenderness
- edema (abnormally large fluid volume in the circulatory system or in tissues).

Rare side effects: may affect up to 1 in 1000 people
- changes in libido
- eye irritation during contact lenses use
- anxiety
- migraine
- bloating (post-prandial abdominal fullness or swelling)
- vomiting (being sick)
- hirsutism (excessive growth of facial or body hair)
- acne (pimples on the face, chest and back)
- muscle cramps
- dysmenorrhea (painful cramps during menstruation)
- vaginal discharge
- premenstrual-like syndrome (physical symptoms that occur between ovulation and the onset of menstruation, such as breast tenderness, back pain, abdominal cramps, headache, and changes in appetite, as well as psychological symptoms of anxiety, depression, and unrest)
- breast enlargement
- fatigue (physical and/or mental exhaustion).

<u>Other adverse reactions have been reported in association with estradiol treatment (frequency unknown):</u>

- Breast cancer, benign or malignant tumours which may be affected by the levels of oestrogens, such as cancer of the womb lining (endometrial cancer), ovarian cancer, increase

in size of leiomyoma (benign tumour of the womb)
- Worsening of fits (epilepsy), muscle twitches you cannot control (chorea)
- Stroke
- Blood clots in the arteries (arterial thromboembolism), angina and heart attack
- Blood clots in the legs or lungs (venous thromboembolism or pulmonary embolism)
- Inflammation of the pancreas (pancreatitis) in women with pre-existing high levels of certain blood fats (hypertriglyceridemia)
- Gastroesophageal reflux disease
- Abnormal liver function, sometimes with yellowing of the skin (jaundice)
- Swelling of the skin around the face and throat, this may cause difficulty in breathing (Angioedema),
- Rash with target-shaped reddening or sores (erythema multiforme)
- Vascular purpura (Blood vessel inflammation that results in the appearance of purplish spots on the skin)
- Discoloration of the skin especially of the face or neck known as "pregnancy patches" (chloasma)
- Application site reactions: skin redness with or without itching
- Urinary incontinence
- Painful/lumpy breasts (fibrocystic breast disease)

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL- Dublin 2; Tel: + 353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store DERMESTRIL-Septem

Keep DERMESTRIL-Septem out of the reach and sight of children.

Do not store DERMESTRIL-Septem above 25°C.

DERMESTRIL-Septem should be stored in its sachet intact.

Do not use DERMESTRIL-Septem after the expiry date which is stated on the carton or on the sachets after EXP. The expiry date refers to the last day of that month.

After use, fold the patch in half, sticky side inwards and throw in a dustbin where children cannot reach it.
The patches left over should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. The measures will help to protect the environment.

6. Contents of the pack and other information

What DERMESTRIL-Septem contains

DERMESTRIL-Septem patches contain the estrogen hormone 17-β estradiol. The adhesive backed patches are applied to the skin and the hormone will then pass continuously through your skin and into your body.

DERMESTRIL-Septem patches are for external use only.

DERMESTRIL-Septem patches are available in three strengths:

DERMESTRIL-Septem 25: contains 2.5 mg of the active ingredient estradiol (as hemihydrate) and releases about 25 micrograms of estradiol per day (in 24 hours).

DERMESTRIL-Septem 50: contains 5.0 mg of the active ingredient estradiol (as hemihydrate) and releases about 50 micrograms of estradiol per day (in 24 hours).

DERMESTRIL-Septem 75: contains 7.5 mg of the active ingredient estradiol (as hemihydrate) and releases about 75 micrograms of estradiol per day (in 24 hours).

The other ingredients are adhesive substances (acrylic copolymers), a backing foil (polyethylene terephthalate) and a protective liner (siliconised polyethylene terephthalate) which is removed prior to use.

What DERMESTRIL-Septem looks like and content of the pack

DERMESTRIL-Septem are transparent transdermal patches individually sealed in a protective sachet.

DERMESTRIL-Septem patches come in cartons which contain 4 or 12 patches.

Marketing Authorisation Holder

Rottapharm Ltd.
Damastown, Industrial Park, Mulhuddart
Dublin 15
Ireland.

Manufacturer responsible for batch release

MEDA Pharma GmbH & Co. KG
Benzstraße 1
61352 Bad Homburg
GERMANY

LTS Lohmann Therapie-Systeme AG
Lohmannstr. 2
56626 Andernach
GERMANY

This medicinal product is authorised in the Member States of EEA under the following names:

Country	**Name**
Belgium	DERMESTRIL-Septem
France	DERMESTRIL-Septem

Germany	DERMESTRIL-Septem
Ireland	DERMESTRIL-Septem
Italy	DERMESTRIL-Septem
Luxembourg	DERMESTRIL-Septem
Portugal	DERMESTRIL-Septem

This leaflet was last revised in August 2020.