Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Estradot Conti 30/95 transdermal patch, 30 micrograms/24 hours and 95 micrograms/24 hours
Estradot Conti 40/130 transdermal patch, 40 micrograms/24 hours and 130 micrograms/24 hours

estradiol (as hemihydrate) and norethisterone acetate

PL 04416/1743-1744

Sandoz Limited

LAY SUMMARY

Estradot Conti 30/95 transdermal patch, 30 micrograms/24 hours and 95 micrograms/24 hours and Estradot Conti 40/130 transdermal patch, 40 micrograms/24 hours and 130 micrograms/24 hours

estradiol (as hemihydrate) and norethisterone acetate

This is a summary of the Public Assessment Report (PAR) for Estradot Conti 30/95 transdermal patch, 30 micrograms/24 hours and 95 micrograms/24 hours and Estradot Conti 40/130 transdermal patch, 40 micrograms/24 hours and 130 micrograms/24 hours. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Estradot Conti in this lay summary for ease of reading.

These products have been authorised by Medicines and Healthcare products Regulatory Agency (MHRA) for the United Kingdom. This procedure takes into account the outcome of mutual recognition (MR) procedures in European Union Member States (and/or Iceland, Liechtenstein, Norway) on 25 March 2008 (NL/H/1155/001-002). This is known as the MR/DC Reliance Procedure.

These applications were approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

For practical information about using Estradot Conti, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Estradot Conti and what is it used for?
These applications are full-dossier applications. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

Estradot Conti is used for the relief of symptoms occurring after menopause.

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

There is only limited experience of treating women older than 65 years with Estradot Conti.

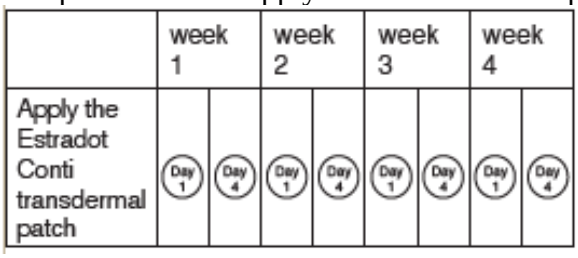
How does Estradot Conti work?
Estradot Conti is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and a progestogen. Estradot Conti is used in postmenopausal women with at least 1 year since their last natural period.

How is Estradot Conti used?
The pharmaceutical form of these medicines is a transdermal patch and the route of administration is through the skin.

The patient's doctor will aim to prescribe the lowest dose to treat their symptoms for as short as necessary. The patient should speak to their doctor if they think this dose is too strong or not strong enough.

Estradot Conti should be applied twice a week, i.e. a new transdermal patch should be applied every 3 or 4 days.

The patient should apply the Estradot Conti patches continuously (without interruption).



When to start treatment
•In women who have never used hormone replacement therapy before or women who change from continuous combined hormone replacement therapy, the treatment can be started on any day.
• In women who are changing form a cyclic or continuous sequential hormone replacement therapy, the treatment should start on the day immediately following completion of the preceding cycle.

Method of use
Where to apply the patch
• The patient should stick the patch on an area of the skin where little wrinkling of skin occurs during movement, such as on the side of the upper thigh. Patients should NOT apply these patches to the breast.
• The skin should not be red or injured.
• The site where the patient sticks the patch should be hair free.
• The patient should avoid areas of the skin where clothing may pinch or under clothing edges.
• The patient should clean the skin thoroughly before they stick the patch on the skin. They should not use body-lotion, body oil, shower gel, suntan products or other products containing a fatty substance. The patient's skin must be dry and not oily.

Open the pack
• The patient should tear the pack open carefully by one of the two corners, along the perforation, just before use.
• The patient should hold the patch by the edge and remove it from the pack.
Note: the drying agent attached to the inner side of the pack is intended to ensure the quality of the product, and must not be used on the skin.

Remove the protective film
• The patient should hold the protective liner with both hands.

• Carefully bend the patch up and down along the perforated curved line.
• Carefully peel off most of the transparent protective liner from the patch.
• The patient should not touch the adhesive layer of the patch.

Sticking the patch on
• The patient should stick the adhesive part of the patch evenly on the body, making sure there are no air bubbles under it.
• Remove the remainder of the protective liner and stick the remaining part of the patch to the skin.
• The patient should press the patch for one minute with the flat of their hand; the Estradiol patch is now applied correctly.

Using the patch
• The patient can take a bath of shower while wearing the patch. The patch may come off in very hot bathwater or in a sauna.
• Avoid the use of fatty crèmes, lotions and powders on the application site of the patch.
• The patch may become less active if exposed to sunlight or artificial sunlight (e.g. in a solarium).

Applied correctly, Estradot Conti adheres well and normally sticks on for at least 4 days without any problem.

If the patch has not been applied correctly or has come off during use, it should not be reused. The patient should use a new patch.

The patch should be changed on the usual day. Forgetting to apply a patch may increase the risk of a breakthrough bleeding or spotting.

New patch
• After use the patch should be taken off, folded up with the sticky side inwards and thrown away.
• Apply a new patch to another area of the skin.

Duration of treatment
The patient’s doctor will tell them how long they should continue the treatment. It is important that the patient should keep to these instructions. If the patient wishes to stop the treatment sooner, they should consult their doctor. Together with their doctor they should have a periodic reassessment of their need for oestrogen treatment. This should be done at least once a year.

Pediatric population
Estradiol/norethisterone is not indicated for use in children.

For further information on how Estradot Conti are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Estradot Conti have been shown in studies?
In clinical studies with Estradot Conti, relief of menopausal symptoms was achieved during the first few weeks of treatment.

Amenorrhoea (no bleeding or spotting) was seen in 33.9 % of the women (about 90% treatment naive, median 2.4 years postmenopausal) during months 10-12 of treatment whereas the cumulative amenorrhoea rate increased from 33.9 % in cycle 10 to 40.2% in cycle 12. Breakthrough bleeding and/or spotting appeared in 63.4 % of the women during the first three months of treatment and in 66.1 % during months 10-12 of treatment.

What are the possible side effects of Estradot Conti?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Estradot Conti (which may affect more than 1 in 10 people) are:
• headache
• skin reactions at the site of application
• breast tension and pain, painful menstruation (dysmenorrhea), menstrual disorder

Why were Estradot Conti approved?
It was concluded that Estradot Conti have been shown to be effective in the treatment of hormone replacement therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women with a uterus and HRT for oestrogen deficiency in women at least 12 months since the last menstrual period.

Furthermore, the side effects observed with use of these products are considered to be typical for this type of treatment. Therefore, the MHRA decided that the benefits are greater than the risks and recommended that these medicines can be approved for use.

What measures are being taken to ensure the safe and effective use of Estradot Conti?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Estradot Conti. The RMP details the important risks of Estradot Conti, how these risks can be minimised, any uncertainties about Estradot Conti (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Estradot Conti.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Estradot Conti are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Estradot Conti
Marketing authorisations were granted in the United Kingdom on 24 March 2025.

The full PAR for Estradot Conti follows this summary.

This summary was last updated in May 2025.

TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Estradot Conti 30/95 transdermal patch, 30 micrograms/24 hours and 95 micrograms/24 hours and Estradot Conti 40/130 transdermal patch, 40 micrograms/24 hours and 130 micrograms/24 hours (PL 04416/1743-1744) could be approved.

The products are approved for the following indication:
Hormone replacement therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women with a uterus.

HRT for oestrogen deficiency in women at least 12 months since the last menstrual period.

Experience treating women older than 65 years is limited.

Estradiol
The active ingredient, synthetic 17ß-estradiol, is chemically and biologically identical to endogenous human estradiol. It substitutes for the loss of oestrogen production in menopausal women and alleviates menopausal symptoms.

Norethisterone acetate
As oestrogens promote the growth of the endometrium, unopposed oestrogens increase the risk of endometrial hyperplasia and cancer. The addition of a progestagen greatly reduces the oestrogen-induced risk of endometrial hyperplasia in non-hysterectomised women.

These products have been authorised by MHRA for the United Kingdom. This procedure takes into account the outcome of mutual recognition (MR) procedures in European Union Member States (and/or Iceland, Liechtenstein, Norway) on 25 March 2008 (NL/H/1155/001-002).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted during the MR procedures, please refer to the Reference Member State (RMS) Public Assessment Report, available on the RMS regulatory agency website or on the Heads of Medicines Agencies website.

These applications were approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Marketing authorisations were granted on 24 March 2025.

II. PRODUCT INFORMATION

Summaries of Product Characteristics (SmPCs)

The SmPCs are in line with current guidelines and are satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for these applications is satisfactory.

The grant of marketing authorisations was recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for these applications is satisfactory.

The grant of marketing authorisations was recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for these applications is satisfactory.

The grant of marketing authorisations was recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the products is acceptable. The non-clinical and clinical data submitted have shown the positive benefit/risk of these products in the treatment of hormone replacement therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women with a uterus and HRT for oestrogen deficiency in women at least 12 months since the last menstrual period.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

IX. TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**