Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Condyline 5 mg/ml Cutaneous Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Condyline Solution contains 5 mg/ml podophyllotoxin in bottles of 3.5 ml.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous Solution.

Each pack of Condyline Solution consists of a 3.5 ml clear, colourless, alcoholic cutaneous solution of 5 mg/ml podophyllotoxin.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the topical treatment of condylomata acuminata (warts) affecting the penis or the female external genitalia.

4.2 Posology and method of administration

By topical administration.

Adults
Apply twice daily for three consecutive days directly to the warts. Allow to dry after treatment.
Use the applicator provided, applying not more than 50 applicators-full for each treatment. This three day treatment may be repeated, if necessary, at weekly intervals for a maximum of five weeks of treatment. Only a small area or number of warts should be treated at any one time.

Special Patient Populations

Elderly
No dose adjustment is needed.

Paediatric population
Not recommended in children under 12 years of age.

4.3 Contraindications

Condyline solution is contraindicated in patients with the following conditions/diseases:
- hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- inflamed or bleeding lesions;
- open wounds following surgical procedures;
- in combination with other podophyllin containing preparations;
- pregnant or breast-feeding women (see section 4.6);
- children under 12 years of age.

4.4 Special warnings and precautions for use

Avoid contact with healthy skin as well as the eyes and face because of severe irritation.

Lesions in the female and lesions greater than 4cm^2 in the male should be treated under direct medical supervision.

The risk of toxicity is increased during simultaneous treatment with other podophyllin containing preparations since these also contain podophyllotoxin and should therefore be avoided.

The risk of systemic toxicity after topical application is increased by the treatment of large areas with excessive amounts for prolonged periods, by the treatment of friable, bleeding or recently removed warts, and by inadvertent application to normal skin or mucous membranes.

4.5 Interaction with other medicinal products and other forms of interactions

None known.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is a limited amount of data from the use of podophyllotoxin in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).
Podophyllotoxin is not recommended during pregnancy or in women of childbearing potential not using contraception (see section 4.3).

Breast-feeding
A risk to the suckling child cannot be excluded. Podophyllotoxin should not be used during breastfeeding (see section 4.3).

Fertility
There are no or limited amount of data on fertility. Animal studies are insufficient with respect to effect on fertility (see section 5.3). Podophyllotoxin is not recommended in women of childbearing potential not using contraception.

4.7 Effects on ability to drive and use machines

Condyline Solution does not interfere has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following convention is used for the classification of the frequency of an adverse drug reaction (ADR) and is based on the Council for International Organizations of Medical Sciences (CIOMS) guidelines: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

System Organ Class (SOC)	Frequency	Preferred term
Nervous system disorders	Not known[1]	Burning sensation
Skin and subcutaneous tissue disorders	Not known[1]	Application site irritation including pruritus, erythema, skin lesion
Reproductive system and breast disorders	Not known[1]	Balanoposthitis
General disorders and administration site conditions	Not known[1]	Pain

1. The adverse drug reactions are based on post-marketing reports. Since these reports are from a population of uncertain size and are subject to confounding factors, it is not possible to reliably estimate their frequency, however in reality systemic reactions are rarely seen.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Symptoms
The risk of systemic toxicity after topical application is increased by the treatment of large areas with excessive amounts for prolonged periods, by the treatment of friable, bleeding, or recently removed warts, and by inadvertent application to normal

skin or mucous membranes. Symptoms including nausea, vomiting, abdominal pain and diarrhoea; thrombocytopenia, leukopenia, hepatotoxicity or renal failure may occur. CNS-related adverse events are delayed in onset and prolonged in duration and include acute psychotic reactions, hallucinations, confusion, dizziness, stupor, ataxia, hypotonia, seizures and coma. Peripheral and autonomic neuropathies develop later and may result in paraesthesias, reduced reflexes, muscle weakness, tachycardia, apnoea, orthostatic hypotension, paralytic ileus and urinary retention.

Management
In topical overdosage, wash well with soap and water; if the eyes are involved, bathe thoroughly with water or if available, with an appropriate eye-cleaning solution. If accidentally ingested, give stomach washout and monitor electrolyte balance, blood gases, liver function and blood picture.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antivirals.
ATC code: D06BB04.

Podophyllotoxin is the therapeutically active component of podophyllin, the resin from the root of Pododphyllum species (Berberidaceae).

Podophyllotoxin is an anti-mitotic agent, with a topical action against genital warts. It is applied locally to the lesion (e.g. wart) and causes destruction of the tissue locally.
Podophyllotoxin and its derivatives have a special affinity for the microtubule protein of the mitotic spindle and thus arrest mitosis in metaphase leading to epithelial cell death. It is also caustic to normal skin if applied to it and can be absorbed into the systemic circulation with resultant toxic effects, in particular nausea, vomiting and thrombocytopenia.

5.2 Pharmacokinetic properties

Absorption
As podophyllotoxin is only absorbed through the skin or mucous membranes to a very limited extent upon local application, no systemic effects are to be expected with the recommended method of use and dosage. The extent of absorption depends on the concentration used.

Topical application of 0.1 ml of 5 mg/ml podophyllotoxin on an area of 4 cm^2 resulted in maximum plasma concentrations of 5 ng/ml after 1-2 hours. After topical application of 0.1-0.15 ml on extreme large lesions the maximum plasma concentrations was 1-17 ng/ml. The serum half-life varies between 1 to 4.5 hours.

Distribution
Owing to its high lipid solubility, it is distributed through the body including the CNS. There is no accumulation of the substance in serum.

Metabolism
No data are available on the metabolism of podophyllotoxin.

Excretion and Elimination
No data are available on the excretion of podophyllotoxin.

5.3 Preclinical safety data

Podophyllotoxin toxicity in animals is related to its cytotoxic activity.

The acute toxicity of podophyllotoxin has been assessed in multiple species and with multiple routes of administration resulting in a wide range of LD50s and described toxicities.

The repeat dose toxicity of podophyllotoxin has been assessed in multiple species and with multiple routes of administration. GLP toxicity studies included those in rats and dogs. In a 90-day dermal toxicity study in rats the higher doses (equivalent to 2 and 10 mg/kg) resulted in necrosis, ulceration and/or hyperplasia at the site of administration and in adjacent skin, as well as corneal lesions, renal pathology, and death at 10 mg/kg due to application site toxicity. The NOAEL was the low dose

equivalent to 0.25 mg/kg. In 26-week dietary toxicity studies in rats and dogs, other than a slight reduction in body weight in the dog study there were no significant podophyllotoxin related effects and the NOELs were the high dose of 0.3 mg/kg.

Carcinogenesis
An *in vitro* cell transformation assay was negative. Long-term topical treatment with podophyllotoxin in mice did not cause skin tumours, but epithelial hyperplasia of the skin was observed.

Dietary carcinogenicity studies in mice and rats for 80 weeks or 104 weeks, respectively, were negative for oncogenic effects induced by podophyllotoxin at doses up to 0.3 mg/kg/day.

Mutagenesis
Although studies to assess the genotoxic potential of podophyllotoxin were conducted, a definitive assessment of the potential for mutagenicity could not be concluded. Other studies suggest that podophyllotoxin has aneugenic activity consistent with its pharmacological action as a microtubule inhibitor.

Reproductive Toxicity
As a cytotoxic agent podophyllotoxin has teratogenic potential. Reproductive toxicity and fertility studies after local application, or oral or intraperitoneal administration, were conducted in rats and rabbits.

Podophyllotoxin was not teratogenic and there was no impact on fertility, pregnancy, lactation, or post-natal development. Fetotoxicity was reported in one rat study with intraperitoneal administration.

Tritiated podophyllotoxin was administered orally or intravenously to pregnant mice and quickly crossed the placenta into the foetus. Radioactivity quickly cleared from the foetuses and at 24 hours after dosing was only present in intestinal contents.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactic acid
Sodium lactate 60%
Solution Ethanol 96%

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.
Shelf-life after opening the immediate container: 6 weeks

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Each pack of Condyline Solution consists of an amber glass bottle fitted with a child resistant polypropylene closure, containing 3.5 ml. The pack is supplied with 30 disposable plastic applicators which have a small hole in one end that holds the solution.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Condyline Solution is flammable and should be kept away from naked flames. A patient information leaflet is provided with the product giving details on the use and handling of the product.

7 MARKETING AUTHORISATION HOLDER

Takeda Products Ireland Ltd
6th Floor
South Bank House
Barrow Street
Dublin 4
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2229/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11th April 1988

Date of last renewal: 11th April 2008

10 DATE OF REVISION OF THE TEXT

May 2021