Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ellura hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One capsule contains 195.7 to 216.9 mg of extract (as dry extract, refined) from the juice of *Vaccinium macrocarpon* Ait., fructus (cranberry fruit), corresponding to 36 mg of proanthocyanidins (PAC), calculated as PAC A2.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard capsule (capsule).
Colourless capsule containing a dark purple powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A traditional herbal medicinal product used to prevent recurrent uncomplicated acute urinary tract infections (UTIs) such as cystitis in women exclusively based on long standing use. Ellura hard capsules are indicated in adult women over the age of 18 years.

4.2 Posology and method of administration

For oral use only.
Ellura hard capsules should always be taken with a large glass of water.

Adult women over 18 years including the elderly
Ellura hard capsules are indicated for use in women who suffer from recurrent uncomplicated acute UTIs, meaning those who have had at least 3 or more episodes in the past 12 months or 2 or more episodes in the past 6 months.

If these acute uncomplicated UTIs recur more often, a doctor should be consulted for advice including advice on the frequency of this prophylactic treatment.

Duration of treatment
One capsule of Ellura to be taken per day as prophylactic treatment for a minimum of 15 consecutive days after the most recent UTI.

Maximum duration of use is 6 months.

If the patient experiences symptoms of a UTI during the use of the medicinal product, a doctor should be consulted.

Children and adolescents under 18 years old:

This product is not recommended in children and adolescents under 18 years old (see section 4.4)

Men:
The use of Ellura hard capsules in men is not recommended (see section 4.4)

4.3 Contraindications

Hypersensitivity to cranberry (*Vaccinium macrocarpon* Ait.) fruit or to any of the excipients.

Current or previous renal disease including kidney stones.

Oedema secondary to heart failure or impaired renal function.

Conditions where a reduced fluid intake is recommended e.g. severe cardiac or renal diseases.

Concomitant use of warfarin and other anticoagulant medicines (see section 4.5).

Concomitant use of immunosuppressant drugs (see section 4.5) Concomitant use with chemotherapy (see section 4.5).

4.4 Special warnings and precautions for use

If the patient experiences symptoms of a UTI during the use of Ellura hard capsules a doctor should be consulted.

A doctor should be consulted **immediately**, if any of the following symptoms develop: fever, dysuria rigors, abdominal pain, back pain, haematuria, urinary retention or urinary incontinence.

Medical advice should be sought if the patient is not sure if she has a UTI.

Cranberry fruit contains oxalic acid, and there may be an increased risk of stone formation in the urinary tract in patients with stone history (see section 4.3).

The use in children and adolescents under 18 years old is not recommended because safety and efficacy data has not been established and medical advice should be sought.

The use in men is not recommended because urinary symptoms in men require medical supervision.

4.5 Interaction with other medicinal products and other forms of interaction

Individual case reports suggest a possible interaction between warfarin and cranberry juice, in most cases leading to an increase in INR or bleeding event.

Other vitamin K antagonists such as acenocoumarol and phenindione are occasionally used instead of warfarin and could also potentially interact with cranberry juice.

There are no reports to date of interactions between cranberry and the new direct- acting oral anticoagulants which are not vitamin K antagonists (such as apixaban, edoxaban, dabigatran, and rivaroxaban) or parenteral anticoagulants (such as heparin, dalteparin, enoxaparin and tinzaparin); however, a clinical study demonstrates a potential pharmacodynamic interaction between cranberry and warfarin.

Therefore, the concomitant use of anticoagulant medicines and cranberry juice products is contraindicated (see section 4.3).

There is no evidence that cranberry juice has a clinically relevant effect on the pharmacokinetics of amoxicillin or cefaclor.
A recent case study reported that concurrent administration of tacrolimus and cranberry juice resulted in a significant reduction in tacrolimus levels. Therefore, patients taking immunosuppressant drugs should not take cranberry preparations (see section 4.3).

An *in vitro* study has suggested that cranberry inhibits CYP2C8, an enzyme pathway for metabolizing many drugs, including paclitaxel. Although there are no human studies showing an interaction between cranberry and paclitaxel, patients receiving chemotherapy should not take cranberry products (see section 4.4).

4.6 Fertility, pregnancy and lactation

The safety of this product during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

No studies on the effects on fertility have been performed.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Gastrointestinal disorders: nausea, vomiting, diarrhoea, constipation, abdominal pain or discomfort.

Skin and subcutaneous tissue disorders: rash (hypersensitivity reaction). The frequency is unknown and cannot be estimated from the available data.

If other adverse reactions not mentioned above occur, a qualified healthcare professional e.g. a doctor, pharmacist or nurse should be consulted.

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 a medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

No cases of overdose have been reported.

Supportive and symptomatic treatment should be provided as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Not required as per Article 16c (1) (a) (iii) of Directive 2001/83/EC as amended.

5.2 Pharmacokinetic properties

Not required as per Article 16c (1) (a) (iii) of Directive 2001/83/EC as amended.

5.3 Preclinical safety data

Reverse mutation assays (Ames test) conducted with cranberry refined dry extract on bacteria indicated that the product was mutagenic in 3 strains of Salmonella typhimurium (TA1537, TA98 and TA100) without metabolic activation, and in 4 strains (TA1537, TA98 and TA100, TA102) with metabolic activation. This positive result was attributed to the presence of flavonoids (quercetin and kaempferol and myricetin) and is not considered relevant to human safety.

Tests on reproductive toxicity and carcinogenicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Magnesium stearate
Colloidal anhydrous silica
Hypromellose (capsule shell)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Store in the original packaging.

6.5 Nature and contents of container

Blister packs of 15, 30, 60 or 90 capsules (PVC/PE/PVDC film-aluminium foil with PVC/PVA copolymer, and butylmethylacrylate coating).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 REGISTRATION HOLDER

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8 REGISTRATION NUMBER(S)

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