1. NAME OF THE MEDICINAL PRODUCT

Micona 2% w/w vaginal cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition

Miconazole nitrate 2% w/w

Preservative:

Benzoic acid…….0.2% w/w

3. PHARMACEUTICAL FORM

White smooth, homogeneous cream. Free from gritty particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Micona 2% w/w is for the local treatment of vulvo-vaginal candidosis and superinfection due to susceptible Gram-positive bacteria.

4.2 Posology and method of administration

Micona 2% w/w cream is for vaginal administration. Adults (aged 18 years and older): The contents of two applicators (10 g of cream) inserted high into the vagina at night for 7 days. Alternatively, the contents of one applicator inserted high into the vagina at night for 14 days. Continue the full 7- or 14-day course of treatment even after pruritus and leukorrhoea have disappeared or menstruation begins. Paediatrics (aged under 18 years) The safety and efficacy of Micona 2% w/w cream in children and adolescents has not been studied.

4.3 Contraindications

Micona 2% w/w cream is contraindicated in individuals with a known hypersensitivity to miconazole/miconazole nitrate, other imidazole derivatives or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with Micona 2% w/w cream and with other miconazole formulations (see section 4.8). If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued. Absorption of the antifungal may occur through denuded mucosa. To date there have been no reports of systematic adverse effects following a single dose. Health Products Regulatory Authority 23 December 2020 CRN00C0PG Page 2 of 6 Appropriate therapy is indicated when the sexual partner is also infected. Micona 2% w/w cream does not stain skin or clothes. The concurrent use of latex condoms or diaphragms with vaginal anti-infective preparations may decrease the effectiveness of latex contraceptive agents. Therefore Micona 2% w/w cream should not be used concurrently with a latex condom or latex diaphragm. Micona 2% w/w cream contains benzoic acid, which is mildly irritant to the skin, eyes and mucous membranes, and butylated hydroxyanisole, which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

4.5 Interaction with other medicinal products and other forms of interactions

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after vaginal application, clinically relevant interactions occur very rarely. In patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored. The effects and side effects of some other drugs (e.g., oral hypoglycemics and phenytoin), when co-administered with miconazole, can be increased and caution should be exercised. Contact should be avoided between certain latex products such as contraceptive diaphragms or condoms and Micona 2% w/w cream since the constituents of the cream may damage the latex (see Section 4.4, Special warnings and special precautions for use).

4.6 Fertility, pregnancy and lactation Pregnancy

Although intravaginal absorption is limited, Micona 2% w/w yno-Daktarin cream should be used in the first trimester of pregnancy only if, in the judgement of the physician, the potential benefits outweigh the possible risks. Breastfeeding It is not known whether miconazole nitrate is excreted in human milk. Caution should be exercised when using Micona 2% w/w cream during breastfeeding (see Section 4.5, Interactions with other medicinal products and other forms of interaction).

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Clinical trial data Adverse events, regardless of causality, reported in 2 Phase 3 clinical trials are shown in Table 1. A total of 537 women with microbiologically confirmed candidiasis and symptoms (e.g., vulvovaginal itching, burning/irritation), or signs of vulvar erythema, edema, excoriation, or vaginal erythema or edema were treated with miconazole intravaginally: randomly assigned to either a single 1200 mg capsule, or a 7-day application of 2% vaginal cream. There was no placebo reference. Safety was self-assessed daily on a diary card. Included in the table are adverse events reported by ≥ 1% of subjects in either treatment group.

Table 1: Adverse events, regardless of causality, reported by ≥ 1% of patients in ei ther treatment group in 2 Phase 3 clinical trials

System Organ Class Preferred terms	Miconazole 2% Vaginal Cream 7-days (n= 265), %	Miconazole 1200 mg Capsule (n=272), %
Nervous system disorders		
Headache	13.6	9.6
Renal and urinary disorders		
Urinary tract infections	0.4	1.1
Reproductive system and breast disorders		
Genital pruritus female	23.0	16.5
Vaginal burning sensation	22.6	22.8
Vulvovaginal discomfort	14.3	16.2
Dysmenorrhea	3.4	3.3
Vaginal discharge	0.4	3.7
Vaginal haemorrhage	0.4	1.1
Vaginal pain	0.4	1.5
Gastrointestinal disorders		
Abdominal pain	2.3	1.8
Abdominal pain upper	1.1	1.5
Nausea	1.1	1.5
Abdominal pain lower	0	1.5
Skin and Subcutaneous Tissue Disorders		
Rash	0.4	1.1
Renal and urinary disorders		
Dysuria	0.4	1.1

Additional adverse reactions that occurred in < 1% of Micona 2% w/w -treated subjects (n=527) in the single-blind clinical datasets are listed in Table 2:

Table 2: Adverse Reactions Reported by < 1% of Micona 2% w/w

-treated Subjects in 2 Single-blind clinical Trials

System Organ Class Preferred terms	Miconazole 2% Vaginal Cream 7-days (n= 265), %	Miconazole 1200 mg Capsule (n=272), %
Skin and Subcutaneous Tissue Disorders Rash pruritic Rosacea Swelling face Urticaria	 0.4 0 0 0	 0 0.4 0.7 0.4

The majority of adverse reactions reported in clinical trials were mild to moderate in severity.

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

In case of accidental ingestion, vomiting and diarrhoea may occur. Treatment In case of accidental ingestion, the treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: (Ant infectives and antiseptics, excl. combinations with corticosteroids, imidazole derivative) ATC code: G01A F04 Miconazole combines a potent antifungal activity against common dermatophytes and yeasts with an antibacterial activity against certain gram-positive bacilli and cocci. Miconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane, resulting in fungal cell necrosis.

5.2 Pharmacokinetic properties

Absorption: Miconazole persists in the vagina for up to 72 hours after a single dose. Systemic absorption of miconazole after intravaginal administration is limited, with a bioavailability of 1 to 2% following intravaginal administration of a 1200 mg dose. Plasma concentrations of miconazole are measurable within 2 hours of administration in some

subjects, with maximal levels seen 12 to 24 hours after administration. Plasma concentrations decline slowly thereafter and were still measurable in most subjects 96 hours post-dose. A second dose administered 48 hours later resulted in a plasma profile similar to that of the first dose.

Distribution: Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).

Metabolism and Excretion:

The small amount of miconazole that is absorbed is eliminated predominantly in feces as both unchanged drug and metabolites over a four-day post-administration period. Smaller amounts of unchanged drug and metabolites also appear in urine. The apparent elimination half-life ranges from 20 to 45 hours in most subjects and likely reflects both absorption from the site of application and metabolism/excretion of the drug.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isopropyl Myristate
Cetodsteararyl Alcohol
Cetomacrogol 1000
Light liquid paraffin
Butylated Hydroxyanisole
Butyated Hydroxytoluene
Dosium EDTA
Benzoic acid
Polysorbet 60
Propylene Glycol
Glycerin, Phosphoric acid
Disodium Hydrogen Phosphate Dodecahydrate
Semithicone Emulsion 30%
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30º C. Protect from light.

6.5 Nature and contents of container

Miconazole Nitarate Vaginal Cream is packed in 40gm Aluminium Collapsible tube packed in printed carton along with insert and applicator.

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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

TAN 20 HM 0099

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

July 29, 2020

10. DATE OF REVISION OF THE TEXT

October 10, 2023