Contents

TITLE PAGE

A Study to evaluate the Safety and Efficacy of Hormonice™ in patients with Polycystic Ovary Syndrome (PCOS), Infertility and Urinary Incontinence.

Protocol No.:	TCR/REE/17/011
Version No.:	Version No.: 1.0 Date:31.08.2017
Investigational Product:	Hormonice™
Indication:	Polycystic Ovary Syndrome, Infertility and Urinary Incontinence
Development Phase:	Post Marketing Survey
Sponsor:	Ree Veda (A division of Ree Labs Pvt. Ltd.)
CRO:	Taiyo Clinical Research
Name of Investigator	Name of Site
Compliance	The study, including the archiving of essential documents has been conducted as per the protocol, GCP, Declaration of Helsinki, Indian Council of Medical Research (ICMR), SOPs and applicable regulatory requirements. We accept the responsibility for the correctness of the project and validity of the data produced in this clinical study report.

SYNOPSIS

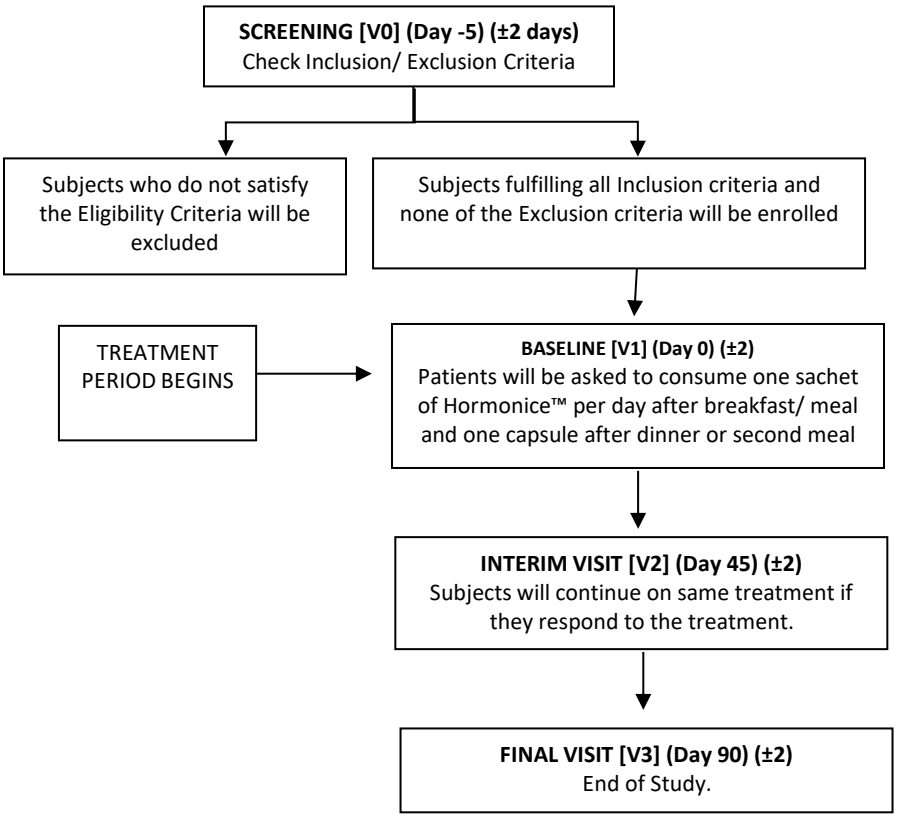
<table>
<tr><td>PROJECT TITLE</td><td>A study to evaluate the efficacy and safety of Hormonice™ in patients with Polycystic Ovary Syndrome (PCOS), Infertility and Urinary Incontinence</td></tr>
<tr><td>PRODUCT</td><td>Hormonice™</td></tr>
<tr><td>DOSAGE</td><td>One sachet whose contents should be mixed with water, stirred thoroughly and taken once a day after breakfast/ meal for 90 days and one capsule to be taken with water once daily after dinner/ second meal for 90 days.</td></tr>
<tr><td>PROJECT ID/NO.</td><td>TCR_REE011C</td></tr>
<tr><td>VERSION & DATE</td><td>Version No. 1.0 Date 31.08.2017</td></tr>
<tr><td>INVESTIGATORS</td><td><table><tr><th>Investigator Name</th><th>Site Name</th></tr><tr><td></td><td></td></tr></table></td></tr>
<tr><td>INDICATIONS</td><td>• Polycystic Ovary Syndrome (PCOS)
• Infertility
• Urinary Incontinence</td></tr>
<tr><td>TREATMENT DURATION</td><td>3 months (90 days)</td></tr>
<tr><td>OBJECTIVES</td><td>Primary Study Objective
To evaluate the effect of Hormonice™ in the following symptoms in patients with PCOS:
• Change in Acne, facial hair growth, weight, insulin resistance and hormonal profile

To evaluate the effect of Hormonice™ on the following in patients with Infertility
• Conception

To evaluate the effect of Hormonice™ on the following in patients with Urinary Incontinence
• Episodes of incontinence

Secondary Study Objective
• To Evaluate Safety and Tolerability of Hormonice™.
• To observe the change in Incontinence Quality of Life (for Urinary Incontinence Patients)
• To observe regulation in Menstrual Cycles (for PCOD patients)</td></tr>
</table>

	• To observe the time frame for conception and improvement in hormonal profile (For Infertility Patients) • Global Assessment for Hormonice™ by Subject and Investigator
NUMBER OF SUBJECTS	75 patients (25 patients with PCOD, 25 patients with Infertility and 25 patients with Urinary Incontinence)
PROJECT RATIONALE	Hormonice™ is a unique nutraceutical formulation that helps correct the turbulent onset of hormonal changes in adolescence during the onset of menstrual cycle and formation of irregular, unhealthy & often clustered ova. Key ingredients in Hormonice™ like soy isoflavones, Evening Primrose Oil, cinnamon, Shatavari (Asparagus Racemosus) and green tea extract help with controlling urinary incontinence, increasing bladder sphincter control, improving urethral health and preventing leakage of urine. PCOS (Polycystic Ovarian Syndrome) is caused under the influence of the changing endocrine system. Hormonice™ helps correct the hormonal changes in the endocrine system and with it the accompanying symptoms. It also helps in the formation of healthy ovaries and restores harmony.

STUDY DESIGN	This is an open label, single arm study. **Study Flow Chart** 
INCLUSION CRITERIA	For PCOD 1. Female adults aged between 18 and 35 years (both inclusive) 2. Diagnosis of Polycystic Ovary Syndrome (PCOS). As confirmed by previous medical reports. 3. Patients with BMI ranging from 22 kg/m2 to 35 kg/m2 4. Patients must be willing to avoid use of all hair removal procedures and products during study participation 5. Patients must be willing to avoid all prescription treatments for acne and not increase the dose or frequency of their current non-prescription acne treatment regimen during study participation. 6. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit. 7. Subjects agreement to comply with study procedures: a. To take the IP as recommended b. To complete the patient diary and study questionnaires 8. Patients willing to give written consent for participation

	9. Patients who are willing to comply with the study procedures. For Infertility 1. Female Adults aged between 21 to 35 years (both inclusive) who have been diagnosed with infertility 2. Patients with PCOD or endometriosis or other hormonal imbalances which affect fertility. 3. BMI ranging from 22 kg/m2 to 30 kg/m2 4. Patient and her partner are desirous of conceiving 5. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit. 6. Subjects agreement to comply with study procedures: a. To take the IP as recommended b. To complete the patient diary and study questionnaires 7. Patients willing to give written consent for participation 8. No deformities in the ovaries, fallopian tubes, uterus. 9. Male partners should not have any fertility issues 10. Patients and their partners should not use any contraception methods for the duration of the study For Urinary Incontinence 1. Female adults aged between 18 and 60 years (both inclusive) 2. Urge or Stress Urinary Incontinence at least twice a week on an average for at least 3 months (as confirmed by medical history and clinical symptoms) 3. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit. 4. Subjects agreement to comply with study procedures: c. To take the IP as recommended d. To complete the patient diary and study questionnaires 5. Patients willing to give written consent for participation 6. Patients who are willing to comply with the study procedures.
EXCLUSION CRITERIA	For PCOD 1. Pregnant women and lactating patients 2. Post-menopausal women 3. Patients with history of severe renal dysfunction 4. Patients with history of severe hepatic impairment 5. Patients with a history of hypersensitivity to the ingredients of the study drug. 6. Hormonal treatment with estrogen or progesterone 3 months prior to or during the study duration 7. Patients with uterine fibroids or congenital anomalies in the female genital tract

	8. Patients who are HIV, VDRL, HbsAg Positive 9. Patients diagnosed with androgen secreting tumours 10. Patients who are inappropriate for research participation for medical reasons (at discretion of treating physician). 11. Patients who have received any study medication or participated in any type of clinical study within 30 days prior to screening 12. Subjects suffering from malabsorption syndrome 13. Alcoholics or drug abusers 14. Untreated or unstable thyroid gland disorder or hypertension 15. Type 1 Diabetes Mellitus or Untreated/ Unstable Type 2 Diabetes Mellitus. 16. Patients who are unwilling to comply with study procedures For Infertility 1. Patients below 21 years or above 35 years of age 2. Pregnant and Lactating patients 3. Post-menopausal women 4. Patients with history of severe renal dysfunction 5. Patients with history of severe hepatic impairment 6. Patients with a history of hypersensitivity to the ingredients of the study drug. 7. Patients whose male partners have fertility issues or low sperm count 8. Patients or their partners who are using contraceptives (Oral, Intra Uterine, Hormonal) 9. Undiagnosed abnormal uterine bleeding 10. Suspicious Ovarian Mass 11. Hemoglobin less than 10g/dL 12. History of DVT, Pulmonary embolus or cerebrovascular event 13. History of alcohol or drug abuse 14. Known or suspecting adrenal or ovarian androgen secreting tumors 15. Medical conditions that are contraindications to pregnancy 16. Presence of severe psychiatric illness (major depression, substance abuse, eating disorder, etc) which according to the PI would interfere with the patient's ability to successfully complete the study. 17. Patients who are unwilling to comply with study procedures 18. Patients who are HIV, VDRL, HbsAg Positive 19. Patients with Uterine abnormalities or congenital abnormalities in their reproductive/ genital tract For Urinary Incontinence

	1. Prior surgical intervention for Urinary Incontinence within the past 6 months 2. Pregnant or Lactating Women 3. Alcoholics or drug abusers 4. Patients who are unwilling to comply with study procedures 5. Patients who are inappropriate for study participation for medical reasons (at the discretion of the PI) 6. Patients with history of severe renal dysfunction 7. Patients with history of severe hepatic impairment 8. Patients with a history of hypersensitivity to the ingredients of the study drug 9. Patients with history of neurological problems such as Parkinsons Disease or Multiple Sclerosis which could impair bladder function
EVALUATION VARIABLES	For PCOD • Regulation of Menstrual Cycles • Changes in PCOS related symptoms such as insulin resistance, weight, acne, facial hair growth, hormonal profile. • Global Assessments by Patient and Investigator • Incidences of any Adverse Events For Infertility • Positive Pregnancy Test (Conception) • Time taken to get pregnant and improvement in hormonal profile For Urinary Incontinence • Episodes of Incontinence • Global Assessments by Patient and Investigator • Incidences of any Adverse Events • Change in Incontinence Quality of Life
PRIMARY ENDPOINT	• Reduction in PCOS related symptoms such as hormonal profile, insulin resistance, weight, acne, facial hair growth • Reduction in episodes of urinary incontinence
SECONDARY ENDPOINT	• Regulation of Menstrual Cycles • Improvement in Quality of Life • Global Assessment by Investigator and Subjects
SAFETY EVALUATIONS	Incidence of adverse events (AE's) and serious adverse events (SAE's) will be noted throughout the study period

DATA CAPTURE	Paper CRFs will be completed for each subject. The treating doctor should ensure that all pages are accurate and submitted. This will indicate a thorough inspection of the data on the CRF has been made and will certify the contents of the form. The data from these forms will be directly entered on to an excel database and analyzed. **Statistical methods** Microsoft Excel

ETHICS

This open label, observational survey was conducted after approval from the Ethics Committee.

Ethics Committee (EC)

Royal Independent Ethics Committee, Pune

List of Administrative Personnel

Sr. No.	Role and Name	Signature
1	**Sponsor: Dr. Rohit Kulkarni**	
2	**Clinical Operations CRO: Kunal Bhatt**	

INTRODUCTION & RATIONALE

INTRODUCTION

Polycystic Ovary Syndrome, or PCOS, is a health condition that affects about 10 million women in the world. It affects one in 10 women of childbearing age. Women with PCOS have a hormonal imbalance and metabolism problems that may affect their overall health and appearance.

Women with PCOS may have infrequent or prolonged menstrual periods or excess male hormone (androgen) levels. The ovaries may develop numerous small collections of fluid (follicles) and fail to regularly release eggs.

Early diagnosis and treatment along with weight loss may reduce the risk of long-term complications such as type 2 diabetes and heart disease

Hormones involved in PCOS include: [3,4]

- Androgens. There are often higher levels of androgens in women with PCOS. The excess androgens are produced mostly by the ovaries, but the adrenal glands can also be involved. Excess androgens are responsible for many PCOS symptoms including acne, unwanted hair, thinning hair, and irregular periods.
- Insulin. This hormone allows the body to absorb glucose (blood sugar) into the cells for energy. In PCOS, the body isn't as responsive to insulin as it should be. This can lead to elevated blood glucose levels and cause the body to make more insulin. Having too much insulin can cause the body to make more androgens.
- Progesterone. In PCOS, a lack of progesterone contributes to irregular periods.

Some of the symptoms of PCOS include: [1]

- Irregular menstrual cycle.
- Too much hair on the face, chin, or parts of the body where men usually have hair. This is called "hirsutism."
- Acne on the face, chest, and upper back
- Thinning hair or hair loss on the scalp; male pattern baldness
- Weight gain or difficulty losing weight
- Darkening of skin, particularly along neck creases, in the groin, and underneath breasts
- Skin tags, which are small flaps of excess skin in the armpits or neck area

The exact cause of PCOS isn't known. Factors that might play a role include:

- Excess insulin. Insulin is the hormone produced in the pancreas that allows cells to use sugar, the body's primary energy supply. If cells become resistant to the action of insulin, then blood sugar levels can rise, and the body might produce more insulin. Excess insulin might increase androgen production, causing difficulty with ovulation
- Low-grade inflammation. This term is used to describe white blood cells' production of substances to fight infection. Research has shown that women with PCOS have a type of low-grade inflammation that stimulates polycystic ovaries to produce androgens, which can lead to heart and blood vessel problems.
- Heredity. Research suggests that certain genes might be linked to PCOS.
- Excess androgen. The ovaries produce abnormally high levels of androgen, resulting in hirsutism and acne.

Complications of PCOS can include: [2]

- Infertility
- Gestational diabetes or pregnancy-induced high blood pressure
- Miscarriage or premature birth
- Non-alcoholic steatohepatitis — a severe liver inflammation caused by fat accumulation in the liver
- Metabolic syndrome — a cluster of conditions including high blood pressure, high blood sugar, and abnormal cholesterol or triglyceride levels that significantly increase your risk of cardiovascular disease
- Type 2 diabetes or prediabetes
- Sleep apnea
- Depression, anxiety and eating disorders
- Abnormal uterine bleeding
- Cancer of the uterine lining (endometrial cancer)
- Obesity is associated with PCOS and can worsen complications of the disorder.

A physical exam will include checking for signs of excess hair growth, insulin resistance and acne.

The doctor might then recommend: [6]

- A pelvic exam - The doctor visually and manually inspects the patient’s reproductive organs for masses, growths or other abnormalities.
- Blood tests – The patient’s blood may be analyzed to measure hormone levels. This testing can exclude possible causes of menstrual abnormalities or androgen excess that mimics PCOS.

Additional blood testing may also be done to measure glucose tolerance and fasting cholesterol and triglyceride levels.

- An ultrasound – This is done to check the appearance of the ovaries and the thickness of the lining of the uterus.
- Periodic monitoring of Blood Pressure, Glucose Tolerance, Cholesterol and triglyceride levels, screening for anxiety and depression are also done for patients who have a diagnosis of PCOS.

PCOS treatment focuses on managing each patient's individual concerns, such as infertility, hirsutism, acne or obesity. Specific treatment might involve lifestyle changes or medication. In case of overweight or obese patients with PCOS, weight loss through a low-calorie diet combined with moderate exercise activities is advised. Losing weight may also increase the effectiveness of medications that have been recommended for PCOS and can help with infertility.

The following treatments are advised for regulation of menstrual cycles: [5]

a. Combination birth control pills. Pills that contain estrogen and progestin decrease androgen production and regulate estrogen. Regulating hormones can lower the risk of endometrial cancer and correct abnormal bleeding, excess hair growth and acne. Instead of pills, patients might use a skin patch or vaginal ring that contains a combination of estrogen and progestin.
b. Progestin therapy. Taking progestin for 10 to 14 days every one to two months can regulate periods and protect against endometrial cancer.

The following treatments are advised in assisting with ovulation:

a. Clomiphene (Clomid). This oral anti-estrogen medication is taken during the first part of the menstrual cycle.
b. Letrozole (Femara). This breast cancer treatment can work to stimulate the ovaries.
c. Metformin (Glucophage, Fortamet, others). This oral medication for type 2 diabetes improves insulin resistance and lowers insulin levels. If a patient doesn't become pregnant using clomiphene, the doctor might recommend adding metformin. If the patient has prediabetes, metformin can also slow the progression to type 2 diabetes and help with weight loss.
d. Gonadotropins.

The following are recommended to reduce excessive hair growth:

a. Birth control pills. These pills decrease androgen production that can cause excessive hair growth.
b. Spironolactone (Aldactone). This medication blocks the effects of androgen on the skin. Spironolactone can cause birth defect, so effective contraception is required while taking this medication. It isn't recommended during pregnancy or if the patient is planning to become pregnant.

c. Eflornithine (Vaniqa). This cream can slow facial hair growth in women.
d. Electrolysis. A tiny needle is inserted into each hair follicle. The needle emits a pulse of electric current to damage and eventually destroy the follicle. Some patients might need multiple treatments.

Infertility:

According to the World Health Organization (WHO), infertility can be described as the inability to become pregnant, maintain a pregnancy, or carry a pregnancy to live birth [7]. A clinical definition of infertility by the WHO and ICMART is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse." [8] Infertility can further be broken down into primary and secondary infertility. Primary infertility refers to the inability to give birth either because of not being able to become pregnant, or carry a child to live birth, which may include miscarriage or a stillborn child.[9, 33] Secondary infertility refers to the inability to conceive or give birth when there was a previous pregnancy or live birth.[9, 10]

Prevalence: Infertility varies widely by geographic location around the world. In 2010, there was an estimated 48.5 million infertile couples worldwide, and from 1990 to 2010 there was little change in levels of infertility in most of the world. [11]

Causes: [13]

About one quarter of female infertility is caused by a problem with ovulation. This can be due to an imbalance of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), an injury to the hypothalamus or pituitary gland (where these hormones are produced), pituitary tumors, or too little or too much body weight.

Other hormonal conditions that can affect fertility include thyroid problems, diabetes, polycystic ovary syndrome (PCOS), premature ovarian failure (POF), and occasionally Cushing's syndrome.

A woman's ability to get pregnant can also be affected by:

- Age (decrease in quantity and/or quality of the eggs)
- Problems with the reproductive tract (e.g., blocked or damaged fallopian tubes; endometriosis, pelvic adhesions, benign uterine fibroids, and complications from surgery or infection)
- Sexually transmitted diseases (e.g., chlamydia and gonorrhea)
- Medical conditions such as sickle cell disease, HIV/AIDS, and kidney disease

- Smoking, drinking alcohol, or using recreational drugs (e.g., cocaine and marijuana)
- Medications such as antidepressants, tranquilizers, calcium channel blockers, narcotics, and anti-cancer drugs
- Exposure to radiation, lead, toxic fumes and pesticides

Treatment: It can be divided into two main categories: One is to bring back fertility through medications or surgery, and the other is to use *assisted reproductive technologies*.

Fertility drugs (clomiphene citrate or FSH and LH hormone injections) are the primary treatment for women with ovulation disorders. These treatments may also be used with an *intrauterine sperm injection (IUI)*, which is when sperm is injected directly into the uterus.

Surgery may also be an option when the cause of infertility is blocked fallopian tubes or endometriosis.

The other category of treatment is *assisted reproductive technology (ART)*. These technologies include egg and embryo donation, in vitro fertilization, and intracytoplasmic sperm injection (the direct injection of a sperm into an egg).

Urinary incontinence [12] is defined by the International Continence Society as "the complaint of any involuntary leakage of urine".

Types:

The International Continence Society further categorizes types of incontinence

- Stress incontinence is the involuntary leakage of urine on effort or exertion, sneezing, or coughing.
- Urge incontinence is the involuntary leakage of urine accompanied by, or immediately preceded by, urgency. Patients describe this type of incontinence as difficulty in holding their urine until they are able to reach a toilet.
- Mixed incontinence involves components of both stress- and urgency-related leakage.
- Continuous incontinence is constant leakage, usually associated with a fistula; it occurs only rarely in males.
- Enuresis refers to any involuntary loss of urine and should be distinguished from nocturnal enuresis, or urinary loss during sleep.

Prevalence:

Although the epidemiology of UI has not been investigated in men as thoroughly as in women, most studies show that the male-to-female ratio is about 1: 2. The type, age distribution, and risk factors differ

greatly between the genders. Age, pregnancy, childbirth, obesity, functional impairment, and cognitive impairment are associated with increased rates of incontinence or incontinence severity

Current means of diagnosis:

Urinary incontinence may be a sign or a symptom. As a symptom, UI may be self-reported or recorded by a third party such as a health care professional or researcher. As a clinical sign, UI may be demonstrated during physical examination, cystoscopy, urodynamics, or video urodynamics, or by pad testing.

Nonpharmaceutical / Nonsurgical: Behavioral therapies, including pelvic floor muscle (PFM) exercises, biofeedback, and bladder training, are the least invasive options and have a low rate of side effects

Pharmacological: The use of medications for the treatment of stress incontinence is anecdotal. Anticholinergic drugs (e.g., oxybutynin and tolterodine) are more effective than placebo in treating overactive bladder syndrome, which may include urgency incontinence. Systematic literature reviews concerning pharmacological treatment of urge incontinence and overactive bladder syndrome with anticholinergic drugs reveal significant symptom improvement.

Surgical: For women with intractable, severe urge incontinence, direct neuromodulation of the sacral spinal cord is an increasingly popular option. Surgical therapy designed to increase bladder capacity and decrease contractility is rarely used. In contrast, surgery is a mainstay of therapy for stress urinary incontinence.

Hormonice is a unique nutraceutical formulation that helps correct the turbulent onset of hormonal changes in adolescence during the onset of menstrual cycle and formation of irregular, unhealthy & often clustered ova.

Key ingredients in Hormonice like soy isoflavones, Evening Primrose Oil, cinnamon, Shatavari (Asparagus Racemosus) and green tea extract help with controlling urinary incontinence, increasing bladder sphincter control, improving urethral health and preventing leakage of urine. Soy Isoflavones have beneficial effects on markers of insulin resistance, total testosterone, androgen index and triglycerides. Evening Primrose Oil can help balance the levels of estrogen and Progesterone, Cinnamon helps in reducing insulin resistance. Shatavari contains steroidal-like saponins that supports the functions of female sex hormones-estrogen and progesterone. It also maintains balance of the endocrine system, which affects the production of hormones that helps to regulate human response to stress, mood swings, helps to maintain the normal adrenal and thyroid function, management of menopausal and pre-menopause symptoms like hot flashes, mood swings, temperamental feels, manage PMS symptoms and works by alleviating pain and controlling the loss of blood during menstruation

Hormonic helps correct the hormonal changes in the endocrine system associated with PCOS and with it the accompanying symptoms. It also helps in the formation of healthy ovaries and restores harmony.

Benefits of Hormonice™

- Care for PCOS.
- Helps control painful menstrual cramps.
- Helps in menstrual regulation.
- Prevents Stress Urinary Incontinence.
- Helps control acne and facial hair growth.

STUDY OBJECTIVES

Primary Study Objective

- To evaluate the effect of Hormonice™ in the following symptoms in patients with PCOS.
    - Change in Acne, facial hair growth, weight, insulin resistance and hormonal profile

- To evaluate the effect of Hormonice™ on the following in patients with Infertility
    - Regulation of menstrual cycles
    - Reduction of menstrual cramps

- To evaluate the effect of Hormonice™ on the following in patients with Urinary Incontinence
    - Episodes of Incontinence

Secondary Study Objectives

- To Evaluate Safety and Tolerability of Hormonice™.
- To observe the change in Incontinence Quality of Life (for Urinary Incontinence Patients)
- Global Assessment for Hormonice™ by Subject and Investigator

Study Outcome Measures

Primary Efficacy Parameters

The indications were assessed on individual evaluation variables:

For PCOD

- Regulation of Menstrual Cycles
- Changes in PCOS related symptoms such as insulin resistance, weight, acne, facial hair growth, hormonal profile.
- Global Assessments by Patient and Investigator
- Incidences of any Adverse Events

For Urinary Incontinence

- Episodes of Incontinence
- Global Assessments by Patient and Investigator
- Incidences of any Adverse Events
- Change in Incontinence Quality of Life

Secondary Efficacy Parameters

The secondary parameters for the study were to evaluate the safety and tolerability as well as the global assessment of Hormonice™.

INVESTIGATIONAL PLAN

Overall Study Design and Plan Description

This was an open label, single arm study conducted to evaluate the efficacy and safety of Hormonice™ in patients with Polycystic Ovary Syndrome (PCOS), Infertility and Urinary Incontinence. A total of 75 subjects were enrolled, with 25 subjects in each of the 3 groups, viz., subjects with PCOS, Infertility and Urinary Incontinence. The duration of the study was 3 months. After the screening visit subjects meeting the inclusion criteria were enrolled in the study. The treatment began on the baseline visit. The interim visit was on the 45th day and the end of study visit was on the 90th day. The subjects had to consume one sachet of Hormonice™ per day after breakfast/ meal and one capsule after dinner or second meal

STUDY FLOW CHART

Flow Chart

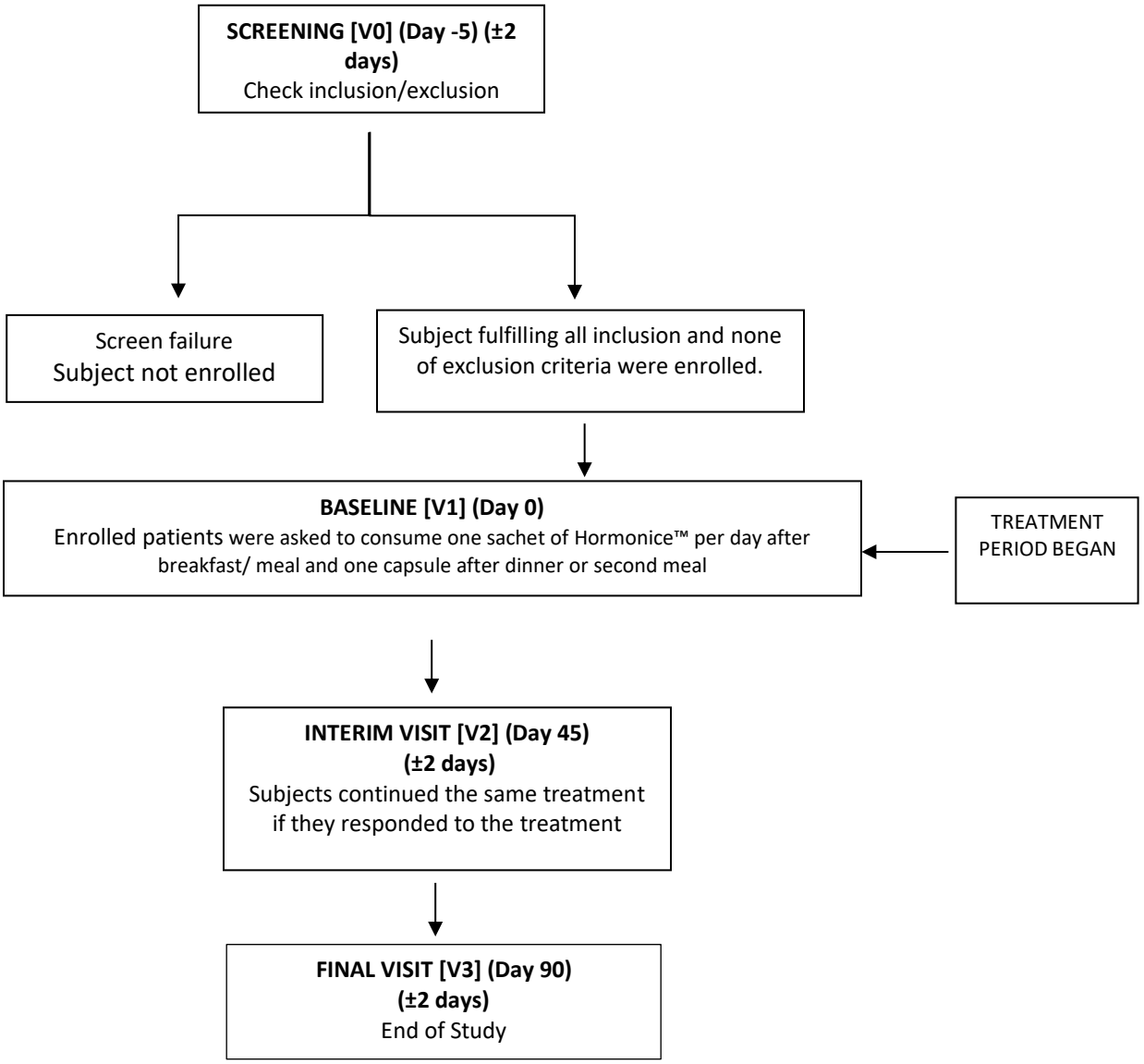


Figure 1: Study Activity Chart

Discussion of Study Design

This study was an open label observational survey to evaluate the efficacy and safety of Hormonice™ in patients with Polycystic Ovary Syndrome (PCOS) and Urinary Incontinence.

Total of 75 subjects were enrolled in the study. Data was collected through-out the study was used for statistical analysis.

Study Period

The observation period in the study was not more than 3 months.

Selection of study population

Inclusion Criteria

Subjects meeting all the following criteria were recruited for the study:

For PCOD

1. Female adults aged between 18 and 35 years (both inclusive)
2. Diagnosis of Polycystic Ovary Syndrome (PCOS). As confirmed by previous medical reports.
3. Patients with BMI ranging from 22 kg/m2 to 35 kg/m2
4. Patients must be willing to avoid use of all hair removal procedures and products during study participation
5. Patients must be willing to avoid all prescription treatments for acne and not increase the dose or frequency of their current non-prescription acne treatment regimen during study participation.
6. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit.
7. Subjects agreement to comply with study procedures:
8. To take the IP as recommended
9. To complete the patient diary and study questionnaires
10. Patients willing to give written consent for participation
11. Patients who are willing to comply with the study procedures.

For Infertility

1. Female Adults aged between 21 to 35 years (both inclusive) who have been diagnosed with infertility
2. Patients with PCOD or endometriosis or other hormonal imbalances which affect fertility.
3. BMI ranging from 22 kg/m2 to 30 kg/m2
4. Patient and her partner are desirous of conceiving

5. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit.
6. Subjects agreement to comply with study procedures:
7. To take the IP as recommended
8. To complete the patient diary and study questionnaires
9. Patients willing to give written consent for participation
10. No deformities in the ovaries, fallopian tubes, uterus.
11. Male partners should not have any fertility issues
12. Patients and their partners should not use any contraception methods for the duration of the study

For Urinary Incontinence

1. Female adults aged between 18 and 60 years (both inclusive)
2. Urge or Stress Urinary Incontinence at least twice a week on an average for at least 3 months (as confirmed by medical history and clinical symptoms)
3. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit.
4. Subjects agreement to comply with study procedures:
5. To take the IP as recommended
6. To complete the patient diary and study questionnaires
7. Patients willing to give written consent for participation
8. Patients who are willing to comply with the study procedures.

EXCLUSION CRITERIA:

Subjects were excluded if ANY of the following conditions applied:

For PCOD

1. Pregnant women and lactating patients
2. Post-menopausal women
3. Patients with history of severe renal dysfunction
4. Patients with history of severe hepatic impairment
5. Patients with a history of hypersensitivity to the ingredients of the study drug.
6. Hormonal treatment with estrogen or progesterone 3 months prior to or during the study duration
7. Patients with uterine fibroids or congenital anomalies in the female genital tract
8. Patients who are HIV, VDRL, HbsAg Positive
9. Patients diagnosed with androgen secreting tumors
10. Patients who are inappropriate for research participation for medical reasons (at discretion of treating physician).
11. Patients who have received any study medication or participated in any type of clinical study within 30 days prior to screening
12. Subjects suffering from malabsorption syndrome

13. Alcoholics or drug abusers
14. Untreated or unstable thyroid gland disorder or hypertension
15. Type 1 Diabetes Mellitus or Untreated/ Unstable Type 2 Diabetes Mellitus.
16. Patients who are unwilling to comply with study procedures

For Infertility

1. Patients below 21 years or above 35 years of age
2. Pregnant and Lactating patients
3. Post-menopausal women
4. Patients with history of severe renal dysfunction
5. Patients with history of severe hepatic impairment
6. Patients with a history of hypersensitivity to the ingredients of the study drug.
7. Patients whose male partners have fertility issues or low sperm count
8. Patients or their partners who are using contraceptives (Oral, Intra Uterine, Hormonal)
9. Undiagnosed abnormal uterine bleeding
10. Suspicious Ovarian Mass
11. Hemoglobin less than 10g/dL
12. History of DVT, Pulmonary embolus or cerebrovascular event
13. History of alcohol or drug abuse
14. Known or suspecting adrenal or ovarian androgen secreting tumors
15. Medical conditions that are contraindications to pregnancy
16. Presence of severe psychiatric illness (major depression, substance abuse, eating disorder, etc) which according to the PI would interfere with the patient's ability to successfully complete the study.
17. Patients who are unwilling to comply with study procedures
18. Patients who are HIV, VDRL, HbsAg Positive
19. Patients with Uterine abnormalities or congenital abnormalities in their reproductive/ genital tract

For Urinary Incontinence

1. Prior surgical intervention for Urinary Incontinence within the past 6 months
2. Pregnant or Lactating Women
3. Alcoholics or drug abusers
4. Patients who are unwilling to comply with study procedures
5. Patients who are inappropriate for study participation for medical reasons (at the discretion of the PI)
6. Patients with history of severe renal dysfunction
7. Patients with history of severe hepatic impairment
8. Patients with a history of hypersensitivity to the ingredients of the study drug
9. Patients with history of neurological problems such as Parkinsons Disease or Multiple Sclerosis which could impair bladder function

Treatment

Treatments Administered

Each patient was given Hormonice™ for no more than 3 months.

STUDY PATIENTS

Disposition of Patients

Total sample size required for the study	=	75 patients
Approximate number of patients in Each Group	=	25 patients

Table: Overall Subject Disposition by Treatment Group - All Participants	
	Total
	(N=75)
Total Patients Screened	75
Screening failure	00
Eligible for enrolment	75
Completed participants	(100.0%)
Not completed participants	0 (00.0%)

Note: Percentages were based on all randomized subjects.

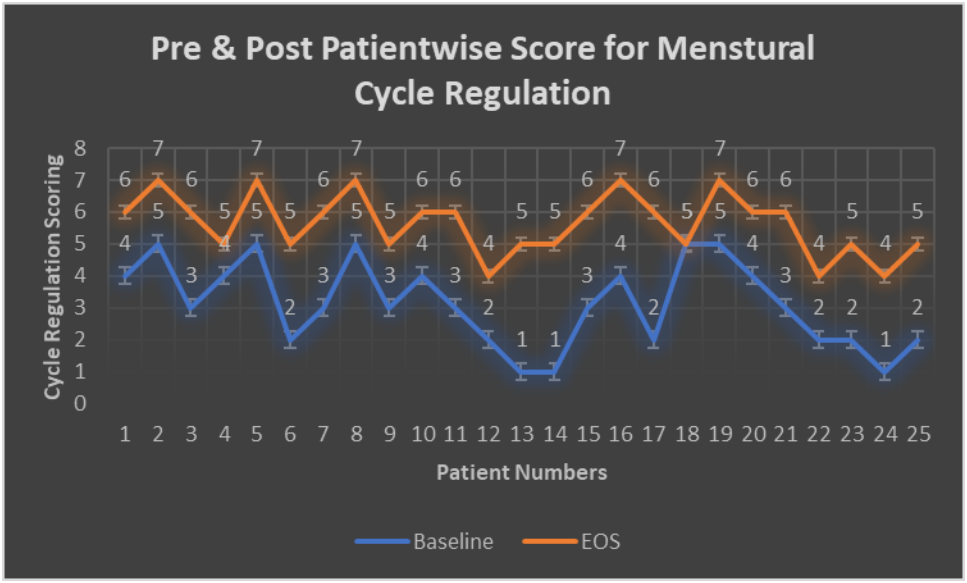
EFFICACY EVALUATION

Efficacy Results

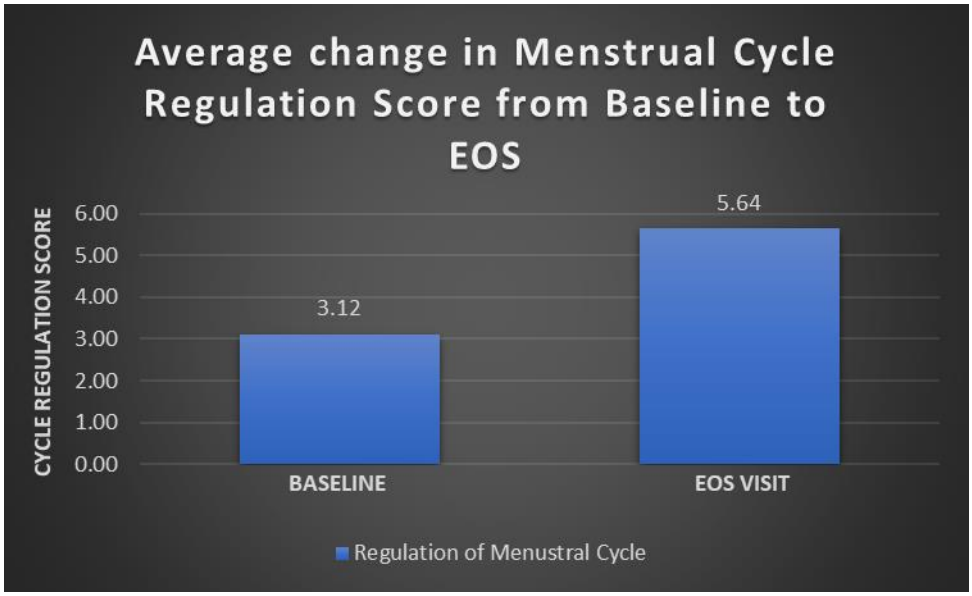
Analysis of Efficacy

For PCOD

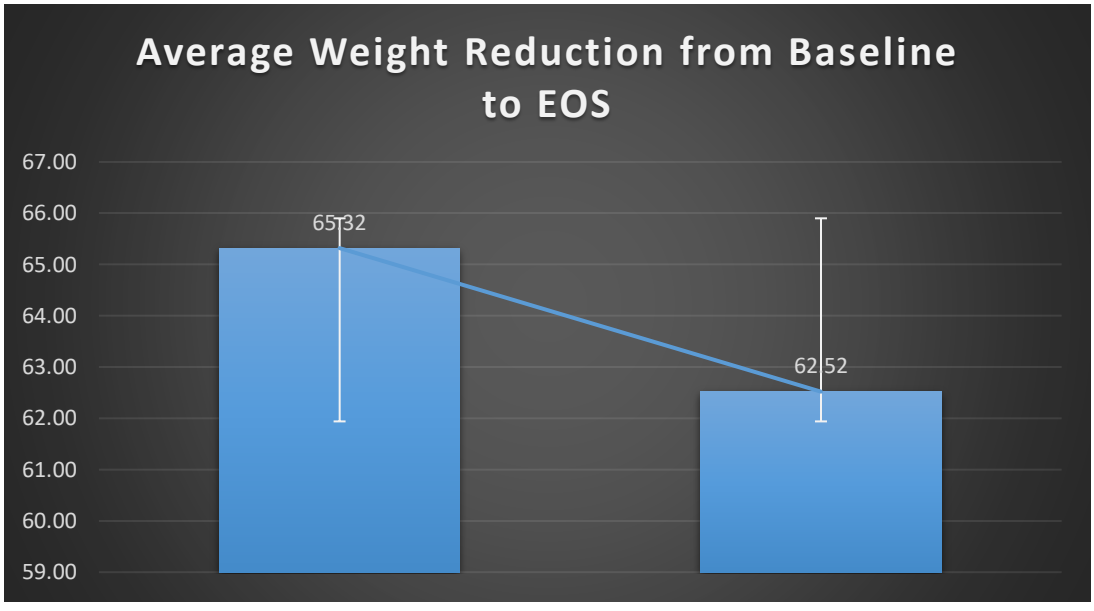
- **Regulation of Menstrual Cycles**

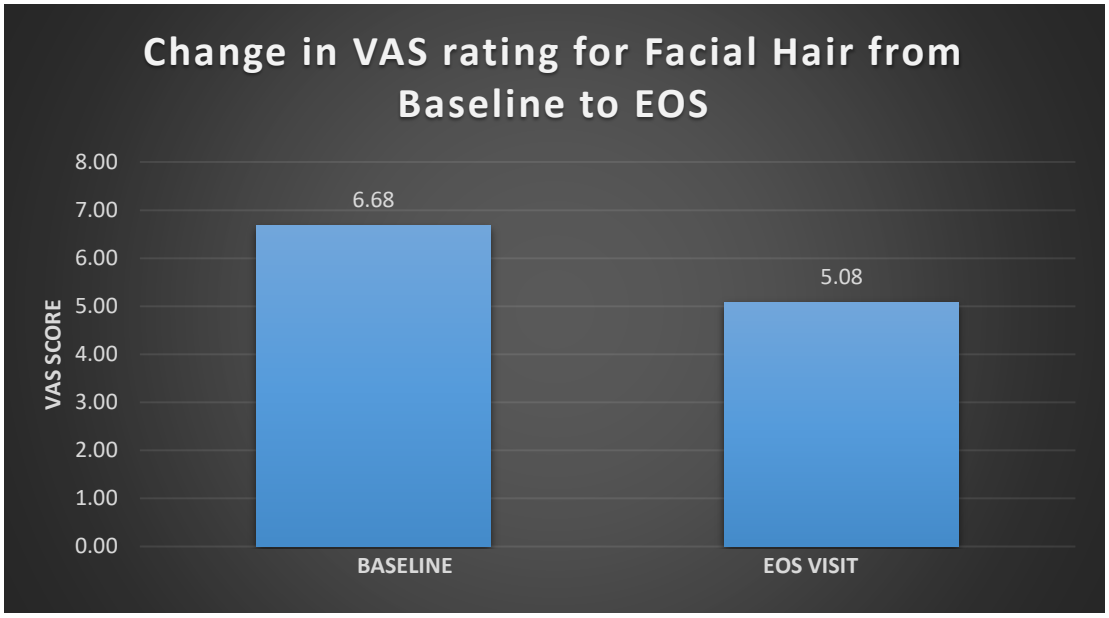


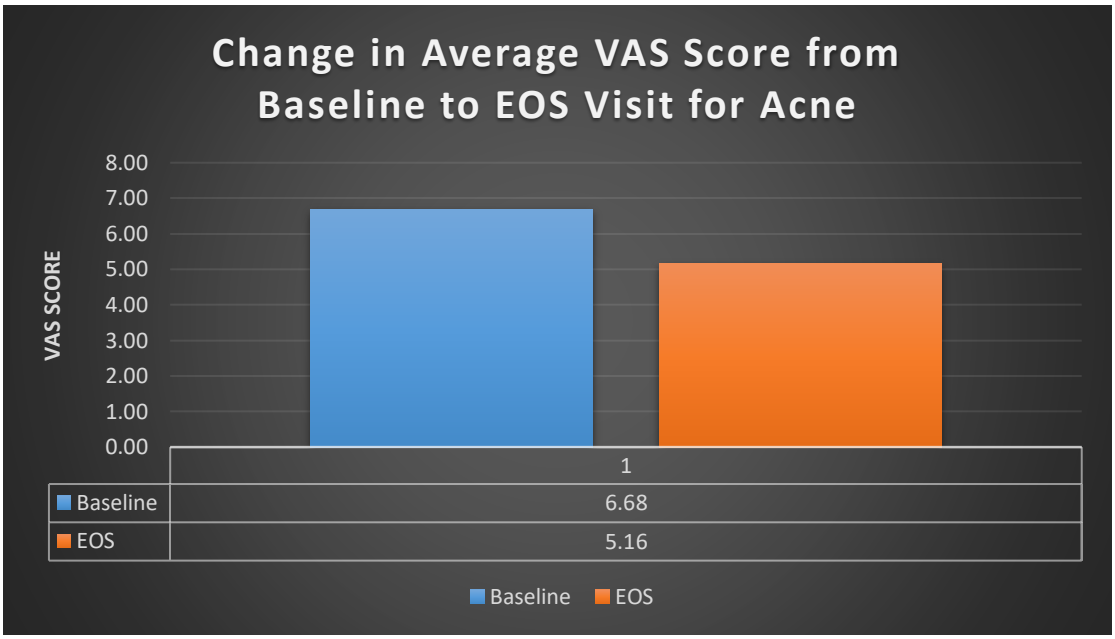
REGULATION OF MENSTRUAL CYCLES
0 to 4 outside the normal range
5 to 10 within the normal range
21 to 35 days in normal with an average of 28 days
No. of females outside of the normal range of 21 to 35 prior to supplement: 20 Females, and 5 on borderline
No. of females within the normal range of 21 to 35 post supplement: 14 Females, 8 border line, 3 had no change



- **Changes in PCOS related symptoms such as weight, acne, facial hair growth, hormonal profile.**



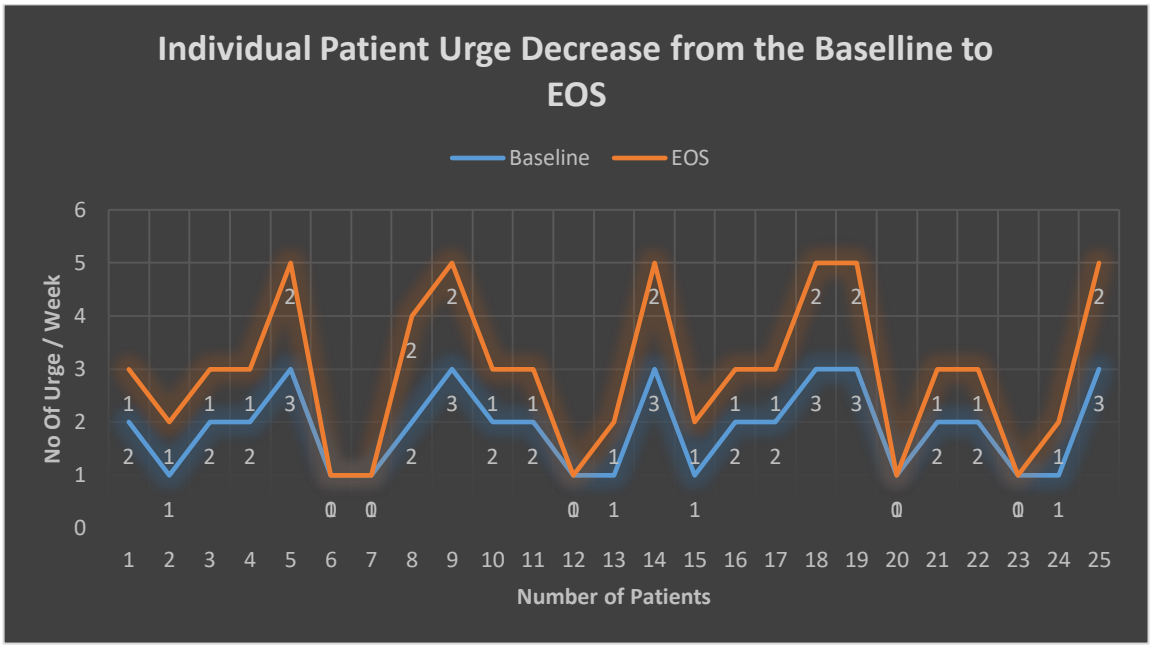


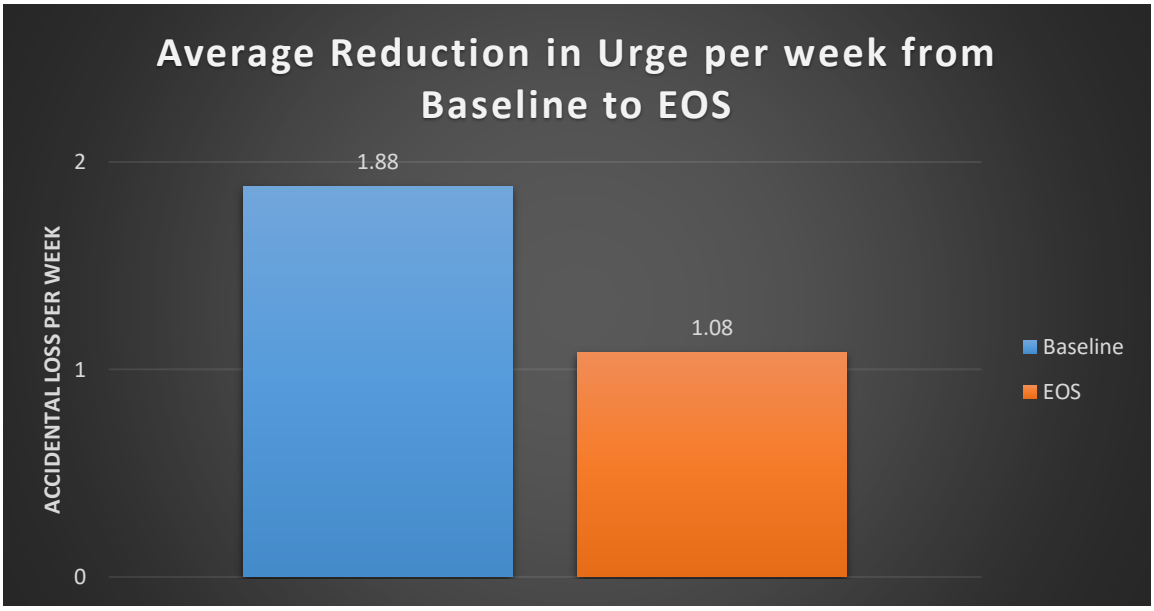


CHANGE IN HORMONAL PROFILE
0 to 4 outside the normal range
5 to 10 within the normal range
21 to 35 days in normal with an average of 28 days
No. of females outside of the normal range of 21 to 35 prior to supplement: 20 Females, and 5 on borderline
No. of females within the normal range of 21 to 35 post supplement: 14 Females, 8 border line, 3 had no change

For Urinary Incontinence

- **Reduction in the Urge**





DISCUSSION AND OVERALL CONCLUSIONS

Polycystic Ovary Syndrome, or PCOS, is a health condition that affects about 10 million women in the world. It affects one in 10 women of childbearing age. The ovaries may develop numerous small collections of fluid (follicles) and fail to regularly release eggs.

Some of the symptoms associated with PCOS are: Irregular menstrual cycle, hirsutism, Acne on the face, chest, and upper back, Thinning hair or hair loss on the scalp, Weight gain or difficulty losing weight, Darkening of skin and Skin tags. The exact cause of PCOS is unknown. However, it could be hereditary, or due to excess of insulin and androgen.

Complications of PCOS can include: Infertility, Gestational diabetes or pregnancy-induced high blood pressure, Miscarriage or premature birth, Type 2 diabetes or prediabetes, Depression, anxiety and eating disorders, Abnormal uterine bleeding, Cancer of the uterine lining (endometrial cancer), Obesity, etc.

A clinical definition of infertility by the WHO and ICMART is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse." Infertility can further be broken down into primary and secondary infertility. About one quarter of female infertility is caused by a problem with ovulation. This can be due to an imbalance of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), an injury to the hypothalamus or pituitary gland (where these hormones are produced), pituitary tumors, or too little or too much body weight.

Other hormonal conditions that can affect fertility include thyroid problems, diabetes, polycystic ovary syndrome (PCOS), premature ovarian failure (POF), and occasionally Cushing's syndrome.

A woman's ability to get pregnant can also be affected by Age, Problems with the reproductive tract (e.g., blocked or damaged fallopian tubes; endometriosis, pelvic adhesions, benign uterine fibroids, and complications from surgery or infection), Sexually transmitted diseases, Medical conditions such as sickle cell disease, HIV/AIDS, and kidney disease, Smoking, drinking alcohol, or using recreational drugs, Medications such as antidepressants, tranquilizers, calcium channel blockers, narcotics, and anti-cancer drugs and exposure to radiation, lead, toxic fumes and pesticides.

Urinary incontinence is defined by the International Continence Society as "the complaint of any involuntary leakage of urine". Age, pregnancy, childbirth, obesity, functional impairment, and cognitive impairment are associated with increased rates of incontinence or incontinence severity.

Hormonice is a unique nutraceutical formulation that helps correct the turbulent onset of hormonal changes in adolescence during the onset of menstrual cycle and formation of irregular, unhealthy & often clustered ova.

Key ingredients in Hormonice like soy isoflavones, Evening Primrose Oil, cinnamon, Shatavari (Asparagus Racemosus) and green tea extract help with controlling urinary incontinence, increasing bladder sphincter control, improving urethral health and preventing leakage of urine. Soy Isoflavones have beneficial effects on markers of insulin resistance, total testosterone, androgen index and triglycerides. Evening Primrose Oil can help balance the levels of estrogen and Progesterone, Cinnamon helps in reducing insulin resistance. Shatavari contains steroidal-like saponins that supports the functions of female sex hormones-estrogen and progesterone. It also maintains balance of the endocrine system, which affects the production of hormones that helps to regulate human response to stress, mood swings, helps to maintain the normal adrenal and thyroid function, management of menopausal and pre-menopause symptoms like hot flashes, mood swings, temperamental feels, manage PMS symptoms and works by alleviating pain and controlling the loss of blood during menstruation

Hormonic helps correct the hormonal changes in the endocrine system associated with PCOS and with it the accompanying symptoms. It also helps in the formation of healthy ovaries and restores harmony.

This study evaluates the efficacy and safety of Hormonice™ in patients with Polycystic Ovary Syndrome (PCOS), Infertility and Urinary Incontinence.

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