Summer Training at
Oaknet Healthcare Pvt. Ltd., Bangalore
(April 3 to June 2, 2017)

To Study Dienogest Usage in Endometriosis Treatment

By
Abhishek Laddha

Under the guidance of
Dr. Nirmal Kumar Gurbani

MBA Pharmaceutical Management
2016-2018

School of Pharmaceutical Management
The IIHMR University, Jaipur
2017

INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
(WHO Collaborating Centre for District Health System Based on Primary Health Care)

IIHMR UNIVERSITY

CERTIFICATE

This is to certify that Mr. **Abhishek Laddha** has undergone summer training in **Oaknet Healthcare Pvt. Ltd., Bangalore** from 3rd April to 2nd June 2017.

The candidate himself completed the project assign to his during summer training. His approach to the project was sincere and proactive. This summer training is in partial fulfillment of the course requirement recommended for the award of MBA in Pharmaceutical Management.

I wish him success in all his future endeavors.

Col. (Dr.) Ashok Kaushik

Dean (Academic & Student Affair

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June 02, 2017

Certificate

This is to certify that Mr. Abhishek Laddha an MBA student of The IIHMR University, Jaipur has successfully completed the Project on "To Study Dienogest Usage in Endometriosis Treatment" in our organisation under the guidance of Mr. Raghavendra KV, Deputy General Manager - Marketing from 10th April 2017 to 2nd June 2017.

We appreciate Mr. Abhishek Laddha for the dedication shown towards his work and the project has come out well.

We found him to be sincere, hardworking, and result oriented.

We take this opportunity to thank him and wish him all the best for his future.

Janardhanan Narayanaswamy
Vice President- Human Resources

Oaknet Healthcare Pvt. Ltd.
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Certificate

TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Mr. Abhishek Laddha** student of MBA in Pharmaceutical Management 2016-2018 from **IIHMR University, Jaipur** had undergone summer training at **Oaknet Healthcare Pvt. Ltd.**, No:64, 3rd Cross, VR Layout, Opposite New Baldwin School, Ramamurthy Nagar Main Road, Banaswadi, Bengaluru, 560043.

The Candidate has successfully carried out the responsibilities and project work designated to him during project and his approach to the study has been sincere, scientific and analytical.

I wish him for great success in all his future endeavours.

Raghavendra Kaggundi

Dy. General Manager, Marketing

Oaknet Healthcare Pvt. Ltd.

Bangalore

Acknowledgement

The satisfaction and euphoria that an organization the successful completion of the project would be incomplete without the mention of the people who made it possible.

First, I express my sage sense of gratitude and indebtedness to our Institute President, **Dr. Vivek Bhandari** IIHMR University.

I would like to extend my sincere and heartfelt thanks to **Mr. Raghavendra Kaggundi**, Dy. General Manager, Marketing, Oaknet Healthcare Pvt. Ltd. for providing me an opportunity to learn and develop professionally.

I would like to thank me collogues of Oaknet Healthcare Pvt. Ltd. for constant support and guidance in each and every step which helped me to understand Pharma market easily.

I would also like to express my deep sense of gratitude to my faculty mentor **Dr. Nirmal Kumar Gurbani**, Professor, The IIHMR University, Jaipur.

I am also thankful to **Dr. Sandeep Narula,** Associate Professor, The IIHMR University, Jaipur. I am greatly indebted to him for providing their valuable guidance at all stages of the study, their advice, constructive suggestions, positive and supportive attitude and continuous encouragement, without which it would not have been possible to complete the project.

To place on record, I owe a debt of gratitude to all my teachers for grooming me and my classmates for the inspiration needed to work with dedication and motivation throughout as a Summer Intern at Oaknet Healthcare Pvt. Ltd.

My thanks and appreciations also go to my family who have willingly supported me throughout the project.

I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards the industry in coming future.

Abhishek Laddha

Executive Summary

The topic assigned was "A Study on Dienogest usage in Endometriosis Treatment" with the primary objectives:

- To study the prevalence and incidence of Endometriosis.
- To identify the preferred choice of line of treatment by doctors.
- To identify the various indications in which dienogest is used.
- To study the duration of treatment of endometriosis by using dienogest.
- To recommend launch of new brand of dienogest by the organization.

The project was carried out in 3 stages:

The first stage was to study about the endometriosis and prepare a questionnaire followed by stage two which involves meeting with the gynaecologist/female infertility specialist in various government and private hospitals and conduct the survey. After the completion of the survey, the last stage followed which includes analysing the data and getting a conclusion.

Company Profile

Oaknet Lifesciences was launched in April 2015 by R S Raghav and a distinguished team of experts combining 150 years of experience, significant achievements & status amongst the top 10 pharma companies in the Indian Pharmaceutical Market (IPM).

The Managing director & Founder of Oaknet Lifesciences has served one of India's leading company and built a business from Rs 50 crores to Rs 1,500 crores and provided significant growth opportunities to more than 2,000 employees. The teams' core strength is NCD business (Non-Communicable Disease) i.e. cardiology, diabetes, neurology, building business & credibility for the team and organization. Value-integrated performance is a core strength of the team.

In November 2016, Oaknet along with Investors scaled up the business by acquiring the Indian Operations of South African MNC Adcock Ingram Healthcare. The new entity thus created, Oaknet Healthcare Pvt Ltd enjoys market presence of a legacy business of the Cosme Farma spanning close to four decades in such specialities as Dermatology, Gynaecology & Orthopaedics. This deal gave Oaknet Healthcare access to the fast-growing dermatology & gynaecology segments with brands having a presence for 40 years in the country. With the acquisition of Adcock Ingram, Oaknet Healthcare became one of the fastest Indian Company to reach amongst the Top 100 Companies in the IPM.

The combined operation of Oaknet Healthcare and Oaknet Lifesciences has a revenue size of around INR 1,500 million. Oaknet with tremendous leadership expertise in the IPM is poised to create history by scaling up revenues to INR 10 billion over the next 5 years through organic and inorganic growth. Specialities of focus are Cardiology, Diabetes, Dermatology, Gynaecology, Pain Management, Ophthalmology and Neurology.

- Company has three internal divisions
  - Oaknet Pharma (Multispeciality)
  - Skin Care (Skin related medications)
  - Cosme Care (Cosmetics & other)

- Head Office – Mumbai (Maharastra)
- Marketing Headquarter – Bangalore (Karnataka)
- Workforce – 1000+ employees
- Brands – 70+ brands

Vision

"To build a sustainable, scalable and speciality focussed pharmaceutical company."

Top Brands

Brand	Mat Sales Value as per Feb'16-17
Cosvate	24.7
Cosmelite	11.9
Flucos	11.5
Jectocos	8.8
Cosklot	7.2
Ferose	4.9

Endometriosis

Endometriosis is a common estrogen-dependent disorder that can result in substantial morbidity, including pelvic pain, multiple operations, and infertility. Current treatment of endometriosis is mainly based on surgery and ovarian suppressive agents. Approximately only half of women with endometriosis get pain relief from existing medical or surgical treatments. Currently available medical therapies are designed to suppress estrogen synthesis, inducing atrophy of ectopic endometriotic implants or interrupting the cycle of stimulation and bleeding. Oral contraceptive, androgenic agents, progestins and gonadotropin-releasing hormone analogues have all been successfully used in the treatment of endometriosis. Unfortunately, these hormonal treatments are often associated with unwanted effects caused by a hypo-estrogenic state. Furthermore, recurrence of disease and symptoms is quite common with all available drugs. An ideal treatment for endometriosis would induce regression of the disease and its symptoms without any adverse effects associated with a hypo-estrogenic state. None of these drugs can eradicate the disease and, in some cases, the substantial side effects limit the long-term use of these therapies. Current medical therapies for endometriosis result in delayed conception and have not been shown to provide any fertile benefit after treatment. For these reasons, new drugs that aim new targets are under development. (Ferrero S, 2005)

Endometriosis may be defined as the presence of heterotopic endometrial tissue that structurally and functionally resembles endometrial glands or stroma. The structures most commonly affected by endometriosis include ovaries, uterosacral ligaments, pelvic peritoneum, rectovaginal septum, and lower genital tract. Other sites that can be involved include small and large bowel, appendix, hernial sacs, umbilicus, perineum, bladder, ureter, sciatic nerve, pleura, lungs, episiotomy scar, caesarean, femoral lymphatic chain, and skin.

Histologically, foci of endometriosis differ somewhat from normally located endometrium throughout the menstrual cycle. Proliferative changes are less pronounced. Although some secretory changes usually are seen, they may not be present at all. However, the ability of this tissue to respond to ovarian hormones forms the basis for its tendency to proliferate and disseminate. Although it is a benign disease, it has a unique capacity to spread and to invade other tissues in a manner remarkably like that of malignancy. True malignancy, however, is very rarely associated with endometriosis.

Endometriosis is one of the most common conditions encountered in gynaecologic patients. It is the second most common gynaecological disorder in the West, after fibromyomata and is found in 9.6% to 18.7% of all gynaecological laparotomies and laparoscopies. Endometriosis is responsible for varied and disabling symptoms, and its adverse effects on reproductive potential are sources of widespread frustration and disappointment. However, there are no characteristic symptoms referable to endometriosis. Menstrual disturbances are often present. Dysmenorrhoea is a frequent symptom and may be moderate or very severe; there being no correlation with extent of disease. When the rectovaginal septum or uterosacral ligaments are involved, the dysmenorrhoea is often referred to the lower sacral or coccygeal region.

Infertility is present in most the cases. The patients whose major complaint is infertility, endometriosis is a major cause. The precise mechanism by which endometriosis causes infertility need to be elucidated. (Rodrigenz EFJ, 1988)

The main symptoms of endometriosis are

- **Pelvic pain.**
- **Pain during or after sex.**
- **Dysmenorrhea**
- **Premenstrual Pain**
- **Dyspareunia**
- **Chronic fatigue**
- **Infertility**

Endometriosis can affect many aspects of a woman's life including her general physical health, emotional wellbeing and daily routine. Endometriosis is common and many women may have no symptoms. An estimated two million women in the UK have this condition. Endometriosis is a long-term condition which affects women of all ages during their reproductive years (from the onset of menstrual periods to the menopause). It affects women from all social and ethnic groups.

Women who do experience symptoms may have one or more conditions :

- **Painful periods (dysmenorrhoea) which do not respond to over-the-counter pain relief. Some women have heavy periods.**
- **Pain during or after sexual intercourse (dyspareunia)**
- **Lower abdominal pain**
- **Pelvic pain which can be long-term**
- **Difficulty in getting pregnant or infertility**
- **Pain related to the bowels and bladder (with or without abnormal bleeding)**
- **Long-term fatigue. Some women do not have any symptoms at all.**

Pain is a common symptom of endometriosis. The pain can be a dull ache in the lower abdomen, pelvis or lower back. Pain affects each woman differently: where it hurts, when it hurts and how much it hurts. The pain, and the effects of endometriosis, can make you feel depressed. Most women with endometriosis get pain in the area between their hips (known as the pelvis) and the tops of their legs. For further information see Long-term pelvic pain: information for you. Some women get pain only at certain times, such as during their periods, when they have sex or when they open their bowels.

Other women have pain all the time. Some women with endometriosis become pregnant easily while others have difficulty getting pregnant. The pain may get better during pregnancy and then recur after the birth of the baby. Some women find that their pain resolves without any treatment. What causes endometriosis? During the menstrual cycle, under the influence of the female hormones estrogen and progesterone, the lining (endometrium) of the womb thickens in readiness for a fertilised egg. If pregnancy does not occur, the lining is shed as a period.

Endometriosis occurs when the cells of the lining of the womb are found in other parts of the body, usually the pelvis. Each month this tissue outside the womb thickens and breaks down and bleeds in the same way as the lining of the womb. This internal bleeding into the pelvis, unlike a period, has no way of leaving the body. This causes inflammation, pain and damage to the reproductive organs. 2 Fallopian tubes Ovary Womb lining (endometrium)

Entrance to the womb (cervix) Patches of endometriosis Womb (uterus) Vagina Reproductive areas where endometriosis can be found Endometriosis commonly occurs in the pelvis.

It can be found:

- **On the ovaries where it can form cysts (often referred to as 'chocolate cysts')**
- **In or on the fallopian tubes**
- **Almost anywhere on, behind or around the womb**
- **In the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen).**

Less commonly, endometriosis may occur on the bowel and bladder, or deep within the muscle wall of the uterus (adenomyosis). It can also rarely be found in other parts of the body. (© Royal College of Obstetricians and Gynaecologists 2007)

Epidemiological Information

Prevalence rate

- 20-25% in women of reproductive age.
- Incidence rate is 10% in women of reproductive age.
- 25-48% in infertile women.
- 3-5% in adolescent girls.
- Post-operative Recurrence rate is 21% at the end of 2 years and 40-50% at end of 5 years.

Demographical Data

- Population of women in India (2011 census). (India, 2011)
  - ✓ Total = 58,74,47,730
  - ✓ Women of age group 15-60 year is 62.8% i.e. 36,89,17,174.
  - ✓ Women of reproductive age i.e. 20-40 years may be 60% of age group 15-60 i.e. 22,13,50,304.
  - ✓ Prevalence rate of endometriosis i.e. 22.5% gives 5,53,37,576.
  - ✓ By the rule of half, women seek for medical assistance in endometriosis are 2,76,68,788 i.e. approx. 30 million patients

Medicinal Treatment for Endometriosis

1. **Dienogest**
2. **NSAIDs**
3. **Combined Oral Contraceptives (COCs)**
4. **Gondotropin releasing hormone agonist (GnRH)**
5. **Danazol**
6. **Progestins**

Dienogest

Dienogest is an oral progestin that has been investigated systematically for the treatment of endometriosis in dose- ranging, placebo-controlled, active comparator- controlled, and long-term trials performed in Europe and Japan (Figure 1). Based on this trial evidence, dienogest has received approval as a monotherapy for the treatment of endometriosis in Europe, Japan, Australia, and Singapore.

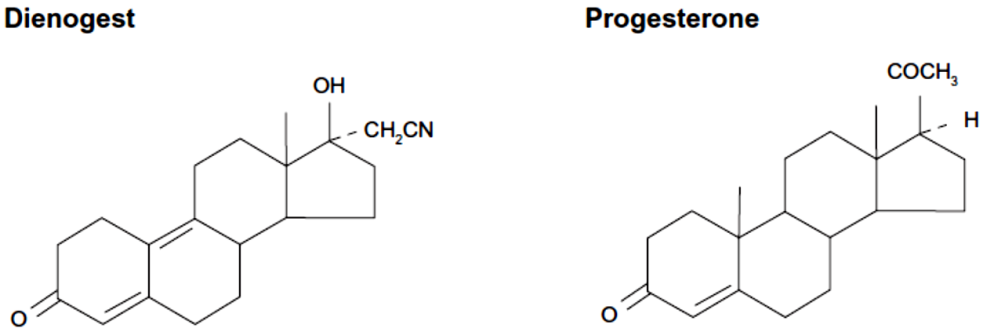


Figure 1 Structural formula of the progestin, dienogest, compared with naturally occurring progesterone.

Preclinical Studies

Dienogest demonstrates several characteristics in preclinical studies that are relevant to its use in endometriosis. Pharmacologically, dienogest combines the advantages of the 19-norprogestin and the progesterone derivative classes. Dienogest binds to the progesterone receptor with high specificity, and produces a potent progestogenic effect related to the high circulating levels of the unbound molecule. Binding affinities of dienogest for estrogen, glucocorticoid, and mineralocorticoid receptors are negligible. Unlike other agents in the 19-norprogestin class, dienogest lacks androgenic effects; rather, dienogest has beneficial antiandrogenic properties typical of the progesterone derivatives, which are associated with minimal changes in lipid and carbohydrate levels. (Kohler G, 2010)

Dienogest is almost completely absorbed, and has a high bioavailability after oral administration, like other 19-norprogestins. Its relatively short half-life of 10 hours means there is no risk of accumulation after repeated dosing. Most orally administered dienogest is excreted within 24 hours, mainly in urine.

Clinical studies

Clinical studies of dienogest with durations between 12 and 24 weeks have provided information on optimal dosing and on efficacy and safety characteristics that are relevant to the long-term management of endometriosis.

The optimal daily dose of dienogest for treating endometriosis was investigated in an open-label, randomized, multicentre, 24-week, dose-ranging study in Europe. Sixty-eight women with endometriosis stage I–III at laparoscopy (i.e., with minimal to moderate disease)

were randomly assigned to treatment with dienogest 1, 2, or 4 mg once daily. Randomization to the 1 mg group was halted prematurely because of unsatisfactory bleeding patterns. Laparoscopy showed that dienogest at 2 mg and 4 mg daily significantly reduced endometriotic lesions. In addition, dienogest at both these doses improved patient-reported symptoms, including the intensity of dyspareunia, dysmenorrhea, and diffuse pelvic pain. The 2 mg and 4 mg dienogest doses were generally well tolerated and rates of discontinuations due to adverse events were low. Irregular uterine bleeding was experienced by 55.2% in the 2-mg group and 68.6% in the 4-mg group, with a trend to decreased intensity over time in both groups. Based on these outcomes, dienogest at 2 mg once daily was recommended as the optimal dose in the treatment of endometriosis. (Kohler G, 2010)

Dienogest and fertility considerations

Most women suffering from endometriosis are of reproductive age and so may require contraception. Based on the available data, dienogest provides complete ovulation inhibition at a daily dose of 2 mg.

However, dienogest monotherapy was not developed as a contraceptive, and women taking dienogest as a treatment for endometriosis are advised to use nonhormonal methods of contraception. Women with endometriosis may desire pregnancy once sufficient pain relief is achieved.

Recent pharmacodynamics data in volunteers indicate that ovarian activity resumes rapidly (range 1–43 days) after cessation of dienogest. These observations support studies that describe a prompt return to fertility (e.g., mean about 30 days) and include cases of successful pregnancy in women with endometriosis following the cessation of dienogest treatment 2 mg daily for durations up to one year.

As with other progestins, there are limited data on the use of dienogest in pregnant women. The available data do not indicate harmful effects for dienogest with respect to reproductive toxicity and reveal no special risks on pregnancy.

However, dienogest should not be administered to pregnant women because there is no need to treat endometriosis during pregnancy. (Visanne, 2010)

Dienogest for the long-term treatment of endometriosis

Effective management of endometriosis over the longer term is an important objective. The painful symptoms and impairment in quality of life associated with endometriosis may persist or deteriorate in the absence of effective treatment. Recurrence is frequent even after successful surgery, while there are only limited trial data to confirm the efficacy and safety of long-term treatment for many medications used in endometriosis.

Dienogest has been investigated as a long-term treatment of endometriosis in two large trials performed in Europe and Japan, which included assessments of efficacy, change in quality of life, safety, and tolerability. Women who completed the 12-week placebo-controlled study in Europe were offered the opportunity to enter an open-label extension study of

dienogest for up to 53 additional weeks, providing an overall treatment period of up to 65 weeks. Notably, of the 188 women completing the placebo-controlled study, a large proportion (n = 168, 89%) consented to enter the long-term extension study.

The intensity of pain showed significant, sustained improvements during the long-term study, in addition to the improvements associated with dienogest during the placebo-controlled phase. Mean visual analogue scores decreased from 56.9 mm at baseline of the placebo-controlled study to 34.1 mm at baseline of the long-term study, to 11.5 mm at the end of the 53 additional weeks of treatment. During a 24-week treatment-free period following the long-term study, visual analogue scores increased only moderately, suggesting that dienogest induces a beneficial effect that may persist after treatment cessation.

Short Form 36 Health Survey scores during the treatment-free period indicated minimal changes in physical or mental indices of quality of life over six months after cessation of dienogest. (Petraglia F, June 17, 2011.)

Effective long-term management of endometriosis is a significant clinical objective in view of the debilitating nature of this often-chronic condition. Among current management approaches, recurrence is common after surgery, while evidence to support the efficacy and safety of many medications is lacking. GnRH agonists, a standard medication in endometriosis, may not be administered continuously for more than six months in the absence of add-back therapy because of the deleterious hypoestrogenic effects.

Problems with other medications are: -

1. NSAIDs- Nonsteroidal anti-inflammatory drugs are frequently used by women with endometriosis to achieve analgesia, although clinical trial evidence to support the efficacy of these agents in endometriosis is lacking. **A major limitation to the long-term use of nonsteroidal anti-inflammatory drugs is their significant side effects, including the risk of gastric ulceration and an anti-ovulatory effect when taken at mid-cycle.**
2. COCs- COCs are widely used to treat the symptoms of endometriosis, although they are not approved for this indication in most countries because of **the absence of supportive trial evidence**. For the same reason, practice guidelines can offer limited guidance on the optimal COC regimens in endometriosis. A recently published review notes that the putative biological effects for COCs include both inhibitions of endometrial cell implantation but also a protective effect against endometrial lesion necrosis. Clinical experience indicates that COCs may be used with safety in many women for the long-term treatment of endometriosis. However, **a common problem with long-term continuous COC regimens is breakthrough bleeding.** This is often treated by discontinuing the COC for a few days and then restarting therapy.
3. GnRH- GnRH agonists are established therapies for endometriosis that can be administered via intramuscular, subcutaneous, or intranasal routes. Depot formulations are available. Although GnRH agonists provide effective pain relief and reduce the progression of endometriotic implants, the hypo estrogenic state that

they induce is associated with effects such as **accelerated bone mineral density loss, hot flushes, and vaginal dryness**. In consequence, the use of GnRH agonists is limited to six months in the absence of "add-back" therapy with steroids. The optimal regimens for add-back therapy are not yet established. For **younger women who have not yet reached maximum bone density, guidelines recommend a careful consideration of the use of GnRH agonists due to their bone demineralizing effects.**

4 Danazol- Danazol is an androgenic steroid that is effective in treating the signs and symptoms of endometriosis, but its use is limited by adverse effects on **lipid metabolism and by weight gain, enema, acne, vaginal dryness, hot flushes, oily skin, hirsutism, liver toxicity, and breast atrophy**. Because of these effects, danazol has today been superseded in many countries by alternative agents.

5 Progestin- Oral, parenteral, intrauterine, or implantable progestin have been used for decades in the treatment of endometriosis, although for many of these agents there is a **lack of supportive evidence from controlled clinical trials**. When administered continuously, progestins are effective in many women for the management of pain and other symptoms of endometriosis, with beneficial effects also relating to amenorrhea and anovulation. However, **certain progestins are effective in endometriosis only at high doses** when compared with use in other indications which may increase the likelihood of adverse effects, **such as weight gain and androgenic effects, and elevate the risk of cardiovascular adverse events.**

Advantages of Dienogest over other medications are:

1 Effective long-term management of endometriosis is a significant clinical objective in view of the debilitating nature of this often-chronic condition. Among current management approaches, recurrence is common after surgery, while evidence to support the efficacy and safety of many medications is lacking.

2 GnRH agonists, a standard medication in endometriosis, may not be administered continuously for more than six months in the absence of add-back therapy because of the deleterious hypoestrogenic effects. Dienogest is a progestin investigated for the treatment of endometriosis. Dienogest at a dose of 2 mg daily has been studied extensively in clinical trial programs performed in Europe and Japan, including two studies with treatment durations of up to 65 weeks. These studies demonstrated that dienogest has an efficacy, safety, and tolerability profile that is favourable for long-term use.

3 The intensity of pain associated with endometriosis decreased progressively, adverse events (mostly mild or moderate in intensity) were predictable and associated with low discontinuation rates, and bleeding irregularities reduced in intensity and frequency over time. Following cessation of dienogest treatment, menses returned to normal.

4 The impact of endometriosis on a woman's quality of life is substantial and wide ranging. Quality of life assessments in the dienogest studies indicated that improvements in both physical and mental indices were attained within 12-week and 24-week treatment durations.

5 Significance to clinical practice, compliance with dienogest treatment was high and rates of discontinuation due to adverse events were low in studies.

6 The dienogest study programs performed in Europe and Japan indicate that dienogest represents a promising new medication for the long-term management of endometriosis.

Market Research Data

This is the market research data given by AWACS as provided by the organization.

BRAND	COMPANY	PACK	STRENGTH	SKU LAUNCH DATE	MRP	Values (in crore INR)					
						MAT VAL MAR 16	MAT VAL MAR 17	GR MAR 17	MAT UNIT MAR 16	MAT UNIT MAR 17	GR MAR 17
DIENOFEM	TTK HEALTHCARE LTD	10	2 MG	Feb-15	480	1.5	0.1	-94.2	40.6	2.4	-94.2
DINOFIRST	AKUMENTIS HEALTHCARE LTD	10	(blank)	Apr-14	499	6.6	4.5	-31.7	174.1	118.9	-31.7
DINOGEST	KOYE PHARMACEUTICALS PVT. LTD.	10	2 MG	Feb-15	499	0.8	0.4	-49.1	20.8	10.6	-49.1
ENDOFIT	AKUMENTIS HEALTHCARE LTD	10	2 MG	Sep-15	499	0.2	0.6	237.9	4.9	16.5	237.9
ENDOHEAL	AKUMENTIS HEALTHCARE LTD	10	2 MG	Apr-15	499	0.4	2.3	421.0	11.6	60.3	421.0
ENDOREG	JAGSONPAL PHARMACEUTICALS LTD	14	2 MG	Jan-15	630	0.7	2.6	305.6	13.1	53.0	305.6
ENDOSIS	PHARMANOVA	10	2 MG	Jun-14	499	1.8	1.6	-11.2	47.9	42.5	-11.2
RUMIGEST	ALEMBIC LTD	10	2 MG	Aug-16	520	0.0	1.2	NA	0.0	31.0	NA
Grand Total						**12.0**	**13.4**	**12.0**	**313.0**	**335.3**	**7.1**

Source: Awacs Market research

Literature Review

1. Endometriosis is a chronic disease primarily affecting women of childbearing age, in which endometriotic lesions form outside the uterus, typically leading to painful symptoms, fatigue, and infertility. The symptoms of endometriosis may cause significant impairment in quality of life and represent a substantial economic burden to patients, families, and society. There is no cure for endometriosis; management consists of alleviating pain and other symptoms, reducing endometriotic lesions, and improving quality of life. Recurrence after surgical intervention is common, while the clinical evidence to support the efficacy and safety of many medications currently used in endometriosis is limited. Dienogest is an oral progestin that has been investigated extensively in the treatment of endometriosis in two clinical programs performed in Europe and Japan, including dose-ranging, placebo-controlled, active comparator-controlled, and long-term (up to 65 weeks) studies. These studies demonstrated that dienogest 2 mg daily effectively alleviates the painful symptoms of endometriosis, reduces endometriotic lesions, and improves indices of quality of life. Dienogest showed a favourable safety and tolerability profile in these studies, with predictable adverse effects, high rates of patient compliance, and low withdrawal rates. This review article describes the clinical trial evidence that characterizes the efficacy and safety of dienogest in endometriosis, including two studies characterizing dienogest in long-term use. The relevance of these findings to the management of endometriosis in clinical practice is discussed. (Schindler, 2011)
2. The prevalence of endometriosis was 5.2% all gynaecological admissions. Our findings of a prevalence of endometriosis of 24.88% in 201 laparotomies/laparoscopies, negates the commonly held view that endometriosis is a rare disease in Pakistan. We have also recorded a high incidence of infertility among patients suffering from endometriosis. The prevalence and pattern of presentation of the patients are comparable with the results reported from all over the world. It is, therefore, concluded that endometriosis is as common among Pakistani women as elsewhere in the world. The pattern of presentation and complications are also similar. (Naseer-ud-Din, 2000)
3. Endometriosis amongst infertile women is increasingly being detected due to greater use of laparoscopy in evaluation of infertility. Though most signs do not correlate with severity of disease however the presence of restricted uterine mobility, adnexal tenderness & chronic pelvic pain should always raise the suspicion of endometriosis. Laparoscopy remains the gold standard for diagnosing and staging endometriosis. (Vineet V Mishra, 2015)
4. Current treatment of endometriosis is mainly based on surgery and ovarian suppressive agents (oral contraceptives, progestin's, GnRh agonist and androgenic agents). Hormonal treatments are often associated with unwanted effects, delayed conception and recurrence of disease and symptoms when stopped. For these reasons, new drugs that aim new targets are required to cause regression of the disease & symptoms without adverse hypo-estrogenic effects. This review aims to provide an update on the new drugs used for treatment of endometriosis. These include the levonorgestrel-releasing intrauterine device, GnRH antagonists, aromatase inhibitors, selective estrogen-receptor modulators, progesterone antagonist, selective progesterone receptor modulators, angiogenesis inhibitors, and immunomodulatory drugs. (Elnashar, 2015)

Objective

1. To study Endometriosis prevalence rate in Banaswadi, Bangalore.
2. To study the treatment(s) preferred by Gynaecologist for treating Endometriosis.
3. To find out indications for which Dienogest will be prescribed.
4. To find out general treatment duration for dienogest.
5. To study dienogest prescription pattern for recommending new brand launch.

Rationale of the study

The purpose of the study is to analyse whether the organization should go for launch of new brand of drug molecule **Dienogest** under gynaecology segment or not. Simultaneously, this study also helps to describe usage of dienogest in treatment of endometriosis because it is the latest drug therapy with minimal side effects and significantly increase quality of life.

Research Methodology

1. **Research Design**: The research was conducted using Descriptive and Exploratory research design.

2. **Data Type:** Primary and Secondary Data

3. **Sample Technique**: Non-probability Purpose Sampling Technique was used.

4. **Sample Size**: Total 50 Gynaecologist/Female Infertility Specialist.

5. **Collection of data**: Survey Questionnaire.

6. **Area of Study**: Banaswadi, Bangalore, 560043.

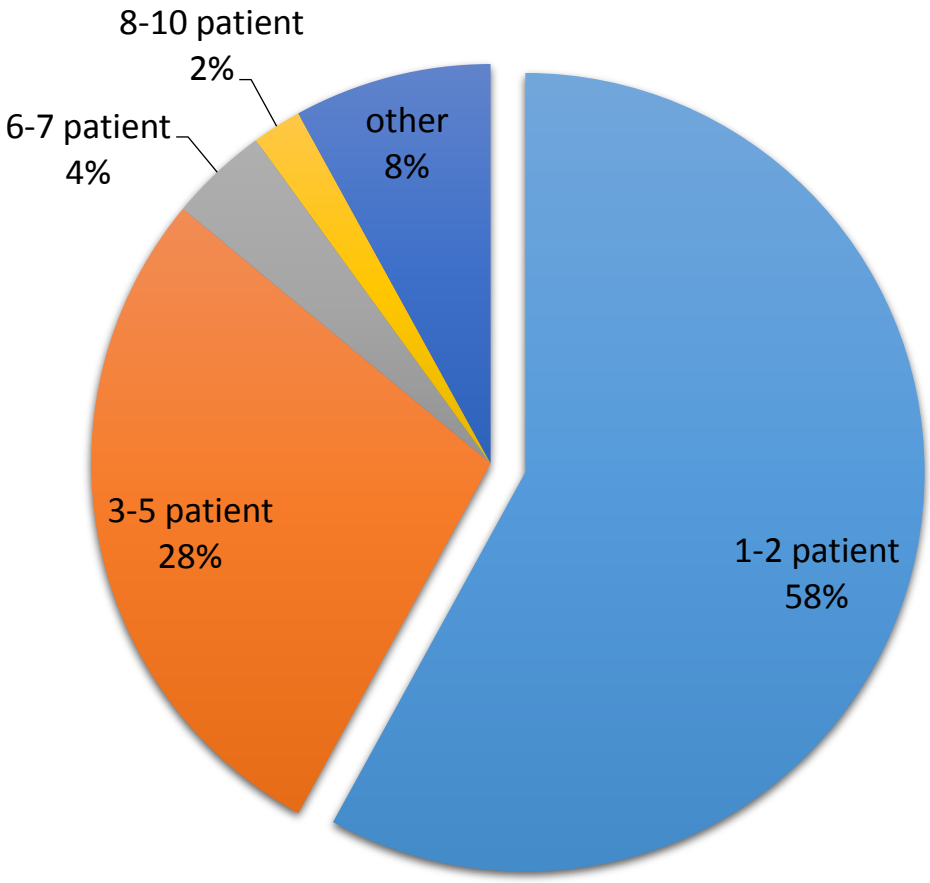
7. **Period of Study**: 60 days

8. **Tools used:** Microsoft Excel is used for analysis

   It is a descriptive study conducted among gynaecologist/female infertility specialist in Banaswadi, Bangalore. This study was done in different part firstly we interacted with doctors who are specialized in gynaecology segment/female infertility and ask them to fill our questionnaire which consist of all the important questions which was design to know the market knowledge about dienogest usage and endometriosis treatments. Market research data was obtained from AWACS market research, which was provided by organization. After getting of all responses, analysis was done by using Microsoft excel. **The study period was 60 days.**
9.

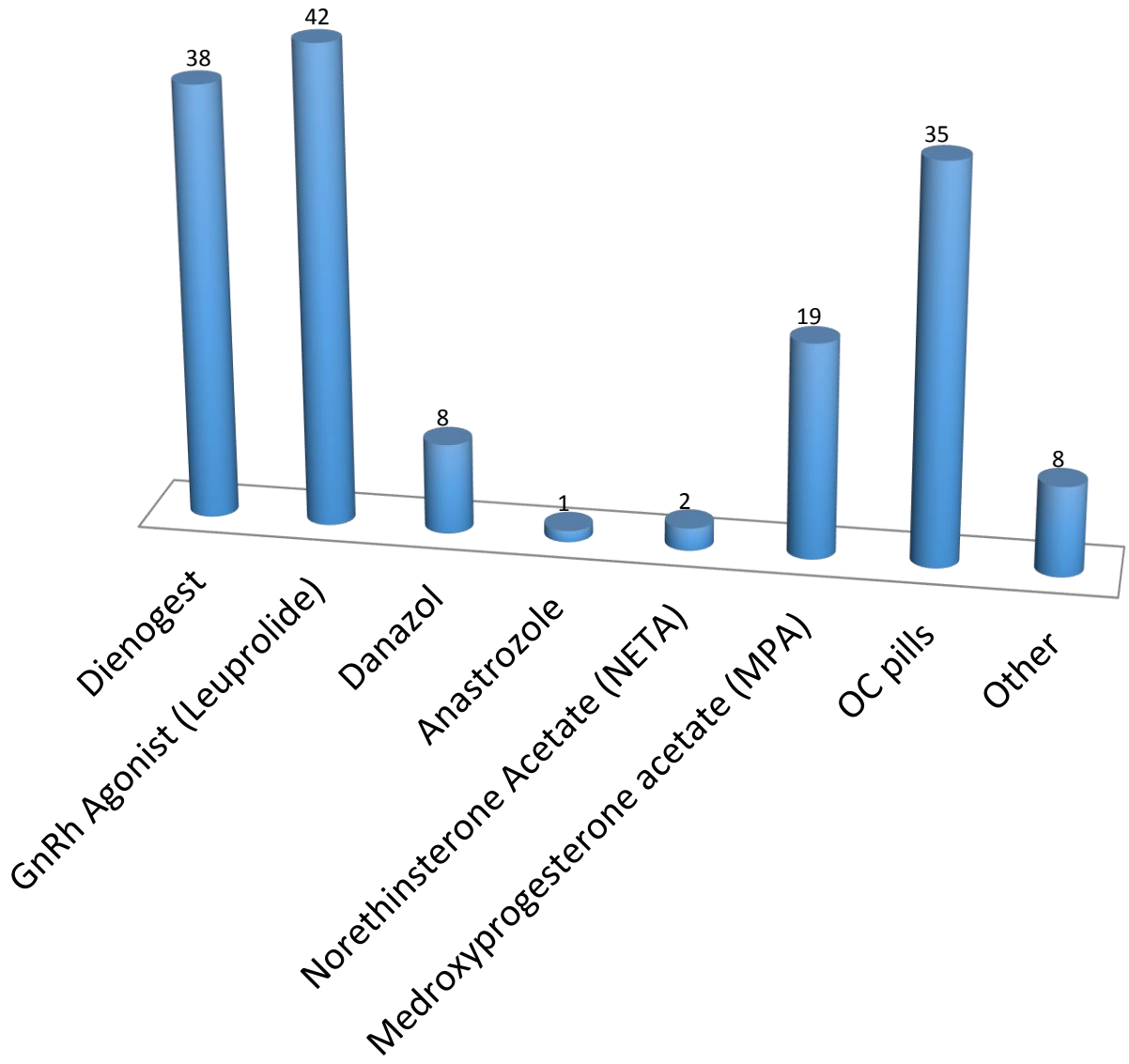
1. Prevalence of Endometriosis Patient in research area as per stated by gynaecologist:

`



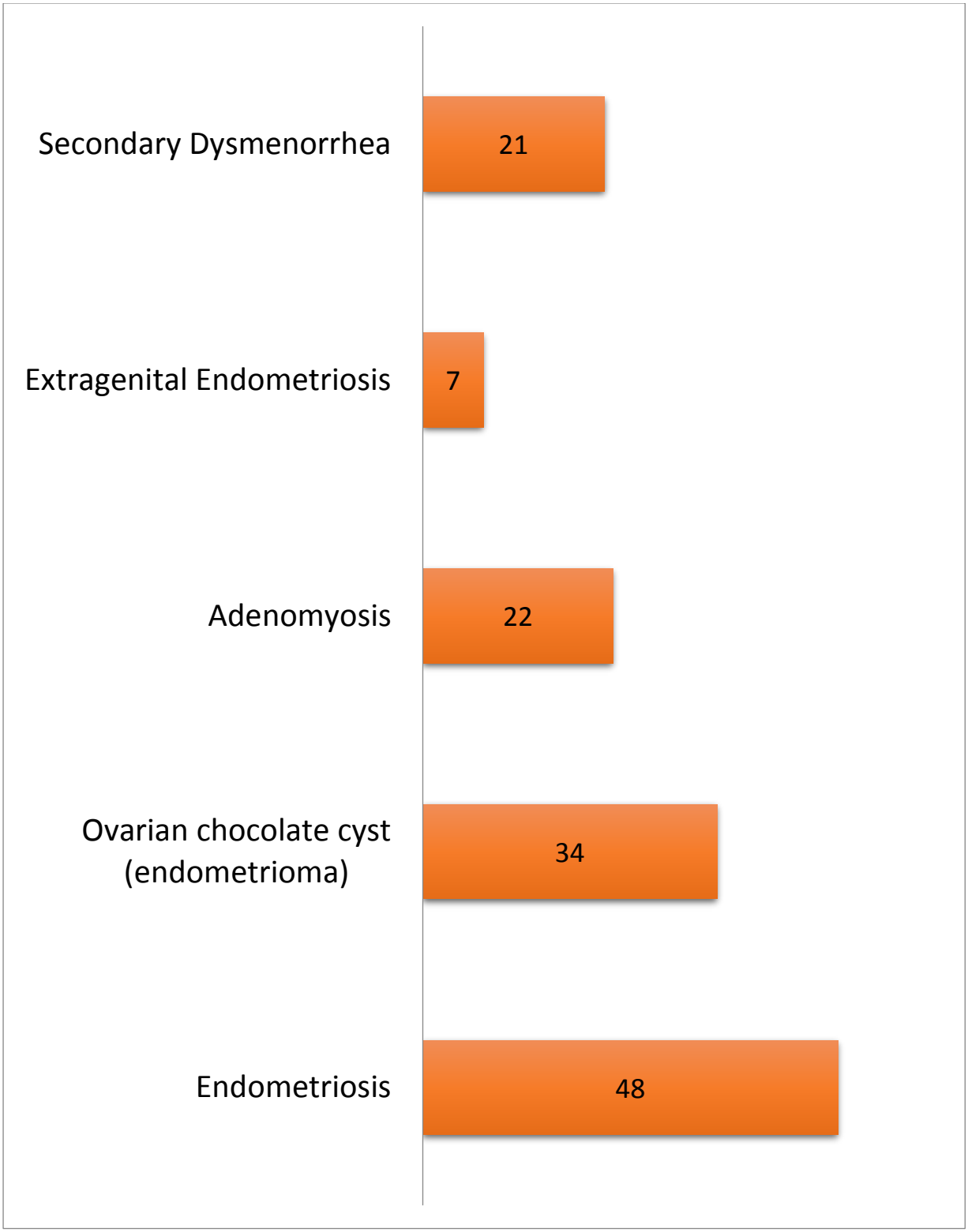
From above chart, it is clearly observed that 58% doctors said that they see 1-2 patients in a week having endometriosis disease. While 28% doctors said 3-5 patients in a week and very few doctors see more than 5 patients in week. However, 8% of doctors said that they have seen only 1 patient in a fortnight or a month.

2. Treatment preference of doctors to treat endometriosis:



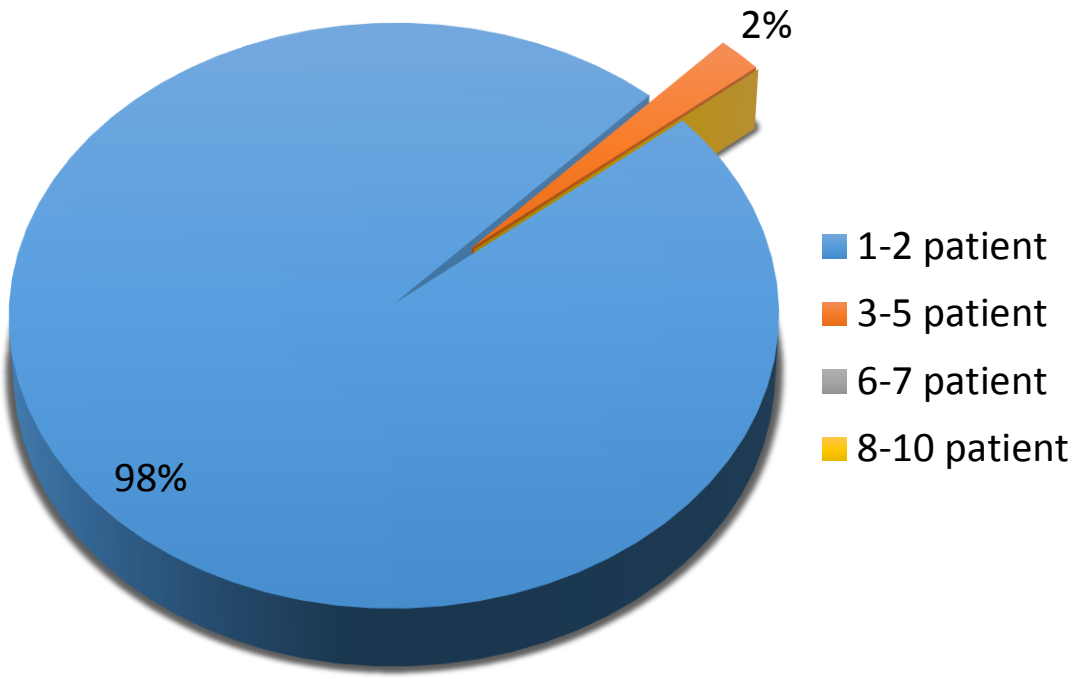
Among 50 Doctors almost 40 prefer dienogest, GnRH agonist (leuprolide) & Oral contraceptives to treat endometriosis. Whether 8 doctors prefer surgical methods such as laparoscopy to treat endometriosis.

3. Use of Dienogest in these indications:



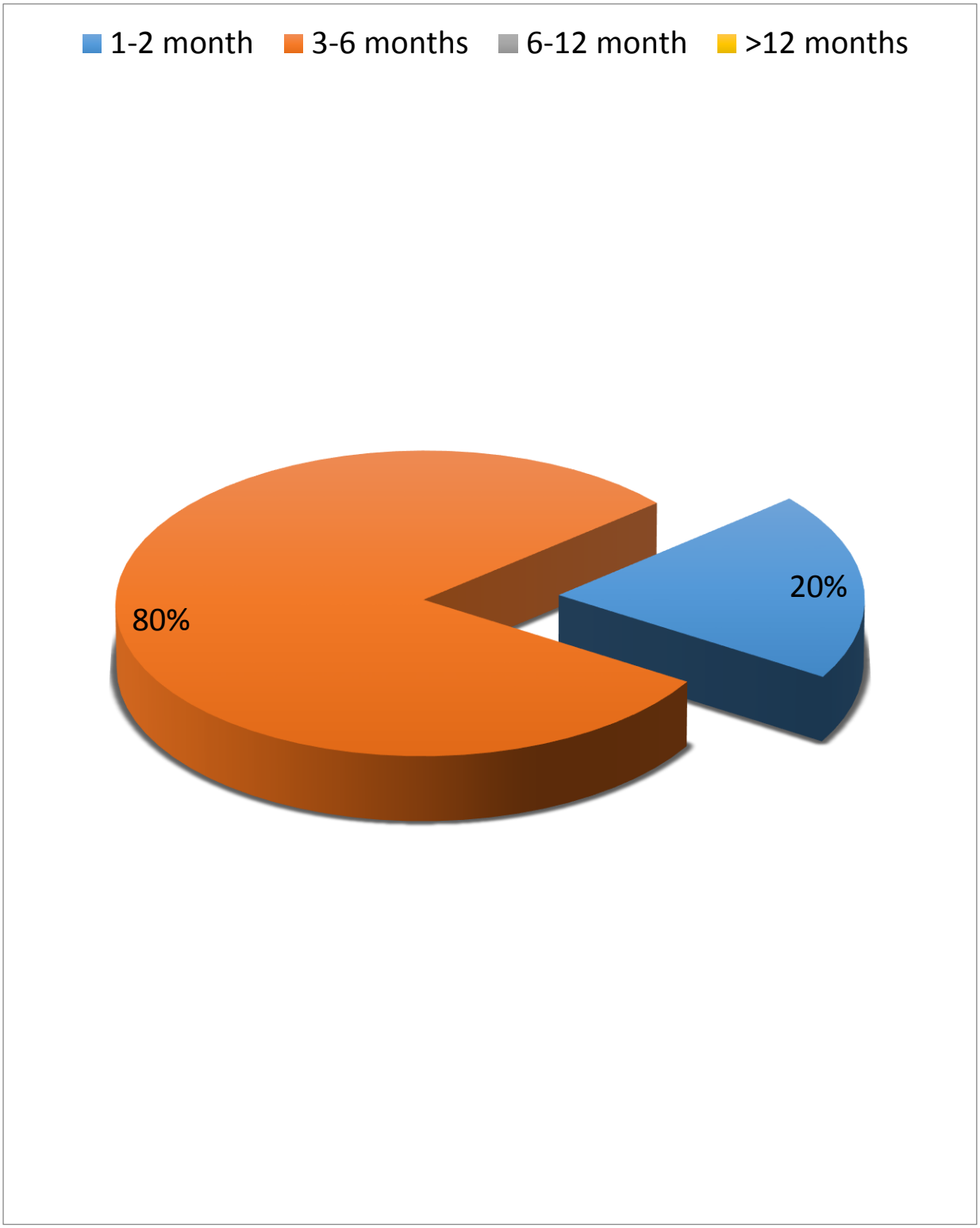
Dienogest is mainly used in treatment of endometriosis disease. Almost 96% doctors said the same. However, it is also used in indications like Ovarian chocolate cyst, Adenomyosis, Extragenital Endometriosis & Secondary dysmenorrhea.

4. Prescription Pattern of Dienogest by Gynaecologist:



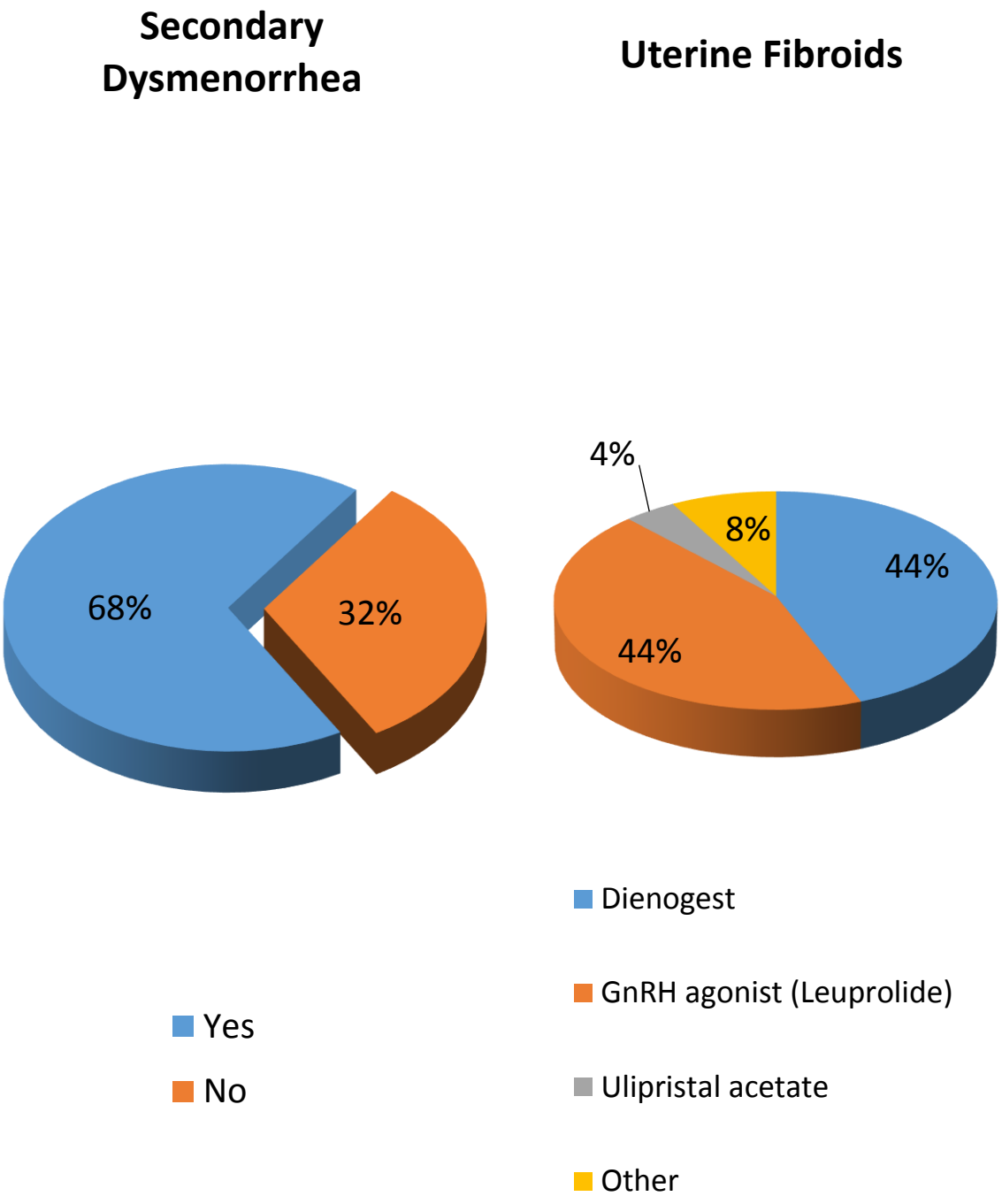
Almost all doctors who were prescribing dienogest in treatment of endometriosis were prescribed dienogest 2mg in a week to 1-2 patients. So, there is huge potential in market.

5. General treatment duration for Dienogest 2mg:



Dienogest is generally prescribed for 3-6 months that means one patient must buy 90-180 tablets for sure.

6. Dienogest use in secondary dysmenorrhea and uterine fibroids:



As illustrated by graphs, 68% doctors prescribed dienogest in Secondary dysmenorrhea whereas for uterine fibroids doctors prescribed both dienogest and GnRH agonist to treat the indications. However, 8% doctors prefer surgical methods such as laparoscopy to treat this indication.

7. Market research facts:

By analysing given market data, following facts were found: -

- Overall market growth was 12% (MAT value) & 7% (MAT volume) for Mar-17. This is considerably excellent growth rate because Indian Pharmaceutical Industry also growing on 15% CAGR. (ibef.com)
- Dienogest Market is dominated by Akumentis healthcare limited. It has 3 brands of this composition and their MAT values are on Mar-17.
    a. DINOFIRST – 4.5 CR (-31.7%)
    b. ENDOFIT – 0.6 CR (237.9%)
    c. ENDOHEAL – 2.3 CR (421%)

DINOFIRST have largest market cap but showing decrease MAT value from last year but other 2 brands showing fast and inclined sales trend.

MRP for all brands are same i.e. Rs. 499/- per strip of 10 tablets and same strength 2 mg.

- ENDOREG by Jagsonpal Pharmaceuticals Ltd. shown growth of 305.6% in MAT value. This is might be because it is the only brand which consists of 14 tabs and Dienogest dose is 1 tab/day.
- RUMIGEST recently launched by Alembic ltd. on Aug-16 and it MAT value for Mar-17 was 1.2 Cr.

So, in accordance with these facts and figures, Dienogest market has a huge growth and few competitor brands in market.

8. Scope of market as per demographical and market research data:

- ✓ Total market of dienogest as on mar-17 is 13.4 Cr (MAT val)
- ✓ MRP of 1 tablet is approx. 50/- rs.
- ✓ Total expense for a patient for 1 year is 18250/-
- ✓ Total expected patients in India approx. to be 30 million.
- ✓ Total expected market for pan India is 50 billion.
- ✓ By rule of half market will be 25 billion approx.

Limitations to the study

- ✓ Doctors were not ready to give information easily.
- ✓ Many doctors were either not aware or not prescribing dienogest refused to fill the forms.

Recommendations

Based on above findings, followed points are recommended:

- Based on Prevalence of disease and Market scope, it is recommended that organization should go for launch of new brand of dienogest in gynaecology segment. But also, keep these following facts on board before taking any decision.
- While doing the survey, it is observed that some doctors are not aware about dienogest treatment. So, this is a great opportunity to place your brand as their first choice of dienogest by informing them all advantages of dienogest over the other medications.
- In addition to above statement, it is also observed that some doctors know about dienogest but do not prescribing it. By informal detailed conversation with some of them, they told that they are not prescribing this drug because of these factors:
    - Price (Higher than GnRH agonist & OC pills).
    - Safety profile not yet established.
    - Efficacy and efficiency of drug not known to a great extent.
    - Newer drug therapy lacks over GnRH agonist and OC pills.
- It is highly recommended that organization should go for a detailed and large survey including those above-mentioned factors to get more details upon those factors. Also, this study was conducted on very less number of doctors so it can't be generalised to pan across India because India is a diverse country in terms of disease prevalence, prescription behaviour, out of pocket expenditure of patients, demographical representation & mind-set of patients as well as doctors.
- It is suggested that most competitor drug to dienogest is GnRH agonist (Leuprolide) so organization also took a closer look on MAT value of this molecule before going for launch of new brand.
- Although, Organization should make a competitive price strategy to gain huge response from market and establish your brand into market.
- Now days, Infertility also a major issue in metro cities more than rural area. Also in metro cities, there are so many infertility clinics are present and they are doing great business. Organization should have to target this infertility clinics and specialist doctors to get more competitive advantage

over the other companies because endometriosis is a major cause of infertility.

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Annexure-I: List of Respondent Doctors

Name of Doctor	Speciality	Address	Contact No.	Email Address
Dr. Anita B R	OBG	Femiint health, Whitefield	9442768940	anita_br@gmail.com
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Annexure-II: Survey Questionnaire Form

A Study on Drugs/Therapies Used in Treatment of Endometriosis.

* Required

1. **Email address** *

_____

2. **How many Endometriosis patients do you see in a week?** *

Mark only one oval.

- ◯ 1-2 Patient
- ◯ 3-5 Patients
- ◯ 6-7 Patients
- ◯ 8-10 Patients
- ◯ Other: _____

3. **Which treatment do you prefer for Endometriosis treatment?** *

Check all that apply.

- ☐ Dienogest
- ☐ GnRH agonist (Leuprolide)
- ☐ Danazol
- ☐ Anastrozole
- ☐ Norethinsterone acetate (NETA)
- ☐ Medroxyprogesterone acetate (MPA)
- ☐ OC pills
- ☐ Other: _____

4. **In which indication(s) do you prescribe Dienogest 2mg?** *

Check all that apply.

- ☐ Endometriosis
- ☐ Ovarian chocolate cyst (endometrioma)
- ☐ Adenomyosis
- ☐ Extragenital Endometriosis
- ☐ Secondary Dysmenorrhea
- ☐ Other: _____

5. **In how many patients do you prescribe Dienogest 2mg in a week?** *
Mark only one oval.

- ◯ 1-2 patient
- ◯ 3-5 patients
- ◯ 6-7 Patients
- ◯ 8-10 Patients

6. **What treatment duration do you prefer for Dienogest 2mg?** *
Mark only one oval.

- ◯ 1-2 month
- ◯ 3-6 months
- ◯ 6-12 months
- ◯ >12 months
- ◯ Other: _____

7. **Approx.40-60% women with secondary dysmenorrhea reported to have Endometriosis. Will you prescribe Dienogest 2mg in secondary dysmenorrhea?** *
Mark only one oval.

- ◯ Yes
- ◯ No

8. **Which treatment do you prefer for women suffering from both endometriosis and uterine fibroids?** *
Mark only one oval.

- ◯ Dienogest
- ◯ GnRH agonist (Leuprolide)
- ◯ Ulipristal acetate
- ◯ Other: _____

9. **Name of Doctor** *

_____

10. **Speciality**

_____

11. **Address** *

_____

12. **Contact No.**

_____

☐ Send me a copy of my responses.

Powered by Google Forms

Annexure-III: Data Tables

Q.2-: How many Endometriosis patients do you see in a week?	
Category	**Responses**
1-2 patient	29
3-5 patient	14
6-7 patient	2
8-10 patient	1
other	4

Q.3-: Which treatment do you prefer for Endometriosis treatment?	
Category	**Responses**
Dienogest	38
GnRh Agonist (Leuprolide)	42
Danazol	8
Anastrozole	1
Norethinsterone Acetate (NETA)	2
Medroxyprogesterone acetate (MPA)	19
OC pills	35
Other	8

Q.4-: In which indication(s) do you prescribe Dienogest 2mg?	
category	**Responses**
Endometriosis	48
Ovarian chocolate cyst (endometrioma)	34
Adenomyosis	22
Extragenital Endometriosis	7
Secondary Dysmenorrhea	21

Q.5-: In how many patients do you prescribe Dienogest 2mg in a week?	
category	**Responses**
1-2 patient	49
3-5 patient	1
6-7 patient	0
8-10 patient	0

Q.6-: What treatment duration do you prefer for Dienogest 2mg?	
Category	**Responses**
1-2 month	10
3-6 months	40
6-12 month	0
>12 months	0

Q.7-: Approx.40-60% women with secondary dysmenorrhea reported to have Endometriosis. Will you prescribe Dienogest 2mg in secondary dysmenorrhea?	
Category	**Responses**
Yes	34
No	16

Q.8-: Which treatment do you prefer for women suffering from both endometriosis and uterine fibroids?	
Category	**Responses**
Dienogest	22
GnRH agonist (Leuprolide)	22
Ulipristal acetate	2
Other	4

Thank You...!!

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