I. YASMIN AND YAZ

Yasmin and Yaz are widely prescribed oral contraceptives used to prevent pregnancy, treat emotional and physical symptoms of PMDD (Premenstrual Dysphoric Disorder) and moderate acne in some cases.

Both drugs are manufactured by Bayer with Yaz being approved by the FDA in 2006. Yasmin is a lower-dose version of the drug and was approved by the FDA in 2001.

Yasmin and Yaz are combination birth control pills using two types of hormones known as estrogen and progestin. The estrogen component, ethinyl estradiol, is common to many combination oral contraceptives. However, the progestin component, Drosperinone is unique to these two drugs. Drosperinone is a spironolactone analog and can cause elevation of potassium levels due to its potassium-sparing diuretic effects.

Because Drosperinone can act like a diuretic, it can cause dehydration which causes increased potassium levels (hyperkalemia) and a decrease in sodium levels (hyponatremia) in the body. Potassium is a key control in the electrical system of the heart and, therefore, the elevated levels cause arrhythmias which can lead to stroke, deep venous thrombosis, pulmonary embolus or heart attack. The dehydration can also lead to kidney stones and gall bladder disease.

II. MENSTRUAL CYCLE, ESTROGEN, PROGESTINS

The menstrual cycle is made up of three phases and it is regulated by hormones released and regulated by the endocrine system. Different types of hormones used in a particular contraceptive determine the way the contraceptive prevents pregnancy. The first stage is Menstruation which is the shedding of the uterine lining. The next phase is the Follicular Phase and is controlled by Estrogens. Estrogens work by preventing the formation of follicles in the ovary. This occurs because the estrogen prevents the release of the follicle stimulating hormone (FSH) which is required for the formation of the follicles. Again, the most common estrogen used in contraceptives is ethinyl estradiol.

The third Phase is the Luteal Phase. This begins with the formation of the egg and ends in either pregnancy or degradation of the egg. This stage is regulated by progesterones. When synthetic progestins are used in combination with an estrogen in an oral
contraceptive like Yasmin and Yaz, the progestin inhibits the luteinizing hormone (LH) which is essential for ovulation.

Progestins are classified into four different generations. Drospirenone is the progestin used in Yasmin and Yaz. Some authorities are now calling Yasmin and Yaz Fourth Generation Progestins.¹

III. PROGESTINS²

Progestin Amounts: Comparing estrogen is fairly simple since all combination birth control pills use the same type of estrogen; this makes it possible to compare dosages simply by quantity. On the other hand, because pills use different types of progestin (each of which has a different strength), it is much harder to compare progestin levels across pills. The amount of progestin found in birth control pills is fairly small, and is usually denoted in milligrams (mg). What this means is that even if two brands have the same progestin dose, they may have different types of progestin, so the potency can vary widely.

Types of Progestin: There are many types of progestins, and each has a different profile in terms of progestational, estrogenic, and androgenic activity and/or effects. The result of these effects is dependent on the combination of the type and level of progestin and the level of estrogen.

¹Below picture at http://embryology.med.unsw.edu.au/wwwhuman/MCycle/images/Mcycle.GIF
²Section from Contraception.About.Com.
To better understand how a progestin may be classified, it is helpful to clarify what effects a progestin may have on the female body.

**Progestational Effects:** Progestational effects refer to how the progestin stimulates the progesterone receptors (thereby helping to prevent ovulation and to lessen menstrual bleeding). A similar term is progestational selectivity, which is the degree to which progestational effects are maximized and androgenic effects are minimized. Typically, the goal of a birth control pill is to achieve a high level of progestational selectivity.

**Androgenic Effects:** Androgenic effects refer to the likelihood that the progestin may cause unpleasant side effects. Progestins with higher androgenic activity may increase the chances of androgen-related side effects which include acne.

Also, progestins with less androgenic activity tend to have little to no effect on carbohydrate metabolism, which is how the body breakdowns and synthesizes simple sugars into smaller units that can then be used by the body for energy.

**Estrogenic Effects:** Estrogenic activity has to do with ethinyl estradiol, the type of synthetic estrogen found in birth control pills. Higher number of micrograms of ethinyl estradiol leads to more potent estrogenic effects. A higher amount of estrogenic activity helps to decrease androgen-related side effects. However, progestins tend to counter some of the estrogenic effects of ethinyl estradiol.

**Classification of Progestins:** Combination birth control pills include an estrogen and one progestin. There are numerous types of progestins. Most of these synthetic progestins are chemical derivatives of testosterone (known as 19-nortestosterone derivatives).

The available birth control pills that are classified under 19-nortestosterone can be further divided into two families: estrane and gonane.

- **The estrane family** (typically, first generation progestins) consist of norethindrone and other progestins that metabolize to norethindrone. These include norethindrone acetate and ethynodiol diacetate.

- **The gonane family:** This classification is further subdivided into two groups:

  Second generation progestins, which have varying degrees of androgenic and estrogenic activities. These include levonorgestrel and norgestrel.

  Newer gonanes, or third generation progestins; these are reported to have the least androgenic effects and include desogestrel and norgestimate.
**Drospirenone**, the last progestin, is also the newest (4th) generation. Drospirenone is a unique progestin as it differs from the others because it is derived from 17α-spirolactone, not from the 19-nortestosterone derivatives.

**IV. DROSPIRENONE**

Yasmin contains 3 mg of Drospirenone and 39 mcg of ethinyl estradiol per tablet. Yaz contains 3 mg of Drospirenone and 20 mcg of ethinyl estradiol. However, Drospirenone is different from the other first three generations of progestins because it works on different chemical receptors than other progestins. In addition, it contains a potassium-sparing diuretic. Since Drospirenone acts as a diuretic, it can cause dehydration which causes an increase in potassium levels (hyperkalemia) and a decrease in sodium levels (hyponatremia) in the body. This imbalance can lead to a whole host of problems including, but not limited to, strokes, deep vein thrombosis, pulmonary embolus and heart attack.

**V. MARKETING AND OVERPROMOTION**

In 2008, sales of Yaz in the United States were $616 million, while Yasmin posted sales of $382 million. The FDA has sent Bayer and Berlex (the company who originally manufactured Yasmin and Yaz before being acquired by Bayer) warning letters regarding their aggressive and controversial marketing efforts. Most recently, the FDA issued Bayer a warning letter for overstating Yaz’s ability to improve women’s moods and clear up acne in misleading commercials. In addition, the FDA required Bayer to run a multi-million dollar television ad campaign to correct the misleading claims, as well as disclose the risks of hyperkalemia and other health problems. The FDA also directed Bayer to address false claims that Yasmin and Yaz were approved to treat Premenstrual Syndrome (PMS) and all forms of acne when it was really just approved for Premenstrual Dysphoric Disorder (PMDD) and moderate to severe acne.

**V. CONCLUSION**

When compared to other oral contraceptives, Yasmin and Yaz unique chemical make-up create an array of new risks and problems. When coupled with Bayer’s aggressive marketing practices, numerous women have been injured and our at an increased risk for life-threatening injuries.