Is Bayer Warning Or Attacking With Its New YAZ / Yasmin Package Insert, Or Label, In The U.S.

Bayer Says YAZ / Yasmin Safety Profile Is Comparable To Older Birth Control Pills, But European Regulators See Possible Increased Risk Of Blood Clot Side Effects

(Posted by Tom Lamb at www.DrugInjuryWatch.com on April 22, 2010; see http://bit.ly/bOwNhX)

On April 9, 2010 Bayer HealthCare Pharmaceuticals announced that that it will update the labels for YAZ® (3 mg drospirenone / 0.02 mg ethinyl estradiol) and Yasmin® (3 mg drospirenone / 0.03 mg ethinyl estradiol) in the United States.

We have not seen the actual new YAZ / Yasmin package insert, or label, but the press release by which Bayer made this announcement, "BAYER UPDATES LABELS FOR YAZ and YASMIN -- Body of Evidence Affirms VTE Risk/Benefit Profile for YAZ and Yasmin Is Comparable to Other Combination Oral Contraceptives", makes us wonder whether Bayer is issuing it to warn doctors and patients or to attack medical researchers who have suggested that these unique "fourth generation" pills containing the progestin drospirenone (DRSP) may be unsafe to use.

From this April 2010 press release we get this "preview" of what the new YAZ / Yasmin label will state about this emerging drug-safety issue:

> ...the new labels now state:
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> • A prospective cohort study (EURAS), conducted in Europe, showed the risk of thromboembolism (particularly venous thromboembolism) and death in Yasmin users to be comparable to that of oral contraceptive preparations, including those containing levonorgestrel.
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> • Another prospective cohort study (Ingenix), conducted in the USA, also showed a comparable risk of thromboembolism in Yasmin users compared to users of other COCs, including those containing levonorgestrel. In this study, COC comparator groups were selected based on having similar characteristics to those being prescribed Yasmin.
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> As part of its evaluation of the risk/benefit of YAZ and Yasmin, the FDA also reviewed data from one case-control study (van Hylckama Vlieg et al.) and one retrospective study (Lidegaard et al.) which suggested that the risk of venous thromboembolism occurring in Yasmin users was between the risk associated with levonorgestrel-containing COCs and desogestrel/gestodene-containing COCs. Based on the FDA's review, the new labels now state that key conclusions from both studies are **unreliable**:
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> • With regard to the case-control study, the label indicates that, "…the number of Yasmin cases was very small (1.2% of all cases) making the risk estimates **unreliable**."
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> • Concerning the retrospective cohort study, the label indicates that, "The relative risk for Yasmin users in the retrospective cohort study was greater than that for users of other COCs when considering women who used the products for less than one year. However, these one-year estimates **may not be reliable** because the analysis may include women of varying risk levels. Among women who used the product for one to four years, the relative risk was similar for users of Yasmin to that for users of other COCs."
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> [Footnotes omitted; emphasis added]

So, essentially, it seems that Bayer is claiming that YAZ and Yasmin are as safe as "second generation" birth control pills which contain the progestin levonorgestrel and that the following two medical journal articles should be disregarded:

- Lidegaard O, Lokkegaard E, Svendsen AL, Agger C. "Hormonal contraception and risk of venous thromboembolism: national follow-up study." *BMJ*. 2009;339:b2890. (hereinafter, "the Lidegaard publication"): and,

- Van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. "The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study." *BMJ*. 2009;339:b2921. (hereinafter, "the Van Hylckama Vlieg publication").

Now let us take a look at what has been happening recently in Europe with regard to YAZ and Yasmin. In March 2010 Bayer said it would update the Yasmin label in Europe to add the results from four medical studies, namely those mentioned in the Bayer press release discussed above.

Again, we have not seen the actual new YAZ / Yasmin package insert, or label, that will be used in Europe. We do, however, have some indication that this European label change by Bayer may need to be different from their U.S. label change.

The April 2010 edition of *Drug Safety Update* published by the Medicines and Healthcare products Regulatory Agency (MHRA) includes an article entitled "Yasmin: Update on risk of venous thromboembolism". From that MHRA article, in relevant part:

> The incidence of VTE in association with the use of levonorgestrel, desogestrel and gestodene-containing pills has been studied extensively. Overall, these studies have shown that women who use desogestrel or gestodene-containing pills have a slightly higher risk of developing VTE than those who use levonorgestrel-containing pills. Because Yasmin was licensed relatively recently, fewer studies on its associated risk have been carried out.
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> In 2006, the results from two large prospective cohort studies (EURAS and Ingenix), suggested that the risk of VTE in Yasmin users is comparable with that for other contraceptives that contain a similar level of oestrogen, including those containing levonorgestrel. More recently, the results from a Danish cohort study and a Dutch case-control study have suggested that this risk may be slightly higher than previously estimated and somewhere between the risk associated with levonorgestrel-containing pills and with desogestrel or gestodene-containing pills (relative risks for the comparison of Yasmin with levonorgestrel-containing pills: 1·64; 95% CI 1·27–2·10 and 1·7; 0·7–3·9, respectively).
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> Because of some limitations in the methodology of these recent studies, further analyses are needed before any firm conclusions can be drawn....
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> [Footnotes omitted]

It remains to be seen whether Bayer will be allowed to use the terms "unreliable" and "may not be reliable" as regards the Lidegaard publication and the Van Hylckama Vlieg publication in Europe, as it apparently intends to do in the U.S. The April 2010 MHRA *Drug Safety Update* article above, however, suggest that the drug company will not be permitted to essentially tell doctors and patients that those two medical articles -- which are among the most recent additions to the medical literature about the safety of YAZ and Yasmin -- should be flat-out disregarded.

Returning to the April 2010 Bayer press release about the YAZ / Yasmin label change in the U.S., we point out this statement:

> “At Bayer, our unwavering commitment to our customers’ health and well-being is always our first priority and we will continue to provide information which will support health care providers and

> their patients in making informed decisions about appropriate treatment choices," said [Kemal Malik, MD, Chief Medical Officer at Bayer HealthCare].

When the actual new YAZ / Yasmin label is finally available for review, we will let you be the judge about the accuracy or sincerity of that particular statement made on behalf of Bayer.

Attorney Tom Lamb represents people in personal injury and wrongful death cases involving unsafe prescription drugs or medication errors. The above article was posted originally on his blog, **Drug Injury Watch** – with live links and readers' Comments.
http://www.DrugInjuryWatch.com