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Enforcement of Method of Use Patents in the United States

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Medical Use Claims in the U.S.

aka Method of Treatment Claims

A method of treating a Disease Y by administering Compound X.

§271 of the U.S. Patent Act

35 USC 271(a): "...makes, uses, offers to sell or sells any patented invention ..." **Direct infringement**

35 U.S.C. §271(b): "Whoever **actively induces** infringement of a patent shall be liable as an infringer"

35 U.S.C. §271(c): "Whoever offers to sell or sells within the United States ..... a component of a patented ... composition, or a material ...for use in practicing a patented process, ..., and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a **contributory infringer.**"

35 U.S.C. §271(e)(2): "It shall be an act of infringement to submit . . . an [ANDA] for a drug claimed in a patent or the use of which is claimed in a patent, . . "**constructive infringement or artificial act of infringement**

Second Medical Use Claims in the U.S.

aka Method of Treatment Claims

A method of treating a Disease Y by administering Compound X.

Who is the infringer?

Doctor? Patient?

Generic Company? Pharmacy? Insurance company?

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use YASMIN safely and effectively. See full prescribing information for YASMIN.

YASMIN (drospirenone/ethinyl estradiol) tablets, for oral use

Initial U.S. Approval: 2001

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS
See full prescribing information for complete boxed warning
- **Women over 35 years old who smoke should not use Yasmin. (4)**
- **Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. (4)**

----------RECENT MAJOR CHANGES----------
Warnings and Precautions, Thromboembolic Disorders (5.1) 2/2012

----------INDICATIONS AND USAGE----------
Yasmin is an estrogen/progestin COC indicated for use by women to prevent pregnancy. (1)

----------DOSAGE AND ADMINISTRATION----------
- Take one tablet daily by mouth at the same time every day. (2.1)
- Tablets must be taken in the order directed on the blister pack. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Yasmin consists of 28 film-coated, biconvex tablets in the following order (3):
- 21 yellow tablets, each containing 3 mg drospirenone (DRSP) and 0.03 mg ethinyl estradiol (EE),
- 7 inert white tablets

----------CONTRAINDICATIONS----------
- Renal impairment (4)
- Adrenal insufficiency (4)
- A high risk of arterial or venous thrombotic diseases (4)
- Undiagnosed abnormal uterine bleeding (4)
- Breast cancer or other estrogen- or progestin-sensitive cancer (4)
- Liver tumors or liver disease (4)
- Pregnancy (4)

----------WARNINGS AND PRECAUTIONS----------
- Vascular risks: Stop Yasmin if a thrombotic event occurs. Stop at least 4 weeks before and through 2 weeks after major surgery. Start no earlier than 4 weeks after delivery, in women who are not breastfeeding. (5.1)
- Hyperkalemia: DRSP has antimineralocorticoid activity. Do not use in patients predisposed to hyperkalemia. Check serum potassium concentration during the first treatment cycle in women on long-term treatment with medications that may increase serum potassium concentration. (5.2, 7.3)
- Liver disease: Discontinue Yasmin if jaundice occurs. (5.4)
- High blood pressure: Do not prescribe Yasmin for women with uncontrolled hypertension or hypertension with vascular disease. (5.5)
- Carbohydrate and lipid metabolic effects: Monitor prediabetic and diabetic women taking Yasmin. Consider an alternate contraceptive method for women with uncontrolled dyslipidemia. (5.7)
- Headache: Evaluate significant change in headaches and discontinue Yasmin if indicated. (5.8)
- Uterine bleeding: Evaluate irregular bleeding or amenorrhea. (5.9)

----------ADVERSE REACTIONS----------
The most frequent adverse reactions (≥ 2%) are premenstrual syndrome (13.2%), headache /migraine (10.7%), breast pain/tenderness/discomfort (8.3%), nausea/vomiting (4.5%), abdominal pain/tenderness/discomfort (2.3%), mood changes (2.3%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bayer HealthCare Pharmaceuticals Inc. at 1-888-842-2937 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------
Drugs or herbal products that induce certain enzymes (for example, CYP3A4) may decrease the effectiveness of COCs or increase breakthrough bleeding. Counsel patients to use a back-up or alternative method of contraception when enzyme inducers are used with COCs. (7.1)

----------USE IN SPECIFIC POPULATIONS----------
Nursing mothers: Not recommended; can decrease milk production. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 2/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

What's in the Label?

Yasmin® Package Insert

1 INDICATIONS AND USAGE

Yasmin is indicated for use by women to prevent pregnancy.

Infringement: Yasmin

Bayer's product ("Yasmin") was approved for contraceptive use *only*.

- Bayer's label -
  - *Clinical Pharmacology section of the label described all three effects.*

Lupin filed ANDA for contraceptive use of the drug.

For method-of-use patents, the 'artificial' infringement claim provided by section 271(e)(2)(A) lies only against a patented use that has been approved by the FDA."

Bayer Schering v. Lupin 676 F.3d 1316 (Fed. Cir. 2012)

Bayer's patent

Achieve three effects together

(1) contraceptive
(FDA approved)

(2) anti-androgenic
(Not FDA approved)

(3) anti-aldosterone effects.
(Not FDA approved)

Infringement: Crestor

Astra Zeneca v Apotex 669 F.3d. 1370 (Fed Cir 2012)

Astra Zeneca's Crestor label:	
Treatment for HeFH	Patent protected
Treatment for CRP	Patent protected
Treatment for HoFe	**Not** patent protected
Treatment for Hypertriglyceriderma	**Not** patent protected

Apotex Label

'Skinny Label"

Induced Infringement: Pulmicort

AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042 (Fed. Cir. 2011) Pulmicort or budesonide

AstraZeneca patents claim methods of administering budesonide "not more than once per day."

Apotex filed ANDA for budesonide for twice-daily use only.

*BUT FDA required inclusion of downward-titration warning:

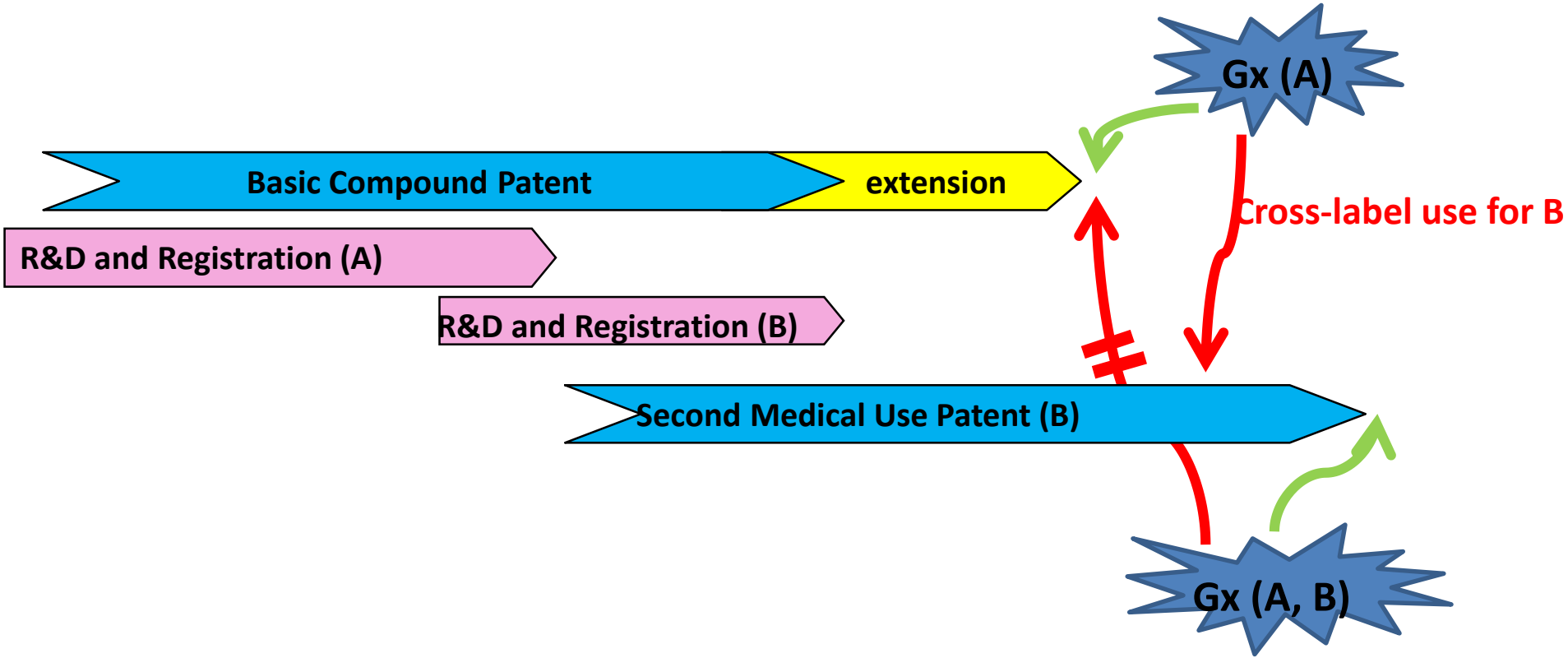
"Once the desired clinical effect is achieved, consideration should be given to tapering to the lowest effective dose."

The pertinent question is whether the proposed label instructs users to perform the patented method. If so, the proposed label may provide evidence of Apotex's affirmative intent to induce infringement.

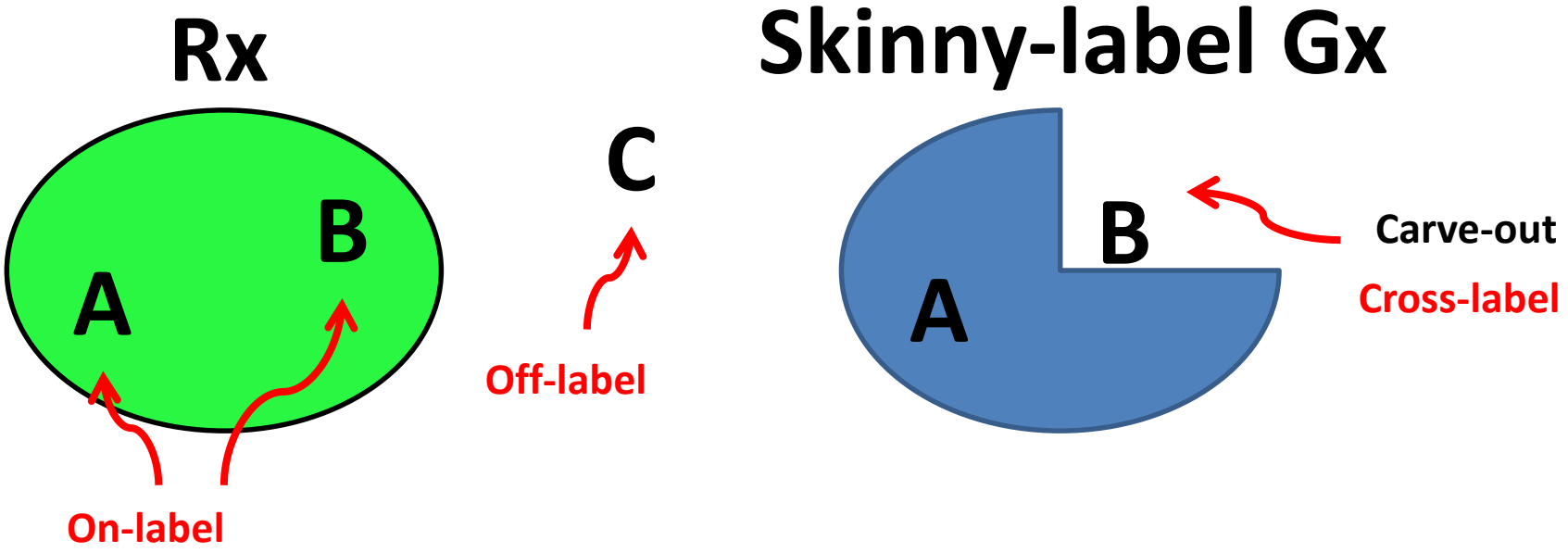
Pharmacies and Payors: Evidence of Infringement?

Can we apply what we've learned from case law against Generic Companies?

Carve-out and Cross-label Use

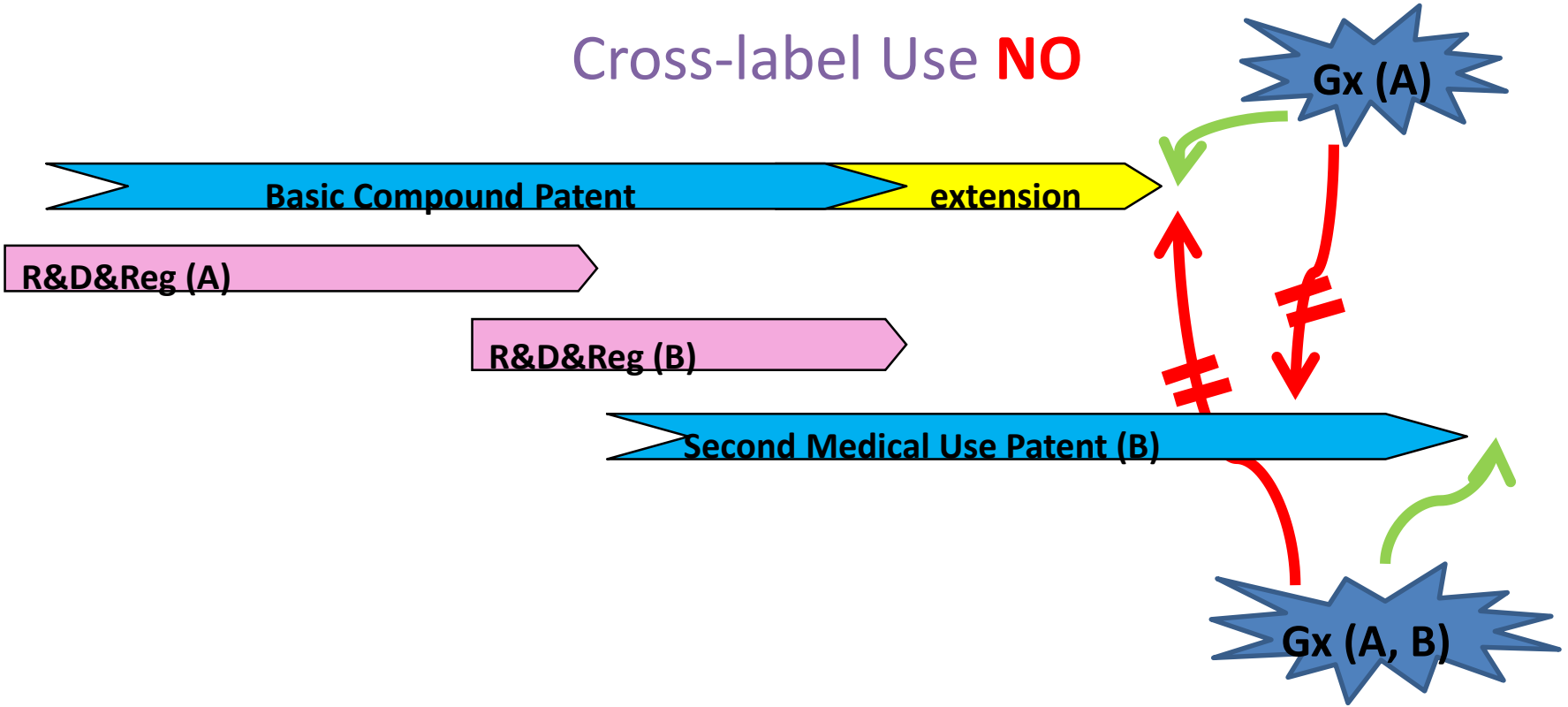


Off- vs. Cross-label Use



Carve-out YES

Cross-label Use NO



Money for old rope or a valuable investment: obtaining and enforcing patents relating to new uses of known products

Reward Fit for the Purpose?

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