

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COALITION FOR AFFORDABLE DRUGS VII LLC,
Petitioner,

v.

HORIZON PHARMA USA, INC.,
Patent Owner.

IPR2015-01718
Patent 8,945,621

DECLARATION OF LEON SHARGEL, PH.D., R.PH.

TABLE OF CONTENTS

I.	Introduction and Bases for Opinions.....	1
A.	Qualifications	1
B.	Materials Reviewed.....	4
C.	Legal Principles Used In Analysis	7
II.	Background	14
A.	State of the Art	14
B.	Overview of the '621 Patent.....	26
C.	Person of Ordinary Skill in the Art (POSA)	27
III.	Claim Construction	28
A.	“Low Dose Aspirin” and “LDA”	29
B.	“Unit Dose Form” and “Unit Dosage Form”	29
C.	All Remaining Terms	30
D.	The Invalidity Grounds	30
1.	Ground 1: Claims 1-16 Are Obvious Under 35 U.S.C. § 103(a)	30
2.	Ground 2: Claims 1-16 Are Obvious Under 35 U.S.C. § 103(a)	31
IV.	Ground 1: Plachetka in view of Graham and Goldstein Renders Obvious Claims 1-16.....	31
A.	A POSA Would Have Combined Plachetka, Graham, and Goldstein	31
B.	Claim 1:	34

1. A method of reducing the incidence of NSAID-associated gastric ulcers in patients taking low dose aspirin who are at risk of developing such ulcers,.....34
2. wherein the method comprises administering to said patient in need thereof a pharmaceutical composition in unit dose form comprising:35
3. (a) 20 mg of esomeprazole, or pharmaceutically acceptable salt thereof,35
4. in a form and route sufficient to raise the gastric pH of said patient to at least 3.5 upon administration of one or more of said unit dose forms and36
5. (b) 500 mg of naproxen, or pharmaceutically acceptable salt thereof;36
6. wherein said unit dose form provides for coordinated release of the esomeprazole and the naproxen,36
7. wherein at least a portion of said esomeprazole, or pharmaceutically acceptable salt thereof, is released independent of the pH of the surrounding medium,37
8. wherein the unit dosage form releases less than 10% of the naproxen or a pharmaceutically acceptable salt thereof after 2 hours when tested using the USP Paddle Method in 1000 ml of 0.1N HCl at 75 rpm at 37° C. +/- 0.5° C.,37
9. wherein said pharmaceutical composition in unit dose form reduces the incidence of NSAID-associated ulcers in said patient and38
10. wherein administration of the unit dose form is more effective at reducing the incidence of the NSAID-associated ulcers in patients taking LDA than in patients not taking LDA who are administered the unit dose form.39

C.	Claim 2: The method according to claim 1, wherein the risk is associated with chronic NSAID treatment.	41
D.	Claim 3: The method according to claim 1, wherein said patient is treated for a disease or disorder selected from pain and inflammation.	42
E.	Claim 4: The method according to claim 1, wherein said patient is treated for a disease or disorder selected from osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and a combination thereof.	42
F.	Claim 5: The method according to claim 1, wherein said unit dose form is at least about 95% free of sodium bicarbonate.	42
G.	Claim 6: The method according to claim 1, wherein said unit dose form begins to release said naproxen, or a pharmaceutically acceptable salt thereof, when the pH of the surrounding medium is at about 4.0 or greater.	43
H.	Claim 7: The method according to claim 1, wherein said unit dose form begins to release said naproxen, or a pharmaceutically acceptable salt thereof, when the pH of the surrounding medium is at about 4.5 or greater.	44
I.	Claim 8:	44
1.	A method of reducing the incidence of NSAID-associated gastric ulcers in patients taking low dose aspirin who are at risk of developing such ulcers,	45
2.	wherein the method comprises administering to the patient a pharmaceutical composition in unit dosage form suitable for oral administration comprising:	45
3.	(a) 20 mg of esomeprazole or a pharmaceutically acceptable salt thereof,	45
4.	that is immediately soluble when the dosage form is placed in an aqueous medium, independent of pH,	45

5.	in an amount effective to raise the gastric pH of the patient to at least 3.5 upon administration of one or more of the unit dosage forms, and.....	46
6.	(b) 500 mg of naproxen or pharmaceutically acceptable salt thereof,.....	46
7.	wherein the unit dosage form releases less than 10% of the naproxen or a pharmaceutically acceptable salt thereof after 2 hours when tested using the USP Paddle Method in 1000ml of 0.1N HCl at 75 rpm at 37° C. +/- 0.5° C.;.....	46
8.	wherein said pharmaceutical composition in unit dose form reduces the incidence of NSAID-related ulcers in said patient and.....	46
9.	wherein administration of the unit dose form is more effective at reducing the incidence of the NSAID-associated ulcers in patients taking LDA than in patients not taking LDA who are administered the unit dose form.	47
J.	Claim 9: The method of claim 8, wherein the risk is associated with chronic NSAID treatment.	47
K.	Claim 10: The method of claim 8, wherein the patient is treated for a disease or disorder selected from pain, inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and combinations thereof.	47
L.	Claim 11: The method of claim 8, wherein the pharmaceutical composition is formulated to be administered to a patient twice daily.	48
M.	Claim 12: The method according to claim 8, wherein the unit dosage form further comprises a pharmacologically inert water soluble coating or film.....	48
N.	Claim 13: The method of claim 12, wherein the inert coating or film comprises a water soluble sugar.	49

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