Clinical Study Synopsis

This Clinical Study Synopsis is provided for patients and healthcare professionals to increase the transparency of Bayer's clinical research. This document is not intended to replace the advice of a healthcare professional and should not be considered as a recommendation. Patients should always seek medical advice before making any decisions on their treatment. Healthcare Professionals should always refer to the specific labelling information approved for the patient's country or region. Data in this document or on the related website should not be considered as prescribing advice.
The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer Healthcare Pharmaceuticals Inc.	
Study Number:	11229	NCT00473460
Study Phase:	IIIb	
Official Study Title:	A double-blind, randomized, placebo controlled study to investigate chronic intermittent "pulse" therapy of moxifloxacin as a prevention of acute exacerbation in out-patients with chronic bronchitis.	
Therapeutic Area:	Anti-Infectives	
Test Product		
Name of Test Product:	Moxifloxacin (Avelox, BAY12-8039)	
Name of Active Ingredient:	Moxifloxacin hydrochloride	
Dose and Mode of Administration:	Moxifloxacin 400 mg was administered per oral (PO) as a capsule daily for 5 consecutive days every 8 weeks.	
Reference Therapy/Placebo		
Reference Therapy:	Matching placebo capsule	
Dose and Mode of Administration:	The placebo was administered PO daily for 5 consecutive days every 8 weeks.	
Duration of Treatment:	The planned duration of the study was 72 weeks, including a 48-week treatment period and a 24-week (untreated) follow-up period. Pulse therapy with moxifloxacin or placebo (a 5-day course every 8 weeks) was given during the 48-week treatment period.	
Studied period:	Date of first subjects' first visit:	13 OCT 2004
	Date of last subjects' last visit:	10 JAN 2007
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 16 JUL 2004) was enacted for the following purposes: • To provide more information on the resistance surveillance • To align the study clinic visit schedule to the visit 2 date • To provide information on spirometry and request for morning clinic visit to ensure good sputum collection • To provide possible reasons for study or center premature termination • To request that narratives be written for withdrawals, episodes of diarrhea, and hospitalizations Amendment no. 2 (dated 24 JUN 2005) was enacted for the following purposes: • Correct inconsistencies within the protocol for collection of serum inflammatory markers, collection and processing of sputum samples	

	• Addition of forced expiratory volume in 6 seconds (FEV_6) within the secondary objectives • Change the primary population for analysis from the Intent-to-Treat to the Per-Protocol population.
Study Center(s):	This study was conducted at 76 centers from 15 countries: Germany (10 centers), France (7 centers), Ireland (1 center), United Kingdom (6 centers), Andorra (1 center), Greece (3 centers), Italy (4 centers), Spain (6 centers), Argentina (4 centers), Brazil (4 centers), Chile (3 centers), Mexico (5 centers), United States (10 centers), Israel (4 centers), and South Africa (8 centers).
Methodology:	The study was conducted at referral centers in which subjects with chronic bronchitis were treated. Following a screening period of up to 7 days, subjects who met the inclusion and exclusion criteria were assigned randomly to receive 6 courses of "pulse" therapy (every 8 weeks) with either moxifloxacin 400 mg PO once daily (od) for 5 days (arm A) or matching placebo PO od for 5 days (arm B) during the treatment period (48 weeks). Subjects were then followed for a 24-week, observation-only, follow-up period. During the course of the study, information and measurements related to Acute Exacerbation of Chronic Bronchitis (AECB) were recorded. Safety was assessed by clinical observation, documentation of all adverse events, and serial monitoring of laboratory tests (renal, hepatic, and hematologic function).
Indication/ Main Inclusion Criteria:	Indication: Prevention of acute exacerbation of chronic bronchitis Main inclusion criteria: • Male or female out-patients, aged ≥ 45 years • Subjects suffering from chronic bronchitis (World Health Organization [WHO] criteria—chronic bronchitis, defined as a cough productive of sputum on most days, for 3 consecutive months, for at least 2 consecutive years) • Forced expiratory volume in 1 second (FEV1) ≤ 70% and [FEV1/Forced vital capacity (FVC)] ≤ 70% predicted based on age, height, and sex • No documented episode of AECB (requiring treatment) within 6 weeks of randomization and not experiencing an exacerbation at the time of screening • Sputum production, on most days, even when exacerbation-free • Presented with at least 2 documented (i.e., requiring antibiotics and / or systemic steroids administration) acute exacerbation episodes during the last 12 months • If receiving chronic therapy with inhaled long-acting bronchodilators and / or inhaled or systemic steroids, the treatment must have remained stable for the preceding 6 weeks prior to screening • Smoking history of at least 20 pack-years • Ability to complete questionnaires and diary as required • Medical condition and social status compatible with study protocol procedures • Subjects willing and able to give fully informed written consent
Study Objectives:	<u>Primary:</u> To assess the frequency of acute exacerbations of chronic bronchitis between the moxifloxacin-treated group and the placebo group during the 48-week treatment period.

	An exacerbation was defined as: • Subject-initiated contact with a health care professional • Increased respiratory symptoms—Anthonisen types 1 and 2 exacerbations • Treatment with systemic antibiotic and /or oral steroids • The definitions of AECB included: 1A) any confirmed AECB or unconfirmed pneumonia or any other lower respiratory tract infection (LRTI) with the exception of confirmed pneumonia, all with intervention (hospitalization within 7 days of the start date of exacerbation, OR [start of systemic respiratory steroid and/or start of systemic antibiotic, within 7 days of the start date of exacerbation]), minimally 2 weeks between start of 2 consecutive exacerbations; 1B) any confirmed AECB or unconfirmed pneumonia or any other LRTI with the exception of confirmed pneumonia, all with intervention (hospitalization within 7 days of the start date of exacerbation, OR [start of systemic respiratory steroid and/or start of systemic antibiotic, within 7 days of the start date of exacerbation]), minimally 4 weeks between start of 2 consecutive exacerbations; 2A) any confirmed AECB, or unconfirmed/confirmed pneumonia, or any other LRTI with intervention (as above), minimally 2 weeks between start of 2 consecutive exacerbations; 2B) Any confirmed AECB, or unconfirmed/confirmed pneumonia, or any other LRTI with intervention (as above), minimally 4 weeks between start of 2 consecutive exacerbations; 3) any confirmed AECB (exclude confirmed/unconfirmed pneumonia and any other LRTIs), minimally 2 weeks between start of 2 consecutive exacerbations; 4) any confirmed AECB (exclude confirmed/unconfirmed pneumonia and any other LRTIs). <u>Secondary:</u> • To compare the impact of the treatment on health-related quality of life between the 2 treatment groups measured by change from baseline in St George's Respiratory Questionnaire (SGRQ) scores at week 48 • To compare any deterioration in lung function between the treatment groups measured by change from baseline in percent predicted forced expiratory volume in 1 second (%PFEV1) at week 48 • To compare frequency of hospitalization through to week 48 between the 2 treatment groups • To compare the mortality rates through to week 48 between the 2 treatment groups • To compare time to first exacerbation between the 2 treatment groups • To assess the frequency of acute exacerbations of chronic bronchitis between the treatment groups after 24 weeks of treatment • To assess the frequency of acute exacerbations of chronic bronchitis between the treatment groups after 72 weeks (after the end of the follow-up period) • To compare the time to next exacerbation from last pulsed dose (at end of 48-week treatment period) between the 2 treatment groups • To compare the length of exacerbations between the 2 treatment groups • To compare percentage of exacerbation free time between the 2 treatment groups

	• To compare changes in other lung function tests (forced vital capacity , %PFEV1/FVC ratio, and forced expiratory volume in 6 seconds [FEV_6]) between the 2 treatment groups • To compare the number and duration of hospitalizations between the 2 treatment groups • To compare the rate of development of resistant pathogens between the 2 treatment groups • To compare the rate of bacterial colonization by potential respiratory pathogens between the 2 treatment groups • To compare the changes in bacterial load/colonization between the 2 treatment groups • To compare the sputum and serum inflammatory parameters between the 2 treatment groups • To compare the changes in symptoms burden assessed by the Acute Exacerbation of Chronic Bronchitis Symptom Scale (AECB-SS) diaries between the 2 treatment groups • To compare the incidence rates of health care resource utilization (HCRU) between the 2 treatment groups • To compare the incidence rates of respiratory steroid and long-acting bronchodilator usage between the 2 treatment groups
Evaluation Criteria:	Efficacy (Primary): Number of exacerbations after 48 weeks of intermittent pulse treatment. Efficacy (Secondary): • Changes from baseline in the SGRQ scores at week 48 • Changes from baseline in %PFEV1 at week 48 • Frequency of hospitalization through week 48 treatment period • Mortality rates through week 48 treatment period Safety: Evaluation of safety was based on adverse events (AEs), including serious adverse events (SAEs) and deaths, determinations of vital signs and clinical laboratory tests.
Statistical Methods:	Demographic variables and baseline characteristics were summarized for each treatment group using N (number of subjects contributing information), arithmetic mean, standard deviation (SD), median, and minimum and maximum values for the Intent To Treat (ITT) and Per Protocol end of treatment (PP [EOT]) populations. The treatment group baseline comparability was to be checked for subjects in the PP (EOT) population and the ITT / safety population. The 2 treatment groups were to be compared with respect to continuous demographic variables (e.g. age, using 2-way analysis of variance [ANOVA]) [main effect model: treatment and geographic region as fixed factors]) and with respect to categorical variables by a Cochran-Mantel-Haenszel (CMH) test adjusted for geographic region. Efficacy (Primary): The primary efficacy variable was the number of exacerbations recorded after 48 weeks of intermittent pulse therapy. The primary population for the efficacy analysis was the PP(EOT) population. All statistical tests were 2-sided and performed at the 0.05 significance level.

	The analysis described for the primary efficacy analysis was also performed using the intent to treat (ITT) / Safety, modified ITT (mITT), and PP populations. These analyses were considered to be supportive. The following assumptions and analyses were supportive of the primary efficacy assessment: • The pre-specified clinically meaningful difference between groups was 30% fewer exacerbations in the moxifloxacin group than in the placebo group • The numbers of exacerbations were grouped into the following four categories: 0, 1, 2 and ≥ 3 • Within these categories, a logistic regression model was used to test the null hypothesis that the number of exacerbations in the moxifloxacin group was not different from that in the placebo group • If the p-value from the test of the null hypothesis was less than 0.05, then it was concluded that the moxifloxacin group was statistically significantly different from the placebo group with respect to the number of exacerbations <u>Efficacy (Secondary):</u> Secondary efficacy analyses were to be performed on secondary efficacy variables using both the PP(EOT) and other populations. All other analyses of efficacy variables were considered to be exploratory. <u>Safety:</u> All analyses of safety endpoints were descriptive only; no formal testing was performed. All safety tabulations were produced for the ITT population (which was equivalent to the valid for safety population).
Number of Subjects:	A total of 1132 randomized subjects were planned. A total of 1157 subjects (573 in the moxifloxacin group and 584 in the placebo group) were actually enrolled and randomized, including 1149 subjects in the intent-to-treat (ITT) / Safety population (569 moxifloxacin subjects and 580 placebo subjects); 738 subjects in the Per Protocol (end of therapy) (PP[EOT]) population (351 moxifloxacin subjects and 387 placebo subjects); 653 subjects in the per protocol (PP) population (310 moxifloxacin subjects and 343 placebo subjects), and 845 subjects in the modified intent-to-treat (mITT) population (406 moxifloxacin subjects and 439 placebo subjects. Subjects who were valid for the PP population and whose only reason for invalidity from the PP population was change in long-acting bronchodilators and/or respiratory steroids up to the end of treatment were included in the mITT population. Consequently, any long-acting bronchodilator and/or respiratory steroid violations during study treatment (up to end of week 48) were accepted for this population.

Study Results
Results Summary — Subject Disposition and Baseline
Of the 1404 subjects enrolled in the study, 247 were not randomized to treatment. The primary reasons for not randomizing subjects were protocol violations in 205 subjects and consent withdrawn in 29 subjects. A significantly higher proportion of moxifloxacin treated subjects (17.8%) did not complete the study as planned in contrast to placebo treated subjects (13.4%). The most common reasons for premature discontinuation from the study during the 48-week treatment period were consent withdrawn (5.8% moxifloxacin versus

4.8% placebo) and AEs (5.1% moxifloxacin versus 2.9% placebo). Four subjects in each of the 2 treatment groups took no study medication. These subjects were excluded from the population valid for safety (ITT population).

There were no statistically significant differences in any of the key demographic and baseline characteristics between treatment groups (subjects valid for safety [ITT/Safety population]). The majority of subjects in both treatment groups were men (74.2% moxifloxacin versus 73.8% placebo). The majority of subjects in the study were Caucasian and Hispanic. The mean age was 66.4 years (range 41 to 88), and mean BMI was 26.5 kg/m^2 (range 12.7 to 47.4).

Results Summary — Efficacy

Primary efficacy analysis:

- The primary objective of the study was met. A statistically significant reduction in the number of AECBs was observed at the end of the pulse therapy in moxifloxacin-treated subjects compared with placebo recipients in the primary efficacy population (i.e., PP population meeting validity criteria up to end of treatment) using the 2 most clinically relevant definitions for AECB, definition 1A (p=0.046) and definition 3 (p=0.028). The estimate of the treatment odds ratio was 0.749 (confidence interval [0.565, 0.994]) using the 1A definition and 0.732 (confidence interval [0.555, 0.966]) using definition 3. Post-hoc subgroup analysis identified that subjects with mucopurulent/purulent sputum especially benefited from therapy with moxifloxacin (p=0.006 and p=0.004, respectively, for treatment differences in number of AECBs at the end of therapy using definition 1A and definition 3). The estimates of the treatment odds ratios were 0.545 (confidence interval [0.355, 0.839]) and 0.533 (confidence interval [0.349, 0.815]) for definition 1A and 3, in this subgroup, respectively. This represents a 45.5% and 46.7% reduction in the odds of a chronic obstructive pulmonary disease (COPD)) exacerbation, active compared to placebo, in the PP(EOT) population by end of treatment, adjusted for baseline %PFEV1 and region for definition 1A and 3.
- The trend for reduced number of exacerbations in the moxifloxacin group at end of therapy was consistent across the different AECB definitions and also in the overall PP, mITT, and ITT populations, although the difference between treatments did not reach statistical significance in all cases.

Secondary efficacy analysis:

- A significant difference was observed between the 2 treatment groups when comparing time to first exacerbation in the PP population.
- No statistical differences were seen in the hospitalization/mortality rates or in %PFEV1 variance at the various assessment visits between the 2 groups.
- Due to the variability in the data and the small number of subjects tested, meaningful interpretation of the inflammatory marker data was not possible.A slight increase in MIC90 values against *P. aeruginosa* isolated from sputum was observed during treatment in both groups, with slightly higher values in moxifloxacin subjects.
- There was no evidence in repeated sputum samples that moxifloxacin pulse therapy was associated with the emergence of in vitro resistance for other organisms, as assessed by the moxifloxacin MICs comparison.
- Results of sputum and rectal swab cultures need further evaluation, especially concerning *E. coli* and *P. aeruginosa* since baseline in vitro resistance was observed for a number of isolates.

Results Summary — Safety

Both moxifloxacin and placebo were well tolerated.

- Commonly reported treatment-emergent adverse events (TEAEs): The proportion of subjects who experienced at least 1 treatment-emergent adverse event was similar in the moxifloxacin (45.3%; 258/569) and placebo (45.7%; 265/580) groups. The most commonly reported adverse events in both treatment groups were COPD, bronchitis acute, diarrhea, and dyspnea. The incidence of each adverse event was generally

similar (≤ 1% difference) between treatment groups, with the exception of diarrhea, dyspnea, vomiting, and nausea, which were higher in the moxifloxacin group, and COPD and acute bronchitis, which were higher in the placebo group..

- Study drug-related AEs: The proportion of subjects who had at least 1 treatment-emergent adverse event that was considered by the investigator to be study drug-related was higher in the moxifloxacin group (9.3%; 53/569 moxifloxacin versus 3.8%; 22/580 placebo). The 3 most commonly reported study drug-related adverse events were diarrhea, nausea, and vomiting. The greatest difference in the incidence of specific drug-related adverse events occurred for diarrhea (2.1% moxifloxacin versus 0.3% placebo) and nausea (1.1% moxifloxacin versus 0% placebo). The incidence of other drug-related adverse events was similar (≤ 1% difference) between treatment groups. Most of the events were rated by the investigator as mild or moderate in intensity.Deaths: A total of 45 subjects died during the study (48-week treatment and post-treatment follow-up), 19 in the moxifloxacin group and 26 in the placebo group. None of the deaths occurred during a pulse in the moxifloxacin group. The serious adverse events reported as the cause of death were assessed not related to study drug therapy.
- Study drug-related SAEs: The incidence of nonfatal treatment-emergent serious adverse events was 16.5% (94/569) in the moxifloxacin-treated group and 16.7% (97/580) in the placebo-treated group. Nine (1.6%) moxifloxacin subjects and 3 (0.5%) placebo subjects experienced serious adverse events that were assessed by the investigator as drug-related.
- Discontinuations due to AEs: The study drug was discontinued prematurely because of adverse events in 21 (3.7%) moxifloxacin-treated and 11 (1.9%) placebo-treated subjects. The most common adverse events that led to discontinuation of moxifloxacin included nausea, vomiting, diarrhea, hypersensitivity, dyspnea, and urticaria.
- Other adverse events of special interest: These included immune system disorders, adverse events suggestive of QT prolongation, and *Clostridium difficile* colitis. Five moxifloxacin-treated subjects experienced a treatment-emergent adverse event in the immune system organ class, including hypersensitivity in 3 subjects and drug hypersensitivity and anaphylactic shock in 1 subject each. All the immune system events were assessed by the investigator as drug-related, with the exception of 1 event of drug hypersensitivity. There is no evidence that repeated courses of moxifloxacin therapy are associated with an increased risk of developing an allergic reaction. There were no reports of QT prolongation and no occurrences of pseudomembranous colitis in subjects treated with moxifloxacin.Laboratory test abnormalities: The incidences of laboratory test abnormalities and clinically significant laboratory test abnormalities were not suggestive of any adverse trends of one treatment over the other.
- Vital signs: In general, for both treatment groups, there was essentially no change from pre-therapy in vital signs measurements.

Conclusion(s)			
In this study, intermittent pulse therapy with moxifloxacin produced a 25% reduction in the odds of an exacerbation compared with placebo therapy. This reduction in exacerbations was comparable to long-acting bronchodilators and inhaled steroids. The reduction in exacerbations was observed for the different AECB definitions and study populations, although it did not reach statistical difference for all analyses. Post-hoc subgroup analysis identified that subjects with mucopurulent/purulent sputum benefited with this therapy. Resistance emergence was rare among subjects treated with moxifloxacin, but further genotyping explorations are needed, especially for *E. coli.* Intermittent pulse therapy with moxifloxacin was safe and well tolerated.			
Publication(s):	Sethi S, Jones PW, Theron MS, Miravitlles M, Rubinstein E, Wedzicha JA, Wilson R; PULSE Study group. Pulsed moxifloxacin for the prevention of exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Respir Res. 2010 Jan 28;11:10.		
Date Created or Date Last Updated:	15 MAR 2012	Date of Clinical Study Report:	02 FEB 2009

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer Vital GmbH
Postal Address	D-51368 Leverkusen, Germany
Sponsor in Germany (if applicable)	
Legal Entity Name	Bayer HealthCare AG
Postal Address	D-51368 Leverkusen, Germany

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	Hospital Ntra. Sra. de Meritxell	Avda. Fitter i Rossell, 1-13		Escaldes - Engordany	ANDORRA
2	Hospital de Clínicas "José de San Martín"	Av. Córdoba 2351	C1120AAF	Buenos Aires	ARGENTINA
3	Hospital Militar Central "CIR. MY. C. Argerich"	Pneumology Department Hospital Militar Central "CIR. MY. C. Argerich" Av. Luis M. Campos 726	1426	Buenos Aires	ARGENTINA
4	Hosp. Municipal de Agudos "Mi Pueblo"	Progreso 240	1888	Florencio Varela	ARGENTINA
5	Policlínico Bancario	Pulmonar Lab. Av. Gaona 2197	1416	Buenos Aires (Capital Federal)	ARGENTINA

6	Hospital das Clínicas da Faculdade de Medicina da USP	Laboratório de Função Pulmonar Av. Dr. Enéas de Carvalho Aguiar, 155, 2 andar, bl 11	05403-900	São Paulo	BRAZIL
7	Pontificia Universidade Católica - Centro Clínico	Centro de Pesquisa Clínica Av. Ipiranga, 6690 4o andar	90610-000	Porto Alegre	BRAZIL
8	UNIFESP/EPM	Lar Escola São Francisco - (Reabilitação) Rua dos Açores, 310 - 1 andar Pneumologia Jardim Luzitânia	04032-060	São Paulo	BRAZIL
9	Universidade Federal de Juiz de Fora-Hospital Universitario	Pneumology Service Rua Catulo Breviglieri, s/n Bairro Santa Catarina	36036-110	Juiz de Fora	BRAZIL
10	Clinica Avansalud	Av. Salvador 130		Santiago	CHILE
11	Hospital Carlos van Buren	Hontaneda 2560	236-3058	Valparaiso	CHILE
12	Hospital Nacional del Tórax	José Miguel Infante 717 Providencia		Santiago	CHILE
13	Cabinet Médical - 22 Gounod - Nice	Cabinet Médical 22 rue Gounod	06000	NICE	FRANCE
14	Cabinet Médical - Bourg - Rosiers d'Egletons	Cabinet Médical Bourg	19300	ROSIERS D'EGLETONS	FRANCE

15	Cabinet médical - Cronstadt - Nice	Cabinet Médical 3 rue Cronstadt	06000	NICE	FRANCE
16	Cabinet Médical - Madame - Orthez	Cabinet Médical 3, rue Madame	64300	ORTHEZ	FRANCE
17	Cabinet Médical - Martinon - Mont de Marsan	Cabinet Médical 26 rue Martinon	40000	MONT-DE-MARSAN	FRANCE
18	Cabinet Médical - Novembre - Arras	Cabinet Médical 50bis rue du 11 Novembre	62000	ARRAS	FRANCE
19	Cabinet Médical - Tauler - Strasbourg	Cabinet Médicla 35 boulevard Tauler	67000	STRASBOURG	FRANCE
20	DRK Krankenhaus Neuwied	Innere Medizin II Marktstr. 74	56564	Neuwied	GERMANY
21	Pneumologisches Forschungsinstitut GmbH	am Krankenhaus Großhansdorf Niederlassung Hamburg Jungestr. 10	20535	Hamburg	GERMANY
22	Praxis Drs. Leonhardt/Molitor	Dieterichsstr. 35 B	30159	Hannover	GERMANY
23	Praxis Drs. Westerhausen/Pettenkofer/Klüppelberg	Markgrafenstr. 20	10969	Berlin	GERMANY
24	Praxis fü Lungen- und Bronchialheilkunde,	Allergologie und Umweltschutz Hohenzollerndamm 2	10717	Berlin	GERMANY
25	Praxis Hr. Dr. A. Colberg	Kurhausstraße 14	23795	Bad Segeberg	GERMANY
26	Praxis Hr. Dr. B. Kroemer	Alte Weberei 2	87600	Kaufbeuren	GERMANY
27	Praxis Hr. Dr. R. Dichmann	Theodor-Heuss-Str. 3	58452	Witten	GERMANY
28	Praxis Hr. Dr. R. Gebhardt	Karl-Marx-Str. 80	12043	Berlin	GERMANY

29	Praxis Hr. Dr. W. Schröder-Babo	Im Ziegelhaus 6-8	63571	Gelnhausen	GERMANY
30	Sotiria General State Hospital of Chest Diseases	2nd Pneumonological Clinic 152 Messogion Avenue	11527	Athens	GREECE
31	Sotiria General State Hospital of Chest Diseases	6th Pneumonological Clinic 152 Messogion Avenue	156 69	Athens	GREECE
32	University General Hospital of Patras	Department of Internal Medicine Infectious Disease	265 00	Rio Patras	GREECE
33	St James' Hospital	CResT Clinical Directorate James' Street	8	Dublin	IRELAND
34	Barzilai Medical Center	3, Hahistadrut Street	78278	Ashkelon	ISRAEL
35	Haemek Medical Center	.	18101	Afula	ISRAEL
36	Maccabbi Sick Fund	37 Katzenelson St.	59512	Bat Yam	ISRAEL
37	Tel Aviv Sourasky Medical Center	6 Weizman St.	64239	Tel - Aviv	ISRAEL
38	A.O. Sacco Polo Universitario	Pneumologia Via G.B. Grassi, 74	20157	Milano	ITALY
39	A.O.U. di Ferrara	Fisiopatologia Respiratoria Arcispedale Sant'Anna Corso Giovecca, 203	44100	Ferrara	ITALY
40	IRCCS Policlinico San Matteo	Malattie Apparato Respiratorio Viale Golgi, 2	27100	Pavia	ITALY

41	Ospedale San Giuseppe FbF Polo Universitario	Pneumologia Via S. Vittore, 12	20123	Milano	ITALY
42	Antiguo Hospital Civil de Guadalajara "Fray Antonio Alcalde"	Infectious Diseases Department Hospital No. 278 Torre de Especialidades 7°Piso Sector Hidalgo	44640	Guadalajara	MEXICO
43	Centro Médico de las Américas	Centro Médico de Las Américas Consultorio 111 Calle 54 N°. 365 por Av. Pérez Ponce	97001	Mérida	MEXICO
44	Clínica Mérida	Av. Itzaes N°. 242 3°piso, consultorio 303 Col. García Gineres	97001	Mérida	MEXICO
45	Hospital Central Universitario	Serv. Medicina Interna/Neumología Rosales 3302 Col. Obrera	31350	Chihuahua	MEXICO
46	Hospital General Regional N°. 12 "Lic. Benito Juárez" IMSS	Servico de Neumología e Inhaloterapia Av. Itzaes por Av. Colón S/N Col. García Gineres	97070	Mérida	MEXICO
47	Clinical Trial Center	14 Malherbe Street	7646	Paarl	SOUTH AFRICA
48	Genclin Corporation	56 Reid Street Westdene	9301	Bloemfontein	SOUTH AFRICA

49	Kraaifontein Medicross Clinic	Arcadia Centre Cnr. Brighton & Kipling Street Kraaifontein	7569	Cape Town	SOUTH AFRICA
50	Morningside Clinic Rocherster Place	Morningside Clinic Rochester Place 173 Rivonia Road Cnr Hill Morningside, Sandton	2057	Johannesburg	SOUTH AFRICA
51	Tiervlei Trial Centre	Karl-Bremer Hospital Ward A1 Mike Pienaar Blvd Belville	7531	Cape Town	SOUTH AFRICA
52	Unitas Hospital	Unitas Hospital Clifton Ave Lyttleton Centurion	0157	Pretoria	SOUTH AFRICA
53	Universitas Hospital	Universitats Hospital Paul Kruger Street	9300	Bloemfontein	SOUTH AFRICA
54	WilMed Medical Research Projects	Beuke Oord 28 Wilgers	0040	Pretoria	SOUTH AFRICA
55	Hospital Clínic i Provincial de Barcelona	C/ Villarroel, 170	08036	Barcelona	SPAIN
56	Hospital Clínico Universitario San Carlos	C/. Dr. Martín Lagos, s/n	28040	Madrid	SPAIN
57	Hospital de la Serranía	Ctra. El Burgo, km 1	29400	Ronda	SPAIN
58	Hospital del Rio Hortega	c/ Cárdenas Torquemada, s/n	47010	Valladolid	SPAIN
59	Hospital Universitari Germans Trias i Pujol	Ctra. del Canyet, s/n	08916	Badalona	SPAIN

60	Hospital Universitari i Politècnic La Fe	Avda. Bulevar Sur, s/n	46026	Valencia	SPAIN
61	Clinical Research Centre	Ground Floor, Start One Building 2 Newark St	E1 2AT	London	UNITED KINGDOM
62	Queen Elizabeth Hospital	QE Medical Centre Bayer Lung Resource Centre First Floor, Nuffield House Edgbaston	B15 2TH	Birmingham	UNITED KINGDOM
63	Royal Free Hospital	Department of Respiratory Medicine Pond Street Hampstead	NW3 2QG	London	UNITED KINGDOM
64	Southmead Hospital	Westbury on Trym	BS10 5NB	Bristol	UNITED KINGDOM
65	St George's Hospital	Jenner Wing Cranmer Terrace	SW17 0RE	London	UNITED KINGDOM
66	St James' Hospital	Beckett Street	LS9 7TF	Leeds	UNITED KINGDOM
67	Bay Pines VA Healthcare System	Building 100/5D-106 10000 Bay Pines Boulevard	33708	Bay Pines	UNITED STATES
68	Hunter Holmes McGuire Veterans Affairs Medical Center	Research Institute Code: 151 1201 Broad Rock Boulevard	23249	Richmond	UNITED STATES
69	Kansas City VA Medical Center	Department of Research (151) 4801 East Linwood Boulevard	64128	Kansas City	UNITED STATES

70	Southern Arizona Veterans Affairs Health Care System	Dep't. of Pulmonary Medicine (111A) 3601 South Sixth Avenue	85723	Tucson	UNITED STATES
71	South Texas Veterans Health Care System	Bldg. I/11E 7400 Merton Minter Boulevard	78284-5799	San Antonio	UNITED STATES
72	VA Greater Los Angeles Healthcare System	Section 111-P Bldg. 200/ Room 3534 16111 Plummer Street	91343	Sepulveda	UNITED STATES
73	VA Long Beach Healthcare System	Pulmonary & Critical Care (II-IIIP) Bldg.126/Room 350 5901 East 7th Street	90822-5201	Long Beach	UNITED STATES
74	VA North Texas Healthcare System	Att'n: Cassie Lusk (8C) Dallas VA Medical Center 4500 South Lancaster Road	75216-7167	Dallas	UNITED STATES
75	VA Western NY Healthcare System	3495 Bailey Avenue Room 829-B	14215	Buffalo	UNITED STATES
76	Veterans Affairs Medical Center	Room 3C-220 2002 Holcombe Blvd.	77030	Houston	UNITED STATES

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Avelox [*Oral formulation*]
Brand/Trade Name(s) ex-US	Avelon® Avelox® Avalox® Actira® Octegra® Izilox® Megaxin® Proflox® Promira®
Generic Name	Moxifloxacin
Main Product Company Code	BAY12-8039
Other Company Code(s)	n/a
Chemical Description	1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.
Other Product Aliases	n/a

Date of last Update/Change: 19 Mar 2014