FDA Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Disclaimers:

Submission of a safety report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event. The information in these reports has not been scientifically or otherwise verified as to a cause and effect relationship and cannot be used to estimate the incidence of these events.

Data provided in the Quarterly Data Extract (QDE) or a FAERS FOIA report are a snapshot of FAERS at a given time. There are several reasons that a case captured in this snapshot can be marked as inactive and not show up in subsequent reports. Manufacturers are allowed to electronically delete reports they submitted if they have a valid reason for deletion. FDA may merge cases that are found to describe a single event, marking one of the duplicate reports as inactive. The data marked as inactive are not lost but may not be available under the original case number.

The FOIA case report information may include both Electronic Submissions (Esubs) and Report Images (Non-Esubs). Case ID(s) will be displayed under separate cover pages for the different submission types.

Cover page Case ID(s) with an asterisk ('*') indicate an invalid status and are not captured in the body of the report.

Esub Case ID(s) Submitted:

17707946	**17746335**	**17750116**	**17778290**	**17800342**	**17801454**

Run by: **STEPPERH**

Date - Time: **12-MAR-2021 14:54 PM**

Total number of cases (Esub): **6**

Total number of inactive cases: **0**

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17707946

Case Information:

Case Type: EXPEDITED (15-DAY) **eSub:** Y **HP:** **Country:** FRA **Event Date:** **Outcomes:** DE,HO,OT, **Application Type:** NDA

FDA Rcvd Date: 08-May-2020 **Mfr Rcvd Date:** 24-Apr-2020 **Mfr Control #:** FR-ADVANZ PHARMA-202004003809 **Application #:** 009768

Patient Information:

Age: **Sex:** **Weight:**

Suspect Products:

#	Product Name	Compounded Drug ?	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date
1	Hydroxychloroquine			Unknown	UNK	COVID-19		
2	AZITHROMYCIN			Unknown	UNK	COVID-19		
3	Hydroxychloroquine					Product use in unapproved indication		

#	Product Name	Interval 1st Dose to Event	DeC	ReC	Lot#	Exp Date	NDC #	MFR/Labeler	OTC
1	Hydroxychloroquine		NA	NA	Unknown			CONCORDIA	
2	AZITHROMYCIN		NA	NA	Unknown				
3	Hydroxychloroquine		NA	NA				CONCORDIA	

Event Information:

Preferred Term (MedDRA Â Version: 23.1)	ReC
Cardiac disorder	NA
Discomfort	NA
Electrocardiogram QT prolonged	NA
Loss of consciousness	NA
Off label use	NA
Ventricular arrhythmia	NA

Case ID: 17707946

Event/Problem Narrative:

Case number 202004003809 is a business partner report (Reference ID:2020SA099420) sent by other healthcare professional on 10-Apr-2020.

Case Description: Upon internal review, the case 2020SA099424, 2020SA098061, 2020SA099422 were identified to be a duplicate of the current case 2020SA099420. The case 2020SA102973 received on 10-Apr-2020 Would be deleted.

The case was cross-referenced with the cases 2020SA099424, 2020SA098061, 2020SA099422 (Duplicate cases).
This case is linked to cases 2020SA099419, 2020SA099411, 2020SA099421 and 2020SA099423 (same reporter).

Initial information regarding this unsolicited valid serious case received from France was received from the healthcare professional on 10-Apr-2020.

This case involves 54 patients with unspecified demographics who experienced cardiac disorder, ventricular rhythm disorders- with discomfort and unconsciousness, prolongation of QT space and off label use indication for covid-19, while he/she was treated with hydroxychloroquine sulfate (Plaquenil) and azithromycin.

The patient's past medical history, medical treatment(s) and family history were not provided.

On an unknown date, the patients started taking hydroxychloroquine sulfate and azithromycin (formulation, strength, lot/batch number, expiry date and other therapy details: unknown) for COVID 19 (corona virus infection, drug use for unapproved indication) (off-label use).

Reportedly since 27-Mar-2020 (onset and latency: unknown), 54 patients of cases of cardiac disorders including 4 fatal, have been identified in France in patients taking this treatment, in some cases associated with azithromycin. Among fifty-four cases of cardiac disorders included seven sudden or unexplained deaths (three of these people were saved by electric shock). The cases reported to the network of thirty-one CRPV in the territory concern hospitalized patients, aged 34 to 88 years. In 36 cases, it was an anomaly measured on the ECG (prolongation of QT space). This reflects a disorder of the cardiac conduction (that is to say the transmission of electrical impulse), which increases the risk of syncope and sudden death. Among these fifty-four cases, ten correspond to ventricular rhythm disorders, which were recorded on the electrocardiogram (ECG) or resulted in symptoms: discomfort, brief unconsciousness. The pharmacologist and cardiologist emphasized at the outset that this was probably only the tip of the iceberg, 95% of the adverse effects of the drugs were not being declared on average to the pharmacovigilance system.

Relevant laboratory test results included:
Electrocardiogram - On an unknown date: ventricular rhythm disorder
Electrocardiogram QT interval - On an unknown date: prolongation of QT space

Action taken: not applicable for off-label use and unknown for rest of the events.

Case ID: 17707946

Corrective treatment: Not reported

Outcome: fatal for cardiac disorder; not applicable for off-label use and unknown for rest of the events

Seriousness criteria: Hospitalization on an unknown date and fatal for Cardiac disorder, medically significant for prolongation of QT space, ventricular rhythm disorders with discomfort, brief unconsciousness.

A query mail was sent to the Business partner regarding the onset date of the event and the commencement of the suspect drug Plaquenil so that an estimated date could be calculated.

Version 0.0 comment: The case is assessed as serious and unlisted as per the company RSI. The company considered the events of cardiac disorder to be unassessable to Hydroxychloroquine (Plaquenil), as per WHO causality classification system, since information is insufficient. Limited information about patient's age and gender, concomitant products, therapy dates, type and course of cardiac disorder, latency, lab data and relevant medical history with confounding other suspect azithromycin precludes comprehensive assessment of the case. The company considered the event of off label use to be possibly related to Hydroxychloroquine (Plaquenil), as per convention.

Follow up information was received on 24-Apr-2020 and version 1.0 was created.

Additional information included: Medical reassessment was made to update the following in this case: The case 2020SA099424, 2020SA098061, 2020SA099422 were found to be a duplicate to this case 2020SA099420. The information of the duplicate case 2020SA099424, 2020SA098061, 2020SA099422 received on 10-Apr-2020 had been incorporated in this active case as follows: Duplicate case ids added. New events added. Lab test added. Outcome updated for the event cardiac disorder as fatal and updated narrative amended accordingly.

Relevant Medical History:

Disease/Surgical Procedure	Start Date	End Date	Continuing?
COVID-19			

Medical History Product(s)	Start Date	End Date	Indications	Events

Case ID: 17707946

Relevant Laboratory Data:

Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail

Concomitant Products:

#	Product Name	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date	Interval 1st Dose to Event

Reporter Source:

Study Report?: No

Sender Organization: ADVANZ PHARMA

503B Compounding Outsourcing Facility?:

Literature Text:

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17746335

Case Information:

Case Type: EXPEDITED (15-DAY) **eSub:** Y **HP:** **Country:** USA **Event Date:** 18-Mar-2020 **Outcomes:** DE, **Application Type:** ANDA

FDA Rcvd Date: 05-May-2020 **Mfr Rcvd Date:** 27-Apr-2020 **Mfr Control #:** US-SLATE RUN PHARMACEUTICALS-20US000055 **Application #:** 203412

Patient Information:

Age: **Sex:** **Weight:**

Suspect Products:

#	Product Name	Compounded Drug ?	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date
1	Azithromycin USP			Intravenous (not otherwise specified)	UNK	Corona virus infection	18-Mar-2020	
2	HYDROXYCHLOROQUINE			Unknown	UNK, single		21-Mar-2020	
3	HYDROXYCHLOROQUINE			Unknown	UNK	Corona virus infection		

#	Product Name	Interval 1st Dose to Event	DeC	ReC	Lot#	Exp Date	NDC #	MFR/Labeler	OTC
1	Azithromycin USP	4 Day	Unk	Unk				HAINAN POLY PHARMACEUTICAL	
2	HYDROXYCHLOROQUINE		NA	Unk					
3	HYDROXYCHLOROQUINE		NA	Unk					

Event Information:

Preferred Term (MedDRA Version: 23.1)	ReC
Electrocardiogram QT prolonged	NA
Electrocardiogram T wave abnormal	NA
Off label use	NA

Case ID: 17746335

Event/Problem Narrative:

This serious literature report (L2005547794; 10.1016/j.hrcr.2020.03.016) was received on 27-Apr-2020, via literature search: An algorithm for managing QT prolongation in coronavirus disease 2019 (COVID-19) patients treated with either chloroquine or hydroxychloroquine in conjunction with azithromycin: Possible benefits of intravenous lidocaine; Mitra RL, Greenstein SA, Epstein LM; Heart Rhythm Case Reports; 2020, pages 1-5.

This literature report refers to a 66-year-old female patient of unspecified ethnicity who experienced the fatal events of Electrocardiogram QT prolonged and Electrocardiogram T wave abnormal after receiving Azithromycin (azithromycin; unknown brand and manufacturer) and Hydroxychloroquine (hydroxychloroquine) for COVID-19 (non-serious event of Off label use).

The patient's medical history included rheumatoid arthritis, pulmonary fibrosis and asthma, all as current conditions. On (b) (6) the consumer was hospitalized with fever and cough after a 2-week course of sinus and upper respiratory tract symptoms initially treated with doxycycline, followed by levofloxacin as an outpatient. Owing to lack of improvement. She presented to the emergency room and was found to be hypoxic. Computed tomography (CT) showed widespread ground-glass opacities as well as honeycombing of the right lung. COVID-19 was suspected and testing was eventually positive. Within 48 hours, she developed profound respiratory failure and required intubation. She also required adrenergic support with norepinephrine.

Concomitant medications included methotrexate and unspecified oral and inhaled steroids for an unknown indication.

While hospitalized, on (b) (6) the patient received Azithromycin (azithromycin; unknown brand and manufacturer) injectable Dry Vial, intravenously for COVID-19. Dosage regimen was not provided. On (b) (6) Hydroxychloroquine (hydroxychloroquine; unknown brand and manufacturer) was started for COVID-19, unknown formulation, dosage regimen and route of administration. On (b) (6) after a single administration of hydroxychloroquine, the patient presented a QTc of 620 ms with a notched broad T wave. No ventricular ectopy was present. Serum potassium and magnesium were 4.4 mM and 2.9 mg/dL, respectively. By the time hydroxychloroquine was initiated, she had already been intubated for 72 hours and she was in severe respiratory failure. After an electrophysiology consultation, 100 mg of intravenous lidocaine were administered followed by a repeat 12-lead electrocardiogram, which revealed a shortening of the QTc to 550 ms. Therefore, Hydroxychloroquine treatment was restarted in conjunction with lidocaine infusion. The patient was able to complete the course of hydroxychloroquine without an arrhythmic event. Despite receiving a full course of hydroxychloroquine, she remained ventilator dependent. On (b) (6) she died owing to progressive metabolic acidosis and multiorgan system failure. Azithromycin and Hydroxychloroquine treatments status at the time of the death was unknown.

The action taken with Azithromycin (unknown brand and manufacturer) was Unknown and for Hydroxychloroquine it was Drug withdrawn with positive dechallenge and rechallenge unknown.

For reference purposes only, this case has been assigned the following tracking number: L2005547794.

Case comment:

Case ID: 17746335

Based on review of available data, the sponsor can neither establish nor exclude the possibility of a cause-and-effect relationship between administration of Azithromycin and the occurrence of the serious events of Electrogram T wave abnormal (notched broad T wave) and Electrogram QT prolonged (QTc of 620 ms). In addition, Azithromycin administration was considered a non-serious event of Off-label use (Azithromycin administered for COVID-19). Even though, prolongation of QT interval is considered an identified risk of Azithromycin per current labeling, the causality is confounded by the subject's concurrent COVID-19 infection and medical history of pulmonary fibrosis and asthma. All of which may have contributed to the subject's progressive metabolic acidosis and multi-organ system failure leading to the fatal outcome.

Relevant Medical History:

Disease/Surgical Procedure	Start Date	End Date	Continuing?
Computerised tomogram	(b) (6)		UNKNOWN
Corona virus infection	(b) (6)		YES
Endotracheal intubation	(b) (6)		UNKNOWN
Hypoxia	(b) (6)		YES
Lung opacity	(b) (6)		YES
Respiratory disorder	(b) (6)		YES
Respiratory failure	(b) (6)		YES
Sinus disorder	(b) (6)		YES
Cough	(b) (6)		YES
Hospitalisation	(b) (6)		UNKNOWN
Pyrexia	(b) (6)		YES
Asthma			YES
Pulmonary fibrosis			YES

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Rheumatoid arthritis			YES	
Medical History Product(s)	**Start Date**	**End Date**	**Indications**	**Events**
DOXYCYCLINE	Mar-2020		Respiratory disorder	Drug ineffective
LEVOFLOXACIN	Mar-2020		Respiratory disorder	Drug ineffective
NOREPINEPHRINE	Mar-2020		Respiratory failure	No adverse event

Relevant Laboratory Data:

Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail
Electrocardiogram QT interval	550	millisecond			N
Electrocardiogram QT interval	620	millisecond			N
Blood potassium	4.4	millimole			N
Blood magnesium	2.9	milligram per decilitre			N
Electrocardiogram					Y

Concomitant Products:

#	Product Name	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date	Interval 1st Dose to Event
1	METHOTREXATE		Unknown		Product used for unknown indication			
2	STEROIDS		Oral	UNK				
3	STEROIDS			UNK	Product used for unknown indication			

Reporter Source:

Study Report?: No

Sender Organization: SLATE PHARMACEUTICALS

503B Compounding Outsourcing Facility?:

Literature Text: Mitra RL, Greenstein SA, Epstein LM.. An algorithm for managing QT prolongation in coronavirus disease 2019 (COVID-19) patients treated with either chloroquine or hydroxychloroquine in conjunction with azithromycin: Possible benefits of intravenous lidocaine. Heart Rhythm Case Reports. 2020;1-5

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17750116

Case Information:

Case Type: EXPEDITED (15-DAY) **eSub:** Y **HP:** **Country:** ESP **Event Date:** 01-Apr-2020 **Outcomes:** DE,HO, **Application Type:** ANDA

FDA Rcvd Date: 06-May-2020 **Mfr Rcvd Date:** 27-Apr-2020 **Mfr Control #:** ES-TEVA-2020-ES-1230679 **Application #:** 040081

Patient Information:

Age: 70 YR **Sex:** Male **Weight:**

Suspect Products:

#	Product Name	Compounded Drug ?	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date
1	HIDROXICLOROQUINA (2143A)		400 MG/QD	Oral	400 Milligram Daily;	Coronavirus infection	26-Mar-2020	30-Mar-2020
2	AZITROMICINA (7019A)					Pneumonia		
3	AZITROMICINA (7019A)		500 MG/QD	Intravenous (not otherwise specified)	500 Milligram Daily;	Coronavirus infection	26-Mar-2020	30-Mar-2020
4	HIDROXICLOROQUINA (2143A)					Pneumonia		
5	TOCILIZUMAB (8289A)					Severe acute respiratory syndrome		
6	TOCILIZUMAB (8289A)		600 MG/	Intravenous (not otherwise specified)	600 MG	Coronavirus infection	27-Mar-2020	27-Mar-2020

#	Product Name	Interval 1st Dose to Event	DeC	ReC	Lot#	Exp Date	NDC #	MFR/Labeler	OTC
1	HIDROXICLOROQUINA (2143A)	12 Day	NA	NA	Unknown			TEVA	
2	AZITROMICINA (7019A)	12 Day	NA	NA	Unknown				
3	AZITROMICINA (7019A)	12 Day	NA	NA	Unknown				
4	HIDROXICLOROQUINA (2143A)	12 Day	NA	NA	Unknown			TEVA	
5	TOCILIZUMAB (8289A)	11 Day	NA	NA	Unknown				
6	TOCILIZUMAB (8289A)	11 Day	NA	NA	Unknown				

Case ID: 17750116

Event Information:

Preferred Term (MedDRA Version: 23.1)	ReC
Atrial flutter	NA
Bundle branch block right	NA
Hypertension	NA
Hypofibrinogenaemia	NA
Pneumonia escherichia	NA
Ventricular tachycardia	NA

Event/Problem Narrative:

27-Apr-2020, Spontaneous, Health authority Serious report. (Report duplicates - AGEMED: ES-AEMPS-624232)
A Physician reported the case of a 70-Years-old Male patient who received AZITROMICINA (7019A) (AZITHROMYCIN, Product cannot be excluded as a Teva product), HIDROXICLOROQUINA (2143A) (HYDROXYCHLOROQUINE, Product cannot be excluded as a Teva product), TOCILIZUMAB (8289A) (TOCILIZUMAB, not Teva's product).
The patient took HIDROXICLOROQUINA (2143A) for NEUMONIA COVID19, PNEUMONIA (HYDROXYCHLOROQUINE, Oral, from (b) (6) (b) (6) until (b) (6) 400Milligram per day) batch: Unknown, AZITROMICINA (7019A) for NEUMONIA COVID19, PNEUMONIA (AZITHROMYCIN, Intravenous (not otherwise specified), from (b) (6) unti (b) (6) 500Milligram per day, 500 MG DIA) batch: Unknown, TOCILIZUMAB (8289A) for CORONAVIRUS INFECTION, SRAS COVID19 (TOCILIZUMAB, Intravenous (not otherwise specified), from (b) (6) unti (b) (6) 600 MG) batch: Unknown.
While on the suspect medication, the patient experienced ATRIAL FLUTTER(Serious , since (b) (6)); COMPLETE RIGHT BUNDLE BRANCH BLOCK(Serious , since (b) (6)); ARTERIAL HYPERTENSION(Serious , since (b) (6)); RECURRENT VENTRICULAR TACHYCARDIA(Serious , since (b) (6) until (b) (6)); PNEUMONIA DUE TO ESCHERICHIA COLI (E. COLI)(Serious , since (b) (6) (b) (6)); HYPOFIBRINOGENEMIA(Serious , since (b) (6) , until (b) (6)) .
At the time of the report the outcome of the AEs were: ATRIAL FLUTTER:Fatal, COMPLETE RIGHT BUNDLE BRANCH BLOCK:Fatal, HYPOFIBRINOGENEMIA:Fatal, RECURRENT VENTRICULAR TACHYCARDIA:Fatal, PNEUMONIA DUE TO ESCHERICHIA COLI (E. COLI):Fatal, ARTERIAL HYPERTENSION:Fatal.
Action taken with suspect drugs: HIDROXICLOROQUINA (2143A) - Drug discontinued; AZITROMICINA (7019A) - Drug discontinued; TOCILIZUMAB (8289A) - Drug discontinued.

The patient's medical history was not reported.
The patient died from ATRIAL FLUTTER, COMPLETE RIGHT BUNDLE BRANCH BLOCK, HYPOFIBRINOGENEMIA, RECURRENT VENTRICULAR TACHYCARDIA, PNEUMONIA DUE TO ESCHERICHIA COLI (E. COLI), ARTERIAL HYPERTENSION. It is unknown whether an autopsy was performed.
The patient's concomitant medication were unspecified.
The patient's past medication were unspecified.

Case ID: 17750116

Lab tests were not reported.
This case was considered serious based on the following criteria: (Death, Hospitalization Required)
Because this is a spontaneous case, regulatory distribution will be handled as though it is a related case.

Relevant Medical History:

Disease/Surgical Procedure	Start Date	End Date	Continuing?	
Medical History Product(s)	**Start Date**	**End Date**	**Indications**	**Events**

Relevant Laboratory Data:

Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail

Concomitant Products:

#	Product Name	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date	Interval 1st Dose to Event

Reporter Source:

Study Report?: No **Sender Organization:** TEVA **503B Compounding Outsourcing Facility?:**

Case ID: 17750116

Literature Text:

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17778290

Case Information:

Case Type: EXPEDITED (15-DAY) **eSub:** Y **HP:** **Country:** ESP **Event Date:** 26-Mar-2020 **Outcomes:** DE,HO, **Application Type:** NDA

FDA Rcvd Date: 13-May-2020 **Mfr Rcvd Date:** 08-May-2020 **Mfr Control #:** ES-PFIZER INC-2020185611 **Application #:** 050733

Patient Information:

Age: 70 YR **Sex:** Male **Weight:**

Suspect Products:

#	Product Name	Compounded Drug ?	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date
1	AZITHROMYCIN		500 MG/	Intravenous (not otherwise specified)	500 mg, daily	COVID-19 pneumonia	26-Mar-2020	30-Mar-2020
2	HYDROXYCHLOROQUINE		400 MG/QD	Oral	400 mg, 1x/day	COVID-19 pneumonia	26-Mar-2020	30-Mar-2020
3	TOCILIZUMAB					SARS		
4	TOCILIZUMAB					COVID-19		
5	TOCILIZUMAB		600 MG/	Intravenous (not otherwise specified)	600 mg, single	Coronavirus infection	27-Mar-2020	27-Mar-2020

#	Product Name	Interval 1st Dose to Event	DeC	ReC	Lot#	Exp Date	NDC #	MFR/Labeler	OTC
1	AZITHROMYCIN	6 Day	NA	NA				PFIZER	
2	HYDROXYCHLOROQUINE	6 Day	NA	NA					
3	TOCILIZUMAB	5 Day	NA	NA					
4	TOCILIZUMAB	5 Day	NA	NA					
5	TOCILIZUMAB	5 Day	NA	NA					

Event Information:

Preferred Term (MedDRA © Version: 23.1)	ReC
Atrial flutter	NA

Bundle branch block right	NA
Hypertension	NA
Hypofibrinogenaemia	NA
Off label use	NA
Pneumonia escherichia	NA
Product use in unapproved indication	NA
Ventricular tachycardia	NA

Event/Problem Narrative:

This is a spontaneous report from a contactable physician downloaded from the European Medicines Agency (EMA) EudraVigilance-WEB (ES-AEMPS-624232).

A 70 year-old male patient started to receive azithromycin (MANUFACTURER UNKNOWN), intravenous from (b) (6) tc (b) (6) at 500 mg daily for pneumonia COVID19, hydroxychloroquine (MANUFACTURER UNKNOWN), orally from (b) (6) to (b) (6) at 400 mg once a day for pneumonia COVID19 and tocilizumab (MANUFACTURER UNKNOWN), intravenous on (b) (6) at 600 mg single for coronavirus infection and severe acute respiratory syndrome (SARS) COVID19. The patient's medical history and concomitant medications were not reported. The patient experienced hypofibrinogenemia on (b) (6) pneumonia due to escherichia coli (E. coli) on (b) (6) arterial hypertension on (b) (6) atrial flutter and complete right bundle branch block on (b) (6) and episodes of ventricular tachycardia with cardiopulmonary resuscitation on (b) (6) which were all reported with the seriousness criteria of being fatal and hospitalization. On (b) (6) the patient received azithromycin for pneumonia COVID19. The action taken in response to the events for azithromycin and hydroxychloroquine was post-therapy and for tocilizumab was not applicable. The outcome of hypofibrinogenemia, pneumonia due to escherichia coli (E. coli), arterial hypertension, atrial flutter, complete right bundle branch block and episodes of ventricular tachycardia with cardiopulmonary resuscitation was fatal. The outcome of patient received azithromycin for pneumonia COVID19 was unknown. The patient died on an unspecified date. It was not reported if an autopsy was performed.

Pfizer is a marketing authorization holder of azithromycin in the country of incidence or the country where the product was purchased (if different). This may be a duplicate report if another marketing authorization holder of azithromycin has submitted the same report to the regulatory authorities.

No follow-up attempts are possible. No further information is expected.

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17778290

Relevant Medical History:

Disease/Surgical Procedure	Start Date	End Date	Continuing?	
Medical History Product(s)	Start Date	End Date	Indications	Events

Relevant Laboratory Data:

Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail

Concomitant Products:

#	Product Name	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date	Interval 1st Dose to Event

Reporter Source:

Study Report?: No

Sender Organization: PFIZER

503B Compounding Outsourcing Facility?:

Literature Text:

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17800342

Case Information:

Case Type: EXPEDITED (15-DAY) **eSub:** Y **HP:** **Country:** USA **Event Date:** **Outcomes:** DE,HO,OT, **Application Type:** NDA

FDA Rcvd Date: 19-May-2020 **Mfr Rcvd Date:** 11-May-2020 **Mfr Control #:** US-ADVANZ PHARMA-202005005269 **Application #:** 009768

Patient Information:

Age: **Sex:** **Weight:**

Suspect Products:

#	Product Name	Compounded Drug ?	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date
1	Hydroxychloroquine				UNK	COVID-19		
2	AZITHROMYCIN				UNK	COVID-19		

#	Product Name	Interval 1st Dose to Event	DeC	ReC	Lot#	Exp Date	NDC #	MFR/Labeler	OTC
1	Hydroxychloroquine		NA	NA				CONCORDIA	
2	AZITHROMYCIN		NA	NA					

Event Information:

Preferred Term (MedDRA Â© Version: 23.1)	ReC
Death	NA
Product use in unapproved indication	NA

Case ID: 17800342

Event/Problem Narrative:

Case number 202005005269 is a literature report (Reference ID: 32351040) send by other healthcare professional on 11/May/2020.

This is one of the linked cases and the case 202005005269 is index case.

This case refers to an adult male Caucasian patient who died on an unknown date, following treatment with Hydroxychloroquine and azithromycin for COVID-19 (off label use).

The patient's medical history non-tobacco user, renal transplant, renal replacement therapy, endotracheal intubation, exposure to communicable disease and historical medications were not provided.

The patient's co-morbid conditions were hypertension and diabetes mellitus.

The patient's concomitant medications were tacrolimus as Immunosuppressant drug therapy and Mycophenolate Mofetil, prednisone and ceftriaxone.

Case report:

There was minimal information on COVID-19 in immunocompromised individuals. they have studied 10 patients treated at 12 adult care hospitals. Ten kidney transplant recipients tested positive for SARS-CoV-2 by PCR, and 9 were admitted. The most common symptom was fever, followed by cough, myalgia, chills, and fatigue. The most common CXR and CT abnormality was multifocal patchy opacities. All hospitalized patients received hydroxychloroquine (HCQ) and azithromycin.

Materials and Methods:

They performed an ongoing study at 12 acute care hospitals in (institution name). All COVID- 19 positive patients with a functioning kidney allograft who presented to the emergency department and were either discharged or hospitalized between 01/Mar/2020, and 27/Mar/2020, were included. Data were collected from the enterprise electronic health record (address) reporting database. COVID-19 positivity was defined as a positive result on real-time polymerase chain reaction (PCR) assay of nasal and/or pharyngeal swab specimens. Kidney transplant status was defined as an active ICD-10 code of T86.1, T86.10, T86.11, T86.12, T86.13, T86.19, or Z94.0. All charts were manually reviewed for demographics, history of recent exposure, immunosuppression changes, clinical signs and symptoms, and laboratory findings. Mycophenolic acid (MPA) doses were converted to mycophenolate mofetil (MMF) (360 milligrams of MPA are equivalent to 500 milligrams of MMF) for dose analysis. Acute kidney injury was graded according to Kidney Disease Improving Global Outcomes (KDIGO) criteria. The study was approved by the institutional review board of (institution name).

Result:

Case ID: 17800342

Ten kidney transplant recipients were found to be COVID-19 positive by PCR. Nine of the ten patients included were hospitalized. Of the nine, five were admitted to the intensive care unit (ICU). Three patients, who required intubation died.

Demographics:
The median age of COVID-19 patients was 57 (interquartile range [IQR] 47-67). The majority of patients were male (60%), Caucasian (40%) and Black or African American (30%) All patients had a history of hypertension, with the majority also having diabetes. None were current smokers, although two had a history of tobacco use. Five patients had undergone living donor transplants, four had received deceased donor organs, and one had an unknown donor type. Median time from transplant to COVID-19 testing was 2,822 days (IQR 1,272-4592). The shortest time from transplant to testing was 124 days with the longest time being 6,290 days.

Presentation and Clinical Course The ten patients with COVID-19 had variable presentations and courses. The most common documented symptom was fever followed by cough, myalgia, chills and fatigue. Two patients had diarrhea and one had nasal congestion. At the time of presentation, seven patients had a temperature greater than 38.3 degrees Celsius. All patients had a chest x-ray (CXR) obtained at the time of admission and 40% had computed tomography (CT) scans. CXR and CT scan findings varied, with multifocal patchy opacities consistent with COVID-19 pneumonia most common seen. Three patients had no abnormal findings on CXR or chest CT. All patients had rapid viral assays performed, no patients had co-existing viral infections at the time of presentation. One patient had influenza diagnosed 13 days prior to admission and was treated at the time with five days of oseltamivir. Three patients (Patients 4, 5 and 10) had positive urine cultures for Enterococcus, Klebsiella pneumonia and E.coli, respectively. None had urinary symptoms at the time of presentation. As was previously noted, one patient (Patient 1) was discharged home from the emergency room without treatment or change in immunosuppression; a follow-up one week later demonstrated resolution of symptoms. Five patients (Patients 5, 6, 8, 9, and 10) required an ICU stay while the others were admitted to a COVID-19 medical floor. Of the ICU patients, three died, and two eventually recovered and were discharged. Patient 5 was initially on a medical floor before decompensating and required intubation and vasopressor support. The patient became anuric, was started on continuous renal replacement therapy, and died two days later after being made DNR. Patient 9 never recovered mental status after mechanical ventilation. She was eventually extubated then died in hospice. Patient 10 developed respiratory decompensation and died of a cardiac arrest. All of the remaining patients were eventually discharged. Median length of stay was 11 days (IQR 4-17 days). One patient resumed MMF at home and was readmitted 2 days later due to fever and shortness of breath. CT upon readmission revealed multifocal pneumonia presumed related to COVID-19. MMF was stopped, fevers resolved and he was discharged on room air after 7 days. Median follow-up for the entire cohort was 25 days (IQR 11-26 days, 2 patients were lost to follow up after discharge). Leukopenia was seen in 20% of patients during hospitalization. Eight of the nine hospitalized patient had at least one ferritin level and c reactive protein checked. Median ferritin was 788 ng/ml (IQR 563-1162) and CRP 13.35 mg/dl (IQR 4.82-23.72). Allograft function was stable in 50% of patients. Five patients had acute kidney injury (AKI): three stage 3, one stage 2, and one stage 1. No kidney biopsies were performed during the hospitalization.

Immunosuppression: All hospitalized patients had their antimetabolite agent stopped. Tacrolimus doses were titrated to a target trough of 3-5ng/ml. Tacrolimus was stopped for Patients 5 and 6 who were intubated in the ICU and sirolimus was stopped for Patient 9. All hospitalized patients received hydroxychloroquine (HCQ) and azithromycin (the latter no longer routinely administered as part of COVID treatment). All patients had an electrocardiogram (EKG) performed before initiation of therapy while only 4 had subsequent EKG's performed. No patient had

Case ID: 17800342

a QTc of 500 or greater. Six patients received at least one dose of an additional antibiotic including ceftriaxone, piperacillin/tazobactam, levofloxacin, cefepime, and vancomycin at the time of presentation. Patient 1 was discharged home without any antiviral or antimicrobial agents. Patients 5, 6, and 10 in the ICU were also placed on thiamine. Patients 6 and 7 were given methylprednisolone and Patient 10 was given high dose prednisone for acute respiratory distress syndrome (ARDS).

Presentation and Hospital Course:

The patient's WBC initial: 4.1; WBC nadir: 4.1; lymphocyte count: 0.32; O2: mechanical ventilation; Ferritin: 2871 ng/mL; C-reactive protein: 30.65 mg/dL; Initial creatinine (ICr): 4.85mg/dL; Peak creatinine (PCr): 6.09 mg/dL; Time from Transplant to infection (days): 7447

At the time of this report, the outcome of the event off label use was unknown and rest of the event was fatal.

The action taken with Hydroxychloroquine was not applicable.

De-challenge and re-challenge result was not applicable for the event with respect to Hydroxychloroquine.

This case is considered to be serious due to seriousness criteria death, hospitalization and medically significant.

The reporter provided the causality as possible for event.

Follow-up information received on 12/May/2020 in the form of Full text article. version 1 was created.

Additional information: Reporters details updated. Reporter details updated. Laboratory details updated. Medical history and concomitant drugs were added. Narrative updated.

Relevant Medical History:

Disease/Surgical Procedure	Start Date	End Date	Continuing?
COVID-19			YES
Diabetes mellitus			YES
Endotracheal intubation			
Exposure to communicable disease			

Case ID: 17800342

Hypertension	YES
Immunosuppressant drug therapy	
Non-tobacco user	
Renal replacement therapy	
Renal transplant	

Medical History Product(s)	Start Date	End Date	Indications	Events

Relevant Laboratory Data:

Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail
C-reactive protein	30.65	mg/dL			N
Serum ferritin	2871	ng/mL			N
Blood creatinine	6.09	mg/dL			N
Blood creatine	4.85	mg/dL			N

Concomitant Products:

#	Product Name	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date	Interval 1st Dose to Event
1	Ceftriaxone							
2	Mycophenolate Mofetil			UNK				
3	Prednisone							
4	Tacrolimus			UNK	Immunosuppressant drug therapy			

Reporter Source:

Study Report?: No

Sender Organization: ADVANZ PHARMA

503B Compounding Outsourcing Facility?:

Literature Text: Nair V, Jandovitz N, Hirsch JS, Nair G, Abate M, Bhaskaran M. et al.. COVID-19 in kidney transplant recipients. Am. J. Transplant.. 2020

FDA - Adverse Event Reporting System (FAERS)

FOIA Case Report Information

Case ID: 17801454

Case Information:

Case Type: EXPEDITED (15-DAY) **eSub:** Y **HP:** **Country:** USA **Event Date:** **Outcomes:** DE,HO,OT, **Application Type:** NDA

FDA Rcvd Date: 19-May-2020 **Mfr Rcvd Date:** 11-May-2020 **Mfr Control #:** US-ADVANZ PHARMA-202005005382 **Application #:** 009768

Patient Information:

Age: **Sex:** **Weight:**

Suspect Products:

#	Product Name	Compounded Drug ?	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date
1	Hydroxychloroquine				UNK	COVID-19		
2	AZITHROMYCIN				UNK	COVID-19		

#	Product Name	Interval 1st Dose to Event	DeC	ReC	Lot#	Exp Date	NDC #	MFR/Labeler	OTC
1	Hydroxychloroquine		NA	NA				CONCORDIA	
2	AZITHROMYCIN		NA	NA					

Event Information:

Preferred Term (MedDRA Â© Version: 23.1)	ReC
Death	NA
Product use in unapproved indication	NA

Case ID: 17801454

Event/Problem Narrative:

Case number 202005005382 is a literature report (Reference ID: 32351040) sent by other healthcare professional on 11/May/2020.

This is one of the linked cases and linked to the case 202005005269.

This case refers to a 74-year-old Caucasian female patient who died on an unknown date, following treatment with Hydroxychloroquine and azithromycin for COVID-19 (Product use in unapproved indication).

The patient's medical history non-tobacco user, renal transplant, renal replacement therapy, extubation, Exposure to communicable disease and historical medications were not provided.

The patient's co-morbid conditions included hypertension, mental status changes and neoplasm malignant, COVID-19.

The patient's concomitant medications included Sirolimus as Immunosuppressant drug therapy and prednisone.

Case report:

There was minimal information on COVID-19 in immunocompromised individuals. they have studied 10 patients treated at 12 adult care hospitals. Ten kidney transplant recipients tested positive for SARS-CoV-2 by PCR, and 9 were admitted. The most common symptom was fever, followed by cough, myalgia, chills, and fatigue. The most common CXR and CT abnormality was multifocal patchy opacities. All hospitalized patients received hydroxychloroquine (HCQ) and azithromycin.

Materials and Methods:

They performed an ongoing study at 12 acute care hospitals in (institution name). All COVID- 19 positive patients with a functioning kidney allograft who presented to the emergency department and were either discharged or hospitalized between 01Mar2020, and 27Mar2020, were included. Data were collected from the enterprise electronic health record (address) reporting database. COVID-19 positivity was defined as a positive result on real-time polymerase chain reaction (PCR) assay of nasal and/or pharyngeal swab specimens. Kidney transplant status was defined as an active ICD-10 code of T86.1, T86.10, T86.11, T86.12, T86.13, T86.19, or Z94.0. All charts were manually reviewed for demographics, history of recent exposure, immunosuppression changes, clinical signs and symptoms, and laboratory findings. Mycophenolic acid (MPA) doses were converted to mycophenolate mofetil (MMF) (360 milligrams of MPA are equivalent to 500 milligrams of MMF) for dose analysis. Acute kidney injury was graded according to Kidney Disease Improving Global Outcomes (KDIGO) criteria. The study was approved by the institutional review board of (institution name).

Result:

Ten kidney transplant recipients were found to be COVID-19 positive by PCR. Nine of the ten patients included were hospitalized. Of the nine,

five were admitted to the intensive care unit (ICU). Three patients, who required intubation died.

Demographics:
The median age of COVID-19 patients was 57 (interquartile range [IQR] 47-67). The majority of patients were male (60%), Caucasian (40%) and Black or African American (30%) All patients had a history of hypertension, with the majority also having diabetes. None were current smokers, although two had a history of tobacco use. Five patients had undergone living donor transplants, four had received deceased donor organs, and one had an unknown donor type. Median time from transplant to COVID-19 testing was 2,822 days (IQR 1,272-4592). The shortest time from transplant to testing was 124 days with the longest time being 6,290 days.

Presentation and Clinical Course The ten patients with COVID-19 had variable presentations and courses. The most common documented symptom was fever followed by cough, myalgia, chills and fatigue. Two patients had diarrhea and one had nasal congestion. At the time of presentation, seven patients had a temperature greater than 38.3 degrees Celsius. All patients had a chest x-ray (CXR) obtained at the time of admission and 40% had computed tomography (CT) scans. CXR and CT scan findings varied, with multifocal patchy opacities consistent with COVID-19 pneumonia most common seen. Three patients had no abnormal findings on CXR or chest CT. All patients had rapid viral assays performed, no patients had co-existing viral infections at the time of presentation. One patient had influenza diagnosed 13 days prior to admission and was treated at the time with five days of oseltamivir. Three patients (Patients 4, 5 and 10) had positive urine cultures for Enterococcus, Klebsiella pneumonia and E.coli, respectively. None had urinary symptoms at the time of presentation. As was previously noted, one patient (Patient 1) was discharged home from the emergency room without treatment or change in immunosuppression; a follow-up one week later demonstrated resolution of symptoms. Five patients (Patients 5, 6, 8, 9, and 10) required an ICU stay while the others were admitted to a COVID-19 medical floor. Of the ICU patients, three died, and two eventually recovered and were discharged. Patient 5 was initially on a medical floor before decompensating and required intubation and vasopressor support. The patient became anuric, was started on continuous renal replacement therapy, and died two days later after being made DNR. Patient 9 never recovered mental status after mechanical ventilation. She was eventually extubated then died in hospice. Patient 10 developed respiratory decompensation and died of a cardiac arrest. All of the remaining patients were eventually discharged. Median length of stay was 11 days (IQR 4-17 days). One patient resumed MMF at home and was readmitted 2 days later due to fever and shortness of breath. CT upon readmission revealed multifocal pneumonia presumed related to COVID-19. MMF was stopped, fevers resolved and he was discharged on room air after 7 days. Median follow-up for the entire cohort was 25 days (IQR 11-26 days, 2 patients were lost to follow up after discharge). Leukopenia was seen in 20% of patients during hospitalization. Eight of the nine hospitalized patient had at least one ferritin level and c reactive protein checked. Median ferritin was 788 ng/ml (IQR 563-1162) and CRP 13.35 mg/dl (IQR 4.82-23.72). Allograft function was stable in 50% of patients. Five patients had acute kidney injury (AKI): three stage 3, one stage 2, and one stage 1. No kidney biopsies were performed during the hospitalization.

Immunosuppression: All hospitalized patients had their antimetabolite agent stopped. Tacrolimus doses were titrated to a target trough of 3-5ng/ml. Tacrolimus was stopped for Patients 5 and 6 who were intubated in the ICU and sirolimus was stopped for Patient 9.

Treatment: All hospitalized patients received hydroxychloroquine (HCQ) and azithromycin (the latter no longer routinely administered as part of COVID treatment). All patients had an electrocardiogram (EKG) performed before initiation of therapy while only 4 had subsequent EKG's

Case ID: 17801454

performed. No patient had a QTc of 500 or greater. Six patients received at least one dose of an additional antibiotic including ceftriaxone, piperacillin/tazobactam, levofloxacin, cefepime, and vancomycin at the time of presentation. Patient 1 was discharged home without any antiviral or antimicrobial agents. Patients 5, 6, and 10 in the ICU were also placed on thiamine. Patients 6 and 7 were given methylprednisolone and Patient 10 was given high dose prednisone for acute respiratory distress syndrome (ARDS).

Presentation and Hospital Course:

The patient's WBC initial: 6.3; WBC nadir: 4.44; lymphocyte count: 0.44; O2: mechanical ventilation

Ferritin: 817 ng/mL; C-reactive protein: 5.14 mg/dL; Initial creatinine (ICr): 1.29; Peak creatinine (PCr): 1.37 mg/dL; Time from Transplant to infection (days): 3127.

At the time of this report, the outcome of the event (Product use in unapproved indication was unknown and rest of the event was fatal.

The action taken with Hydroxychloroquine was not applicable.

De-challenge and re-challenge result was not applicable for the event with respect to Hydroxychloroquine.

This case is considered to be serious due to seriousness criteria death, hospitalization and medically significant.

The reporter reported that causality assessment possibly related with event.

Follow-up information received on 12/May/2020 via Full text article. Version 1.0 was created.

Additional information: Author's details updated. Laboratory details and treatment drugs added. Medical history and concomitant drugs were added. Narrative amended accordingly.

Relevant Medical History:

Disease/Surgical Procedure	Start Date	End Date	Continuing?
COVID-19			YES
Exposure to communicable disease			
Extubation			

Case ID: 17801454

Hypertension	YES
Immunosuppressant drug therapy	
Mental status changes	YES
Neoplasm malignant	YES
Non-tobacco user	
Renal replacement therapy	
Renal transplant	

Medical History Product(s)	Start Date	End Date	Indications	Events

Relevant Laboratory Data:

Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail
C-reactive protein	5.14	mg/dL			N
Serum ferritin	817	ng/mL			N
Blood creatinine	1.29	mg/dL			N
Blood creatinine	1.37	mg/dL			N

Concomitant Products:

#	Product Name	Dose/ Frequency	Route	Dosage Text	Indications(s)	Start Date	End Date	Interval 1st Dose to Event
1	Prednisone			UNK				
2	Sirolimus			UNK	Immunosuppressant drug therapy			

Reporter Source:

Study Report?: No

Sender Organization: ADVANZ PHARMA

503B Compounding Outsourcing Facility?:

Literature Text: Nair V, Jandovitz N, Hirsch JS, Nair G, Abate M, Molmenti EP et al.. COVID-19 in kidney transplant recipients. Am. J. Transplant.. 2020

Printer: CDPEDQ5
User: STEPPERH
Date - Time: 12-Mar-2021 02:56 PM
Total Number of Cases (Non-Esub): 7
Total Number of Pages: 34
Print Job Number: 23830

Disclaimers:
Submission of a safety report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event. The information in these reports has not been scientifically or otherwise verified as to a cause and effect relationship and cannot be used to estimate the incidence of these events.

Data provided in the Quarterly Data Extract (QDE) or a FAERS FOIA report are a snapshot of FAERS at a given time. There are several reasons that a case captured in this snapshot can be marked as inactive and not show up in subsequent reports. Manufacturers are allowed to electronically delete reports they submitted if they have a valid reason for deletion. FDA may merge cases that are found to describe a single event, marking one of the duplicate reports as inactive. The data marked as inactive are not lost but may not be available under the original case number.

Processed Case Id's for Images:
17605425 17614765 17675095 17782864 17784015 17858758 18251897

Failed Case Id's for Images:

Total Failed Cases: 0

All dates displayed in the report are in EST(GMT-05:00) time zone

Basic Details

Company Unit	CDER-CTU	Originating Account	FAERS
Source Medium	MWO (Drug)	Source Form Type	E2B XML 3500
Priority	Routine		
Override Auto Calculation Rule	No		
FDA Received Date	30-Mar-2020	CTU Received Date	30-Mar-2020
CTU Triage Date		CTU Data Entry Date	
Report Type	Spontaneous	Report Classification	Drug
Assign To	User		
User/Group			
Forward to Department	☑ CDER (CDER-OSE-RSS-CTU@fda.hhs.gov) (E2B)		
Case Priority	Direct		

Contact

Case Reporter	First Name	Last Name	Email Address	Phone
☑	(b) (6)	(b) (6)	(b) (6)	

A. PATIENT INFORMATION

	Patient Identifier (In Confidence)	(b) (6)
	Age	87 Year(s)
	Date of Birth	
	Gender	Male
	Weight	84.5 kg
	Ethnicity (Check single best answer)	Not Hispanic/Latino
	Race (Check all that apply)	☐ Asian ☐ American Indian or Alaskan Native ☑ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

	Type of Report (check all that apply)	☑ Adverse Event ☐ Product Use/Medication Error ☐ Product Problem (e.g., defects/malfunctions) ☐ Problem with Different Manufacturer of Same Medicine
	Serious	Yes
	Outcome Attributed to Adverse Event (Check all that apply)	☐ Death ☑ Life Threatening ☐ Hospitalization (initial or prolonged) ☐ Other Serious or Important Medical Events ☐ Disability or Permanent Damage ☐ Congenital Anomaly/Birth Defects ☐ Required Intervention to Prevent Permanent Impairment/Damage

Date of Death	
Date of Event	27-Mar-2020
Date of this Report	30-Mar-2020

Describe Event, Problem or Product Use Error

Describe Event, Problem, or Product Use Error: Report from Clinical Pharmacist: QTc increased from 397 on (b) (6) at 2240 to 468 on (b) (6) at 0453, which is a >15% increase leading to increased EKG moniroting. Chart review: Admitted: (b) (6) Expired: (b) (6) Weight: 84.5 kg Height: 69 inches CrCL: 12 mL/min COVID positive test: (b) (6) Home medications: ? Amlodipine 5 mg daily ? Atenolol 100 mg daily ? Atorvastatin 40 mg nightly ? Chlorthalidone 25 mg daily ? Furosemide 20 mg daily prn swelling of legs ? Loratadine 10 mg daily ? Losartan 50 mg dily ? Meclizine 25 mg three a day as prn for dizziness ? TiZANidine 4 mg q6 hrs prn muscle spasms Information from H&P: pleasant 87 y.o. old male with CAD, HTN, history of prostate cancer, CKD stage III who presented to the (b) (6) ED with complaints of malodorous urine. He has had prior hx UTIs. He also complains of mild cough. He denies known ill contacts. He denies myalgias. Further history is limited; pt is a poor historian. ED course: vancomycin, meropenem, 900 ml LR bolus ? Hydroxychlorquine: 400 mg given (b) (6) at 1817; (b) (6) at 0951 ? Hydroxychlorquine: 200 mg given (b) (6) at 1648, (b) (6) at 0936 and 1750, missed both doses on (b) (6) (RN comments state pt on bipap); (b) (6) at 0829 ? One dose of azithromycin 250 mg tablet given ? (b) (6) at 0830 No treatment of QTc prolongation noted in chart

Relevant Test/Laboratory Data 1 of 1

Test Name		Test Date	
Test Result		Test Unit	
Low Test Range		High Test Range	
More Information Available?			

Additional Comments

Other Relevant History, Including Preexisting Medical Conditions

C. PRODUCT AVAILABILITY

Product Available for Evaluation? (Do not send product to FDA)	No
Returned to Manufacturer on	
Do you have a picture of the product? (check yes if you are including a picture)	No

D. PRODUCT(S) 1 of 2

Suspect	Yes
Does this report involve cosmetic, dietary supplement or food/medical food?	
Primary?	Yes
Type	Drug/Biologic
Product Name	hydrochlorquine

	Strength		If Other		
	Manufacturer/Compounder				
	NDC# or Unique ID				
	Product Type(check all that apply)	☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar			
	Event Abated After Use Stopped or Dose Reduced?				
	Event Reappeared after Reintroduction ?				

Drug Therapy 1 of 1

	Dose or Amount		If Other		
	Frequency		If Other		
	Route		If Other		
	Dosage Form				
	Start	24-Mar-2020			
	Stop	28-Mar-2020			
	Therapy Duration		If Other		
	Is therapy still on-going?	No			
	Lot Number				
	Expiration Date				

Diagnosis for Use (indication) 1 of 1

	COVID-19

D. PRODUCT(S) 2 of 2

	Concomitant	Yes			
	Does this report involve cosmetic, dietary supplement or food/medical food?				
	Primary?				
	Type	Drug/Biologic			
	Product Name	azithromycin 250 mg tablet			
	Strength		If Other		
	Manufacturer/Compounder				
	NDC# or Unique ID				
	Product Type(check all that apply)	☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar			
	Event Abated After Use Stopped or Dose Reduced?				
	Event Reappeared after Reintroduction ?				

Drug Therapy 1 of 1

Dose or Amount		If Other		
Frequency		If Other		
Route		If Other		
Dosage Form				
Start	27-Mar-2020			
Stop	27-Mar-2020			
Therapy Duration		If Other		
Is therapy still on-going?				
Lot Number				
Expiration Date				

Diagnosis for Use (indication) 1 of 1

E. SUSPECT MEDICAL DEVICE

Brand Name	
Common Device Name	
Procode	
Manufacturer Name	
City	
State	
Model #	
Lot #	
Catalog #	
Expiration Date	
Serial #	
Unique Identifier (UDI)#	
Operator of Device	☐ Health Professional ☐ Patient/Consumer ☐ Other
Other	
If Implanted, Give Date	
If Explanted, Give Date	
Is this a single-use device that was reprocessed and reused on a patient?	
If Yes for the above field, Enter Name and Address of Reprocessor	
Was this device serviced by a third party?	

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

CONCOMITANT MEDICAL PRODUCT DESCRIPTION

G. REPORTER 1 of 1

Primary?	Yes	
Reporter is Patient?		
Title		
Last Name	(b) (6)	
Middle Name		
First Name	(b) (6)	
Address	(b) (6)	
City	(b) (6)	
State/Province/Region	(b) (6)	
Country	UNITED STATES	If Other
ZIP/Postal Code	(b) (6)	
Phone	(b) (6)	
Email	(b) (6)	
Fax		
Reporter Organization		
Department		
Reporter Speciality		
Health Professional?	Yes	
Occupation	Pharmacist	If Other
Also Reported to	☐ Manufacturer/Compounder ☑ User Facility ☐ Distributor/Importer	
If you do NOT want your identity disclosed to the manufacturer, please mark this box (Confidentiality Requested):	No	

Reset Form

CaseID: 17614765

U.S. Department of Health and Human Services
Food and Drug Administration

MEDWATCH

FORM FDA 3500 (10/18)

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use/medication errors

Form Approved OMB No 0910 0291 Expires 9 30 2021
See PRA statement on reverse

FDA USE ONLY

Triage unit sequence #

FDA Rec Date

Note: For date prompts of "dd mmm yyyy" please use 2 digit day 3 letter month abbreviation and 4 digit year; for example 01 Jul 2018

A. PATIENT INFORMATION

1 **Patient Identifier**
(b) (6)

n Confidence

2 **Age**
65 ☐ Year(s) ☐ Month(s) ☐ Week(s) ☐ Day(s)

or Date of Birth *(e g 08 Feb 1925)*

3 **Gender**
☐ Female ☑ Male ☐ ntersex ☐ Transgender ☐ Prefer not to disclose

4 **Weight**
105.3 ☐ lb ☐ kg

5 **Ethnicity** *(check one)*
☐ Hispanic/Latino ☐ Not Hispanic/Latino

6 **Race** *(check all that apply)*
☐ Asian ☐ American ndian or Alaskan Native ☐ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific slander

B. ADVERSE EVENT, PRODUCT PROBLEM

1 **Type of Report** *(check all that apply)*
☑ Adverse Even ☐ Produc Problem *(e g defects/malfunctions)* ☐ Produc Use/ Medica ion Error ☐ Problem wi h Differen Manufac urer of Same Medicine

2 **Outcome Attributed to Adverse Event** *(check all that apply)*
☑ Death *Date of death (dd mmm yyyy):*
☑ Life threatening ☐ Disability or Permanent Damage
☐ Hospitalization (initial or prolonged) ☐ Congenital Anomaly/Birth Defects
☐ Other Serious or mportant Medical Events
☐ Required ntervention to Prevent Permanent mpairment/Damage

3 **Date of Event** *(dd mmm yyyy)*
17 - Mar - 2020

4 **Date of this Report** *(dd mmm yyyy)*
31 - Mar - 2020

5 **Describe Event, Problem or Product Use/Medication Error**

FDA/CDER/OSE Follow-up for FAERS Case ID#:

17591609: follow-up report from pharmacist

(Continue on page 2)

6 **Relevant Tests/Laboratory Data** **Date** *(dd-mmm-yyyy)*

(Continue on page 2)

7 **Other Relevant History, Including Preexisting Medical Conditions** *(e g allergies pregnancy smoking and alcohol use liver/kidney problems etc)*

Hypertension, ESRD on hemodialysis, CAD, s/p percutaneous transluminal coronary angioplasty, hypercholesteremia, sleep apnea,

(Continue on page 2)

C. PRODUCT AVAILABILITY

1 **Product Available for Evaluation?** *(Do not send product to FDA)*
☐ Yes ☐ No ☐ Returned to Manufacturer on *(dd mmm yyyy)*

2 **Do you have a picture of the product?** *(check yes if you are including a picture)* ☐ Yes

D. SUSPECT PRODUCTS

1 **Name, Strength, Manufacturer/Compounder** *(from product label)*
Does this report involve cosmetic dietary supplement or food/medical food? **#1** ☐ Yes **#2** ☐ Yes

#1 Name and Strength	#1 NDC # or Unique D
#1 Manufacturer/Compounder	#1 Lot #
#2 Name and Strength	#2 NDC # or Unique D
#2 Manufacturer/Compounder	#2 Lot #

2	Dose or Amount	Frequency	Route
#1	400 - 200 mg	BID	PO
#2			

3 **Treatment Dates/Therapy Dates** *(give length of treatment (to/from) or your best estimate)*
#1 Start 15 - Mar - 2020
#1 Stop 17 - Mar - 2020
s therapy still on going? ☐ Yes ☑ No

#2 Start
#2 Stop
s therapy still on going? ☐ Yes ☐ No

4 **Diagnosis for Use** *(Indication)*
#1 COVID-19
#2

5 **Product Type** *(check all that apply)*
#1 ☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar
#2 ☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar

6 **Expiration Date** *(dd mmm yyyy)*
#1
#2

7 **Event Abated After Use Stopped or Dose Reduced?**
#1 ☐ Yes ☐ No ☐ Doesn t apply
#2 ☐ Yes ☐ No ☐ Doesn t apply

8 **Event Reappeared After Reintroduction?**
#1 ☐ Yes ☐ No ☐ Doesn t apply
#2 ☐ Yes ☐ No ☐ Doesn t apply

E. SUSPECT MEDICAL DEVICE

1 **Brand Name**

2a **Common Device Name** 2b **Procode**

3 **Manufacturer Name, City and State**

4 **Model #** **Lot #** 5 **Operator of Device**
☐ Health Professional ☐ Patient/Consumer ☐ Other

Catalog # **Expiration Date** *(dd-mmm-yyyy)*

Serial # **Unique Identifier** *(UDI) #*

6a **If Implanted, Give Date** *(dd mmm yyyy)* 6b **If Explanted, Give Date** *(dd mmm yyyy)*

7a **Is this a single-use device that was reprocessed and reused on a patient?** ☐ Yes ☐ No

7b **If Yes to Item 7a, Enter Name and Address of Reprocessor**

8 **Was this device serviced by a third party servicer?** ☐ Yes ☐ No

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

1 **Product names and therapy dates** *(Exclude treatment of event)*

(Continue on page 2)

G. REPORTER *(See confidentiality section on back)*

1 **Name and Address**

Last Name Swank First Name Kim

Address 10903 New Hampshire Ave

City Silver Spring State/Province/Region MD

Z P/Postal Code 20993 Country US

Phone # 301-796-2887 Email kimberley.swank@fda.hhs.gov

2 **Health Professional?** ☑ Yes ☐ No

3 **Occupation** Pharmacist

4 **Also Reported to:** ☐ Manufacturer/ Compounder ☐ User Facility ☐ Distributor/ mporter

5 **If you do NOT want your identity disclosed to the manufacturer, please mark this box:** ☐

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event
* Please see instructions

MEDWATCH

FORM FDA 3500 (10/18) *(continued)*

The FDA Safety Information and Adverse Event Reporting Program

B 5 **Describe Event or Problem** *(continued)*

see overflow on page 3

Back to Item B.5

B 6 **Relevant Tests/Laboratory Data** *(continued)*

	Date *(dd-mmm-yyyy)*	Relevant Tests/Laboratory Data	Date *(dd-mmm-yyyy)*
WBC 12.1	(b) (6)	ALT 19	(b) (6)
BUN 33	(b) (6)	AST 53	(b) (6)
creatinine 3.88	(b) (6)	Alk phos 212	(b) (6)
potassium 3.1	(b) (6)	Total bilirubin 1.1	(b) (6)

Additional comments

Back to Item B.6

B 7 **Other Relevant History** *(continued)*

Back to Item B.7

F.1 **Concomitant Medical Products and Therapy Dates** *(Exclude treatment of event) (continued)*

(b) (6) (b) (6) (b) (6) (b) (6)

Back to Item F.1

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

(b) (6)

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(b) (6)

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(b) (6)

(b) (6)

(b) (6)

CTU #: FDA-CDER-CTU-2020-36131 | Department: CDER | RCT #: RCT-798011 | CTU Triage Date: 01-Apr-2020 | AER #: 17614765 |
Total Pages: 4

ADVICE ABOUT VOLUNTARY REPORTING

Detailed instructions available at: http://www.fda.gov/medwatch/report/consumer/instruct.htm

Report adverse events, product problems or product use errors with:

- Medications (drugs or biologics)
- Medical devices (including diabetes glucose-test kit, hearing aids, breast pumps, and many more)
- Combination products (medication & medical devices)
- Blood transfusions, gene therapies, and human cells and tissue transplants (for example, tendons, bone, and corneas)
- Special nutritional products (dietary supplements, medical foods, infant formulas)
- Cosmetics (such as moisturizers, makeup, shampoos and conditioners, face and body washes, deodorants, nail care products, hair dyes and relaxers, and tattoos)
- Food (including beverages and ingredients added to foods)

Report product problems – quality, performance or safety concerns such as:

- Suspected counterfeit product
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures (product didn't work)

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability or permanent damage
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment or damage
- Other serious (important medical events)

Report even if:

- You're not certain the product caused the event
- You don't have all the details
- Just fill in the sections that apply to your report

How to report:

- Use section D for all products except medical devices
- Attach additional pages if needed
- Use a separate form for each patient
- Report either to FDA or the manufacturer (or both)

How to submit report:

- To report by phone, call toll-free: 1-800-FDA (332)-1088
- To fax report: 1-800-FDA(332)-0178
- To report online: www.fda.gov/medwatch/report.htm

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

If your report involves an adverse event with a vaccine, go to http://vaers.hhs.gov to report or call 1-800-822-7967.

Confidentiality:

The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise.

The information in this box applies only to requirements of the Paperwork Reduction Act of 1995

The burden time for this collection of information has been estimated to average 40 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed, and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

Please DO NOT RETURN this form to the PRA Staff e-mail above.

OMB statement:

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

All dates displayed in the report are in EST(GMT-05:00) time zone

Basic Details

Company Unit	CDER-CTU	Originating Account	FAERS
Source Medium	MWO (Drug)	Source Form Type	E2B XML 3500
Priority	Urgent		
Override Auto Calculation Rule	No		
FDA Received Date	15-Apr-2020	CTU Received Date	15-Apr-2020
CTU Triage Date		CTU Data Entry Date	
Report Type	Spontaneous	Report Classification	Drug
Assign To	User		
User/Group			
Forward to Department	☑ CDER (CDER-OSE-RSS-CTU@fda.hhs.gov) (E2B)		
Case Priority	Direct		

Contact

Case Reporter	First Name	Last Name	Email Address	Phone
☑	(b) (6)	(b) (6)	(b) (6)	(b) (6)

A. PATIENT INFORMATION

	Patient Identifier (In Confidence)	Unspecified
	Age	
	Date of Birth	(b) (6)
	Gender	Female
	Weight	56.25 kg
	Ethnicity (Check single best answer)	Not Hispanic/Latino
	Race (Check all that apply)	☐ Asian ☐ American Indian or Alaskan Native ☐ Black or African American ☑ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

	Type of Report (check all that apply)	☑ Adverse Event ☐ Product Use/Medication Error ☐ Product Problem (e.g., defects/malfunctions) ☐ Problem with Different Manufacturer of Same Medicine
	Serious	Yes
	Outcome Attributed to Adverse Event (Check all that apply)	☑ Death ☐ Life Threatening ☐ Hospitalization (initial or prolonged) ☐ Other Serious or Important Medical Events ☐ Disability or Permanent Damage ☐ Congenital Anomaly/Birth Defects ☐ Required Intervention to Prevent Permanent Impairment/Damage
	Date of Death	(b) (6)

Date of Event	10-Apr-2020
Date of this Report	15-Apr-2020

Describe Event, Problem or Product Use Error

Describe Event, Problem, or Product Use Error: This report was mandated through the fact sheet EUA for use of hydroxychloroquine. We feel that the patient was doing better the very next morning after receiving just one dose of 200 mg. She died (b) (6) likely from a pulmonary embolism. She unexpectedly had drop in BP to 60/40 and became unresponsive just hours after she felt better and was smiling and conversing normally. This lady had nearly died three times in the past 18 months for various lung problems including COPD, CHF, pneumonia with sepsis and amiodarone toxicity and I feel that the medication hydroxychloroquine had nothing to do with her passing away.

Relevant Test/Laboratory Data 1 of 1

Test Name	COVID-19 TEST	Test Date	(b) (6)
Test Result	negative	Test Unit	
Low Test Range		High Test Range	
More Information Available?			

Additional Comments

Patient was dying and fragile. Order was given for hydroxychloroquine since I was highly suspicious that patient had Covid-19 and a negative test result would not have changed my mind to give my patient the best chance possible to survive her illness (false negative rate known to be 30-40% at the time of my decision. The EUA was given by our pharmacist who spoke with the patient.

Other Relevant History, Including Preexisting Medical Conditions

Severely fragile patient with COPD, CHF, PAD, Amiodarone lung toxicity, AF, DM type II with recent above knee amputation and recurrent pneumonia.

C. PRODUCT AVAILABILITY

Product Available for Evaluation? (Do not send product to FDA)	No
Returned to Manufacturer on	
Do you have a picture of the product? (check yes if you are including a picture)	No

D. PRODUCT(S) 1 of 1

Suspect	Yes		
Does this report involve cosmetic, dietary supplement or food/medical food?			
Primary?	Yes		
Type	Drug/Biologic		
Product Name	hydroxychloroquine		
Strength	200 mg milligram(s)	If Other	
Manufacturer/Compounder			
NDC# or Unique ID			
Product Type(check all that apply)	☐ OTC		

	☐ Compounded ☑ Generic ☐ Biosimilar
Event Abated After Use Stopped or Dose Reduced?	Doesn't Apply
Event Reappeared after Reintroduction ?	Doesn't Apply

Drug Therapy 1 of 1

Dose or Amount		If Other	
Frequency	Twice a day	If Other	
Route	Oral	If Other	
Dosage Form			
Start	09-Apr-2020		
Stop	10-Apr-2020		
Therapy Duration		If Other	
Is therapy still on-going?	No		
Lot Number			
Expiration Date			

Diagnosis for Use (indication) 1 of 1

suspect covid-19

E. SUSPECT MEDICAL DEVICE

Brand Name	
Common Device Name	
Procode	
Manufacturer Name	
City	
State	
Model #	
Lot #	
Catalog #	
Expiration Date	
Serial #	
Unique Identifier (UDI)#	
Operator of Device	☐ Health Professional ☐ Patient/Consumer ☐ Other
Other	
If Implanted, Give Date	
If Explanted, Give Date	
Is this a single-use device that was reprocessed and reused on a patient?	

	If Yes for the above field, Enter Name and Address of Reprocessor	
	Was this device serviced by a third party?	

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

CONCOMITANT MEDICAL PRODUCT DESCRIPTION

G. REPORTER 1 of 1

	Primary?	Yes		
	Reporter is Patient?			
	Title			
	Last Name	(b) (6)		
	Middle Name			
	First Name	(b) (6)		
	Address	(b) (6)		
	City	(b) (6)		
	State/Province/Region	(b) (6)		
	Country	UNITED STATES	If Other	
	ZIP/Postal Code	(b) (6)		
	Phone	(b) (6)		
	Email	(b) (6)		
	Fax			
	Reporter Organization			
	Department			
	Reporter Speciality			
	Health Professional?	Yes		
	Occupation	Physician	If Other	
	Also Reported to	☐ Manufacturer/Compounder ☐ User Facility ☐ Distributor/Importer		
	If you do NOT want your identity disclosed to the manufacturer, please mark this box (Confidentiality Requested):	No		

All dates displayed in the report are in EST(GMT-05:00) time zone

Basic Details

Company Unit	CDER-CTU	Originating Account	FAERS
Source Medium	MWO (Drug)	Source Form Type	E2B XML 3500
Priority	Urgent		
Override Auto Calculation Rule	No		
FDA Received Date	14-May-2020	CTU Received Date	14-May-2020
CTU Triage Date		CTU Data Entry Date	
Report Type	Spontaneous	Report Classification	Drug
Assign To	User		
User/Group			
Forward to Department	☑ CDER (CDER-OSE-RSS-CTU@fda.hhs.gov) (E2B)		
Case Priority	Direct		

Contact

Case Reporter	First Name	Last Name	Email Address	Phone
☑	(b) (6)	(b) (6)	(b) (6)	

A. PATIENT INFORMATION

	Patient Identifier (In Confidence)	(b) (6)
	Age	72 Year(s)
	Date of Birth	
	Gender	
	Weight	127 kg
	Ethnicity (Check single best answer)	Not Hispanic/Latino
	Race (Check all that apply)	☐ Asian ☐ American Indian or Alaskan Native ☑ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

	Type of Report (check all that apply)	☑ Adverse Event ☐ Product Use/Medication Error ☐ Product Problem (e.g., defects/malfunctions) ☐ Problem with Different Manufacturer of Same Medicine
	Serious	Yes
	Outcome Attributed to Adverse Event (Check all that apply)	☑ Death ☐ Life Threatening ☐ Hospitalization (initial or prolonged) ☐ Other Serious or Important Medical Events ☐ Disability or Permanent Damage ☐ Congenital Anomaly/Birth Defects ☐ Required Intervention to Prevent Permanent Impairment/Damage
	Date of Death	(b) (6)

Date of Event	10-Apr-2020
Date of this Report	14-May-2020

Describe Event, Problem or Product Use Error

Describe Event, Problem, or Product Use Error: Hydroxychloroquine Sulfate treatment under Emergency Use Authorization (EUA):patient had cardiac pulmonary arrest

Relevant Test/Laboratory Data 1 of 1

Test Name		Test Date	
Test Result		Test Unit	
Low Test Range		High Test Range	
More Information Available?			

Additional Comments

Other Relevant History, Including Preexisting Medical Conditions

C. PRODUCT AVAILABILITY

Product Available for Evaluation? (Do not send product to FDA)	Yes
Returned to Manufacturer on	
Do you have a picture of the product? (check yes if you are including a picture)	No

D. PRODUCT(S) 1 of 1

Suspect	Yes		
Does this report involve cosmetic, dietary supplement or food/medical food?			
Primary?	Yes		
Type	Drug/Biologic		
Product Name	hydroxychloroquine		
Strength	200 mg milligram(s)	If Other	
Manufacturer/Compounder	sandoz cs		
NDC# or Unique ID	0781599401		
Product Type(check all that apply)	☐ OTC ☐ Compounded		

	☑ Generic ☐ Biosimilar
Event Abated After Use Stopped or Dose Reduced?	No
Event Reappeared after Reintroduction ?	Doesn't Apply

Drug Therapy 1 of 1

Dose or Amount	400 mg milligram(s)	If Other	
Frequency	Daily	If Other	
Route	Oral	If Other	
Dosage Form			
Start			
Stop			
Therapy Duration	0.93 Day	If Other	
Is therapy still on-going?	No		
Lot Number	JN1834		
Expiration Date	30-Nov-2020		

Diagnosis for Use (indication) 1 of 1

covid-19

E. SUSPECT MEDICAL DEVICE

Brand Name	
Common Device Name	
Procode	
Manufacturer Name	
City	
State	
Model #	
Lot #	
Catalog #	
Expiration Date	
Serial #	
Unique Identifier (UDI)#	
Operator of Device	☐ Health Professional ☐ Patient/Consumer ☐ Other
Other	
If Implanted, Give Date	
If Explanted, Give Date	
Is this a single-use device that was reprocessed and reused on a patient?	

	If Yes for the above field, Enter Name and Address of Reprocessor	
	Was this device serviced by a third party?	

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

CONCOMITANT MEDICAL PRODUCT DESCRIPTION

G. REPORTER

	Primary?	Yes		
	Reporter is Patient?			
	Title			
	Last Name	(b) (6)		
	Middle Name			
	First Name	(b) (6)		
	Address	(b) (6)		
	City	(b) (6)		
	State/Province/Region			
	Country	UNITED STATES	If Other	
	ZIP/Postal Code	(b) (6)		
	Phone			
	Email	(b) (6)		
	Fax			
	Reporter Organization			
	Department			
	Reporter Speciality			
	Health Professional?	Yes		
	Occupation	Pharmacist	If Other	
	Also Reported to	☐ Manufacturer/Compounder ☐ User Facility ☐ Distributor/Importer		
	If you do NOT want your identity disclosed to the manufacturer, please mark this box (Confidentiality Requested):	No		

All dates displayed in the report are in EST(GMT-05:00) time zone

Basic Details

Company Unit	CDER-CTU	Originating Account	FAERS
Source Medium	MWO (Drug)	Source Form Type	E2B XML 3500
Priority	Urgent		
Override Auto Calculation Rule	No		
FDA Received Date	14-May-2020	CTU Received Date	14-May-2020
CTU Triage Date		CTU Data Entry Date	
Report Type	Spontaneous	Report Classification	Drug
Assign To	User		
User/Group			
Forward to Department	☑ CDER (CDER-OSE-RSS-CTU@fda.hhs.gov) (E2B)		
Case Priority	Direct		

Contact

Case Reporter	First Name	Last Name	Email Address	Phone
☑	(b) (6)	(b) (6)	(b) (6)	

A. PATIENT INFORMATION

	Patient Identifier (In Confidence)	60
	Age	74 Year(s)
	Date of Birth	
	Gender	Male
	Weight	89.8 kg
	Ethnicity (Check single best answer)	Not Hispanic/Latino
	Race (Check all that apply)	☐ Asian ☐ American Indian or Alaskan Native ☐ Black or African American ☑ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

	Type of Report (check all that apply)	☑ Adverse Event ☐ Product Use/Medication Error ☐ Product Problem (e.g., defects/malfunctions) ☐ Problem with Different Manufacturer of Same Medicine
	Serious	Yes
	Outcome Attributed to Adverse Event (Check all that apply)	☑ Death ☐ Life Threatening ☐ Hospitalization (initial or prolonged) ☐ Other Serious or Important Medical Events ☐ Disability or Permanent Damage ☐ Congenital Anomaly/Birth Defects ☐ Required Intervention to Prevent Permanent Impairment/Damage
	Date of Death	(b) (6)

Date of Event	14-Apr-2020
Date of this Report	14-May-2020

Describe Event, Problem or Product Use Error

Describe Event, Problem, or Product Use Error: Hydroxychloroquine Sulfate treatment under Emergency Use Authorization (EUA):patient had cardiac pulmonary arrest

Relevant Test/Laboratory Data 1 of 1

Test Name		Test Date	
Test Result		Test Unit	
Low Test Range		High Test Range	
More Information Available?			

Additional Comments

Other Relevant History, Including Preexisting Medical Conditions

C. PRODUCT AVAILABILITY

Product Available for Evaluation? (Do not send product to FDA)	Yes
Returned to Manufacturer on	
Do you have a picture of the product? (check yes if you are including a picture)	No

D. PRODUCT(S) 1 of 1

Suspect	Yes		
Does this report involve cosmetic, dietary supplement or food/medical food?			
Primary?	Yes		
Type	Drug/Biologic		
Product Name	hydroxychloroquine		
Strength	200 mg milligram(s)	If Other	
Manufacturer/Compounder	sandoz cs		
NDC# or Unique ID	0781599401		
Product Type(check all that apply)	☐ OTC ☐ Compounded		

	☑ Generic ☐ Biosimilar
Event Abated After Use Stopped or Dose Reduced?	No
Event Reappeared after Reintroduction ?	Doesn't Apply

Drug Therapy 1 of 1

Dose or Amount	400 mg milligram(s)	If Other	
Frequency	Daily	If Other	
Route	Oral	If Other	
Dosage Form			
Start			
Stop			
Therapy Duration	1.02 Day	If Other	
Is therapy still on-going?	No		
Lot Number	JN1834		
Expiration Date	30-Nov-2020		

Diagnosis for Use (indication) 1 of 1

covid-19

E. SUSPECT MEDICAL DEVICE

Brand Name	
Common Device Name	
Procode	
Manufacturer Name	
City	
State	
Model #	
Lot #	
Catalog #	
Expiration Date	
Serial #	
Unique Identifier (UDI)#	
Operator of Device	☐ Health Professional ☐ Patient/Consumer ☐ Other
Other	
If Implanted, Give Date	
If Explanted, Give Date	
Is this a single-use device that was reprocessed and reused on a patient?	

	If Yes for the above field, Enter Name and Address of Reprocessor	
	Was this device serviced by a third party?	

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

CONCOMITANT MEDICAL PRODUCT DESCRIPTION

G. REPORTER

	Primary?	Yes		
	Reporter is Patient?			
	Title			
	Last Name	(b) (6)		
	Middle Name			
	First Name	(b) (6)		
	Address	(b) (6)		
	City	(b) (6)		
	State/Province/Region			
	Country	UNITED STATES	If Other	
	ZIP/Postal Code	(b) (6)		
	Phone			
	Email	(b) (6)		
	Fax			
	Reporter Organization			
	Department			
	Reporter Speciality			
	Health Professional?	Yes		
	Occupation	Pharmacist	If Other	
	Also Reported to	☐ Manufacturer/Compounder ☐ User Facility ☐ Distributor/Importer		
	If you do NOT want your identity disclosed to the manufacturer, please mark this box (Confidentiality Requested):	No		

CTU #: FDA-CDER-CTU-2020-52602 | Department: CDER | RCT #: RCT-814860 | CTU Triage Date: 03-Jun-2020 | AER #: 17858758 | Total Pages: 9

MedWatch 3500 Health Professional Report

The FDA Safety Information and Adverse Event Reporting Program

FDA Safety Report ID #	513013	FDA Received Date	03-Jun-2020

A. PATIENT INFORMATION			
A1. Patient Identifier:	(b) (6)		
A2. Age:	59	Year(s)	
A2. Date of Birth:			
A3. Gender:	Female	Yes	
	Male		
	Intersex		
	Transgender		
	Prefer not to disclose		
A4. Weight:	99.3	kg	
A5. Ethnicity:	Hispanic/Latino		
	Not Hispanic/Latino	Yes	
A6. Race:	Asian		
	American Indian or Alaskan Native	Yes	
	Black or African American		
	White		
	Native Hawaiian or Other Pacific Islander		

B. ADVERSE EVENT, PRODUCT PROBLEM			
B1. Type of Report:	Adverse Event	Yes	
	Product Use/Medication Error		
	Product Problem (e.g., defects/malfunctions)		
	Problem with Different Manufacturer of Same Medicine		
B2. Outcome Attributed to Adverse Event:	Death *(Date of Death)*	Yes	(b) (6)
	Life-threatening		
	Hospitalization (initial or prolonged)		
	Disability or Permanent Damage		
	Congenital Anomaly/Birth Defects		
	Other Serious or Important Medical Events		
	Required Intervention to Prevent Permanent Impairment/Damage		
B3. Date of Event:	22-Apr-2020		
B4. Date of this Report:	03-Jun-2020		

CTU #: FDA-CDER-CTU-2020-52602 | Department: CDER | RCT #: RCT-814860 | CTU Triage Date: 03-Jun-2020 | AER #: 17858758 |
Total Pages: 9

B5. Describe Event, Problem or Product Use/Medication Error:

COVID-19 patient was on azithromycin 500mg IV q24h from 4/18/20 to 4/22/20 and hydroxychloroquinine 200mg oral twice daily from 4/19/20 to 4/22/20. Patient a recorded QTc interval recorded as 522 ms on (b) The patient went into cardiac arrest and expired on (b) at 23:44

CTU #: FDA-CDER-CTU-2020-52602 | Department: CDER | RCT #: RCT-814860 | CTU Triage Date: 03-Jun-2020 | AER #: 17858758 | Total Pages: 9

B6. Relevant Tests/Laboratory Data:	
Test 1	
Test Date:	(b) (6)
Test Name:	EKG
Test Result:	522
Test Unit:	
Low Test Range:	
High Test Range:	
Test 2	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	
Test 3	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	
Test 4	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	

CTU #: FDA-CDER-CTU-2020-52602 | Department: CDER | RCT #: RCT-814860 | CTU Triage Date: 03-Jun-2020 | AER #: 17858758 |
Total Pages: 9

B6. Relevant Tests/Laboratory Data:	
Test 5	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	
Test 6	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	
Test 7	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	
Test 8	
Test Date:	
Test Name:	
Test Result:	
Test Unit:	
Low Test Range:	
High Test Range:	

B6. Additional Comments:

B7. Other Relevant History, Including Preexisting Medical Conditions:

This 59 years old female came in with a complaint of shortness of breath. Patient had not been feeling well for the last week to 10 days time. On presentation her O2 sat was 82% on room air. Patient complained of intermittent dry cough. Past Medical History: • Breast cancer 06/18/2008 • Chronic kidney disease • Congestive heart failure • COVID-19 virus detected (b) (6) • Family history of coronary artery disease 9/1/2011 • GERD (gastroesophageal reflux disease) • Hypertension • Insulin-requiring dependent type 2 diabetes mellitus • Myocardial infarction 2009

C. PRODUCT AVAILABILITY	
C1. Product Available for Evaluation?	No
C1. Returned to Manufacturer on:	
C2. Do you have a picture of the product?	

D. SUSPECT PRODUCTS				
Product 1				
D1. Does this report involve cosmetic, dietary supplement or food/medical food?				
D1. Name:	hydroxychloroquinine			
D1. Strength:	200	MG		
D1. Manufacturer/Compounder:				
D1. NDC # or Unique ID:				
D1. Lot #:				
D2. Dose or Amount:	200	MG		
D2. Frequency:	BID			
D2. Route:	Oral			
D3. Treatment Dates/Therapy Dates:	Start	19-Apr-2020	Stop	22-Apr-2020
	Give best estimate of duration			
	Is therapy still on-going?	No		
D4. Diagnosis for Use:	COVID-19			
D5. Product Type:	OTC (Over-the-counter)			
	Compounded			
	Generic	Yes		
	Biosimilar			
D6. Expiration Date:				
D7. Event Abated After Use Stopped or Dose Reduced?	No			
D8. Event Reappeared After Reintroduction?	Doesn't apply			
Product 2				
D1. Does this report involve cosmetic, dietary supplement or food/medical food?				
D1. Name:	azithromycin			
D1. Strength:	500	MG		
D1. Manufacturer/Compounder:				
D1. NDC # or Unique ID:				
D1. Lot #:				
D2. Dose or Amount:				
D2. Frequency:				
D2. Route:				
D3. Treatment Dates/Therapy Dates:	Start	18-Apr-2020	Stop	22-Apr-2020
	Give best estimate of duration			
	Is therapy still on-going?	No		
D4. Diagnosis for Use:	COVID-19			
D5. Product Type:	OTC (Over-the-counter)			
	Compounded			
	Generic			
	Biosimilar			
D6. Expiration Date:				
D7. Event Abated After Use Stopped or Dose Reduced?	No			
D8. Event Reappeared After Reintroduction?	Doesn't apply			

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E. SUSPECT MEDICAL DEVICE			
E1. Brand Name:	na		
E2a. Common Device Name:			
E2b. Procode:			
E3. Manufacturer Name, City and State:			
E4. Model #:			
E4. Catalog #:			
E4. Serial #:			
E4. Lot #:			
E4. Expiration Date:			
E4. Unique Identifier (UDI) #:			
E5. Operator of Device:	Health Professional		
	Patient/Consumer		
	Other		
E6a. If Implanted, Give Date:			
E6b. If Explanted, Give Date:			
E7a. Is this a single-use device that was reprocessed and reused on a patient?			
E7b. If Yes to Item 7a, Enter Name and Address of Reprocessor:			
E8. Was this device serviced by a third party servicer?			

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product Name	Therapy Start Date	Therapy End Date
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
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18.		
19.		
20.		
21.		

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G. REPORTER		
G1. Name and Address	Last Name	(b) (6)
	First Name	(b) (6)
	Address	(b) (6)
	City	(b) (6)
	State/Province/Region	(b) (6)
	ZIP/Postal Code	(b) (6)
	Country	US
	Phone #:	(b) (6)
	Email:	(b) (6)
G2. Health Professional?	Yes	
G3. Occupation:	Pharmacist	
G4. Also Reported To:	Manufacturer/Compounder	
	User Facility	
	Distributer/Importer	
G5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box (Confidentiality Requested):	Yes	

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CUREID mobile application report

FDA Received date: 27-May-2020

Patient Identifier (A.1): (b) (6)

Age (A.2): 51-60 years

Sex (A.3): Male

Ethnicity (A.5)/Race (A.6): None/

Type of Report (B.1): Torsades de pointes, cardiac arrest

Outcome (B.2): Patient died

Narrative field B.5

Description: Covid 19 preliminary clinical reports suggest significant acute therapeutic efficacy for the combination of AZ and HC(1) above that of HC alone(2). The putative mechanism might be prevention of secondary bacterial infection in cytokine-insulted alveoli however it may be due to macrolide CYA-3A4 inhibition with elevation of hydroxychloroquine levels, perhaps unpredictably.

Case Report: Patient was male in 50s with no prior medical condition presenting 3/27/20 with fever and dyspnea negative for influenza A and B and RSV but positive for COVID 19 (PHI removed by moderator MD). Patient in moderate respiratory distress with bilateral crackles. Lab values: WBC 20.7k/■L with neutrophilic predominance (92%) and lymphopenia (2.8%). Lab values: PaO2 44 on FiO2 100%. Serum K (5.0mg/dL, normal 3.5–5.1 mg/dL) and Mg (1.9 mg/dL, normal 1.6–2.3 mg/dL). Serum Ca was low (7.7 mg/dL, normal 8.4-10.4 mg/dL) and phosphate high (9.0 mg/dL, normal < 4.5 mg/dL) in keeping with acute renal failure with Cr rising from 2.4 to 6.5mg/dl (normal < 1.1 mg/dL) within 24h of admission. AST

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(166 U/L, normal <59 U/L) and LDH (3546 U/L, normal <618 U/L) and PT/ INR 14.6s/1.3 (normal <12.9s/<1.16) but normal ALT. Imaging: CXR revealed bilateral peripheral focal consolidation and right pleural effusion. Baseline EKG sinus rhythm QT/QTc 298/403 msec figure 1a). Treatment & Outcome: Patient was admitted to ICU telemetry, intubated and started on hydroxychloroquine 400 mg BID day one then 200mg BID and azithromycin 500 mg day one then 250mg daily. Day 2 EKG revealed repeated torsades de pointes though QT/QTc remained normal (250/427 msec fig 1b). (b) (6) later patient experienced cardiac arrest. Resuscitation efforts were unsuccessful, despite defibrillation.

Discussion: Both HC and AZ are capable of prolonging QT(3,4) and macrolide (AZ) is a well-known CYA-3A4 inhibitor which may decrease HC metabolism raising the potential for cardiotoxic accumulation and arrhythmia. Doses of HC as high as 1200mg are being suggested(1). In view of the beneficial results with HC alone(2) perhaps the initial loading dose of AZ might be omitted particularly in patients with multiorgan failure. Prophylactic mexiletine might also be considered based on the prior efficacy of quinidine mexiletine combinations(5). Notably, there was no premonitory QT prolongation documented prior to or concurrent with torsades.

How diagnosis was made:

Why infection is difficult to treat?: There is no standard/approved therapy for this disease; Unusual disease presentation; Drug toxicity on recommended therapy(Oth

Adverse Event: Torsades de pointes, cardiac arrest

Country Contracted: United States

Country Treated: United States

Sites of Infection:

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Clinical Syndrome: torsades de pointes

Unusual in this case: No premonitory or concurrent QT/QTc prolongation documented

Organisms: Coronavirus - covid-19

Resistant Drugs:

Drugs used in new way: Hydroxychloroquine: To treat a disease other than the one for which the drug is approved

Azithromycin: To treat a disease other than the one for which the drug is approved

Drug Treatment Setting: Hydroxychloroquine: ICU/Critical Care

Azithromycin: ICU/Critical Care

Surgery: No

Previous Drugs:

How Outcome:

When Outcome: At the time the treatment was completed

Disease Relapse: No

Abstract:

Article URL: None

Journal:

Publication Year: None

Published Authors:

Unusual Adverse Events: No premonitory or concurrent QT/QTc prolongation documented

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Past Medical History (B.7): Other Relevant Co-Morbidities: Nil prior to admission

Other Relevant Co-Infections: Acute renal failure, Hepatic transaminitis

Suspect Drug (D.1): Drug: Hydroxychloroquine / Dose: 400 mg x24h then 200mg/ Frequency: BID/ Route: NG/ Approximate Duration: 1 Day(s)

Drug: Azithromycin / Dose: 500mg x1 then 250mg/ Frequency: QD/ Route: NG/ Approximate Duration: 2 Day(s)

Treatment Dates (D.3): 2020

Diagnosis for Use/Indication (D.4): COVID-19

Confidentiality Requested (G.5): No