

1. APPENDIX 6

1.1. Narratives for Cases of Suicides in Clinical Trials

Table 1.1 Patient Identifiers of Patients who Completed Suicide during Paroxetine Clinical Trials

| Patient Number | Study | Study Treatment |
|-----------------------|-------------------------|----------------------------|
| 083.003.1090 | 29060/083 | Paroxetine |
| 1 13 126 | MDUK 13 Wade | Paroxetine |
| 2206 005 | Belgian MC Open | Paroxetine |
| 2406.149 | German MC Comparative | Paroxetine |
| 245.161.0163 | 29060/245 | Paroxetine |
| 502.037.05146 | 29060/502 | Paroxetine |
| 6 47 003 | HP 82 47a Vervarcke | Paroxetine |
| 650.307.06282 | 29060/650 | Paroxetine |
| 7124.012 | DFG 124 P32 | Paroxetine |
| 057.012.1217 | 29060/057 | Placebo |
| 627.605.01012 | 29060/627 | Placebo |
| 785.721.00716 | 29060/785 | Placebo |
| 197.045.0322 | 29060/197 | Comparator – Imipramine |
| 2371 054 | MDF 1727 MC Comparative | Comparator –Clomipramine |
| 6 67 002 | HP 83 67 Margo | Comparator – Amitriptyline |
| 7124 023 | DFG 124 P32 | Comparator – Imipramine |
| 7124 060 | DFG 124 P32 | Comparator – Imipramine |

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Seroxat Article 31 - Consolidated Response Document - January 04

Table 1.2 Study Treatment Start and Stop Dates and Date of Death for Patients who Committed Suicide during Paroxetine Clinical Trials

| Patient Number | Study Treatment | Study Type | Study Treatment | | Suicide |
|----------------|-----------------|--------------|-----------------|-------------|-------------|
| | | | Start Date | Stop Date | Date Died |
| 083.003.1090 | Paroxetine | Uncontrolled | 10 Apr 1989 | 17 Apr 1989 | 18 Apr 1989 |
| 1 13 126 | Paroxetine | Active Cont | 28 Feb 1984 | 19 Jul 1984 | 20 Jul 1984 |
| 2206 005 | Paroxetine | Uncontrolled | 13 Jul 1985 | 10 Jan 1986 | 10 Jan 1986 |
| 2406.149 | Paroxetine | Active Cont | 11 May 1987 | 17 Jun 1987 | 24 Jun 1987 |
| 245.161.0163 | Paroxetine | Active Cont | 20 Jan 1994 | 22 Jan 1994 | 22 Jan 1994 |
| 502.037.05146 | Paroxetine | Placebo Cont | 10 Jun 1997 | 14 Jul 1997 | 14 Jul 1997 |
| 6 47 003 | Paroxetine | Active Cont | 16 Feb 1983 | 27 Mar 1983 | 03 Apr 1983 |
| 650.307.06282 | Paroxetine | Uncontrolled | 24 Mar 2000 | 30 Mar 2000 | 30 Mar 2000 |
| 7124.012 | Paroxetine | Active Cont | 08 May 1987 | 16 May 1987 | 17 May 1987 |
| 057.012.1217 | Placebo | Placebo Cont | 27 Apr 1991 | 16 Jul 1991 | 18 Aug 1991 |
| 627.605.01012 | Placebo | Placebo Cont | 13 Feb 1999 | 01 Mar 1999 | 18 Mar 1999 |
| 785.721.00716 | Placebo | Placebo Cont | 31 May 2001 | 10 Jul 2001 | 29 Jul 2001 |
| 197.045.0322 | Imipramine | Active Cont | 06 Dec 1994 | 27 Dec 1994 | 28 Dec 1994 |
| 2371 054 | Clomipramine | Active Cont | 29 May 1987 | 10 Jul 1987 | 10 Aug 1987 |
| 6 67 002 | Amitriptyline | Active Cont | 18 Oct 1983 | 15 Nov 1983 | 29 Nov 1983 |
| 7124 023 | Imipramine | Active Cont | 13 Feb 1987 | 02 Mar 1987 | 02 Mar 1987 |
| 7124 060 | Imipramine | Active Cont | 01 Dec 1987 | 27 Dec 1987 | 27 Dec 1987 |

Patient 083.003.1090

Study Medication: Paroxetine

Cause of Death: Suicide (by hanging)

This 58 year old female had hypertension on entry to the study. She had been receiving metoprolol 100mg daily and amiloride plus hydrochlorothiazide from day -54. She had suffered five or six previous episodes of depression for which she had received treatment with bi/tri/tetracyclic antidepressants and benzodiazepines. The duration of the present episode of depression was recorded as 1 to 3 months. She had received previous treatment for this episode with bi/tri/tetracyclic antidepressants, which were stopped on day -1, and benzodiazepines, which were stopped on day -4.

The patient received 20mg paroxetine from days 0 to 8. She also received temazepam 20mg, twice or three times daily, from day 0, and chloral hydrate 500mg daily from day 1.

The patient experienced a moderately decreased appetite and mild dryness of the mouth from day 2; both events were considered to be probably related to study treatment.

The patient did not have any double flagged changes in vital signs data and only baseline laboratory assessments were performed.

On day 8 the patient committed suicide by hanging (preferred term: emotional lability). The investigator considered this to be unrelated to study treatment.

Patient 1 13 126

Study Medication: Paroxetine

Cause of Death: Suicide (by hanging)

This 50 year old male had been depressed since his wife was last admitted to the Oncology Department just after Christmas 1982. His wife died due to breast cancer on 15 Jan 1983.

His depression was worsened by being made redundant in Dec 1983. Since becoming unemployed he had been very depressed, only slept 3-4 hours per night, and said he wished he developed a fatal illness but would not consider suicide. When the patient was widowed he was left with only one of two sons at home. This son is going abroad to work and the patient was not looking forward to him leaving.

The patient received study treatment (30mg paroxetine) for over 4 months. He was taking Mogadon (nitrazepam) at night to help him sleep. He occasionally used alcohol, and had no history of drug abuse.

On 20 Jul 1984 the patient committed suicide by hanging. He had made no previous suicide attempts. The investigator considered the suicide was not directly related to study medication

Patient 2206 005

Study Medication: Paroxetine

Cause of Death: Death (by hanging)

This patient was a 58 year old female who was diagnosed with depression with psychotic features. She was admitted to hospital on 09 Jul 1985. The duration of the episode on admission was 6 months. She had had two previous episodes and had received amitriptyline and lithium.

Her family history includes a brother who committed suicide (after a bankruptcy) and her mother had a few psychiatric hospitalisations. She had a compulsive personality, could not cope with the difficulties of each day, and felt worthless since the death of her husband in 1984.

She had made a previous suicide attempt shortly before her admission to hospital. The patient returned home from hospital on 22 Nov 1985. She committed suicide on 10 Jan 1986 by hanging herself. She had taken paroxetine 30mg/day for over 4 months.

Patient 2406.149

Study Medication: Paroxetine

Cause of Death: Suicide (overdose)

This 18 year old female had no concurrent illness and was not receiving concurrent medication at baseline.

She experienced a mild dry mouth, which the investigator considered to be drug related, from day 5 for 25 days and a mild eye disorder of unknown relationship to therapy.

The patient received diazepam from day 32 because of increasing restlessness (agitation) and on day 38 she stopped paroxetine treatment and left the clinic. On day 44 the patient committed suicide by overdosage. No further details were available.

The patient had no double flagged laboratory or vital signs data.

Patient 245.161.0163

Study Medication: Paroxetine

Cause of Death: Suicide (jumped from window)

The patient was a 67 year old female with no previous episodes of depression. She had had her current episode for approximately 3 months on entry into the study. The patient was started on paroxetine. She was not taking any concomitant medication.

On day 2, the patient committed suicide by throwing herself out of a third floor window. The investigator considered the suicide to be unrelated to study medication

Patient 502.037.05146

Study Medication: Paroxetine

Cause of Death: Suicide (suspected overdose)

Case reference 97017163-1 is a clinical trial report from study 29060/502 which is a double blind study, referring to a male patient aged 23 years.

On the 10 June 1997, the patient started taking study medication for social phobia. He received paroxetine at daily doses of 20mg from 10 Jun 1997 to 23 Jun 1997, 30mg from 24 Jun 1997 to 30 Jun 1997, 40mg from 01 Jul 1997 to 07 Jul 1997, and 50mg from 08 Jul 1997 to 14 Jul 1997. The patient failed to present for a scheduled appointment on 15 July 1997; the investigator was later informed that the patient committed suicide on 14 July 1997.

According to the patient's mother, the patient had stolen a large amount of his grandmother's medication (bisporolol hemifumarate, isosorbide dinitrate, nitrazepam). An autopsy has been refused by the patient's parents.

The investigator considered that the events were probably unrelated to study medication and could possibly be associated with the patient's primary condition

Patient 6 47 003

Study Medication: Paroxetine

Cause of Death: Suicide (by drowning)

This patient was a 56 year old female who received 30 mg/day paroxetine from days 7 to 47, having previously received 10mg and 20mg/day. Medical history included a myocardial infarction 4 years previously. Isosorbide dinitrate (15mg daily) and metoprolol tartrate (300mg daily) were taken as concomitant medication throughout the study. There was a family history of mental illness. Her mother was suffering from mental disease when she died at 65 years, her father died at 62 years by committing suicide, and two brothers and two sisters have present recurrent depression.

The patient overdosed (on flunitrazepam) on day 40. She committed suicide by drowning on day 47 of the study period during treatment with active medication. Relationship to study treatment was given as "unknown". Her clinical state, as measured by the Hamilton Depression Rating Scale, had improved during the course of the trial, potentially giving her the volition to kill herself. It is known that 15% of patients with depressive illness die by suicide.

Patient 650.307.06282

Study Medication: Paroxetine

Cause of Death: Suicide (Shooting)

Case reference number 2000009299-1 is a clinical trial report from the single blind phase of blinded study 29060/650 for the treatment of post traumatic stress disorder. This report refers to a 35 year old male (patient identification number (650.307.06282).

The patient's medical history included a suicide attempt in 1993.

The patient received oral single blind paroxetine from 24 March 2000 until 30 March 2000 at dose 20mg daily. On 30 March 2000, 7 days after the first dose of study medication, the patient committed suicide with a gun in his car after his wife told him that she wanted a divorce.

The investigator considered this to be a serious event because it was fatal. An autopsy was not performed.

The investigator reported the suicide with a fire weapon as unrelated to treatment with study medication and to be probably associated with the family condition.

Patient 7124.012

Study Medication: Paroxetine

Cause of Death: Suicide (overdose)

This 42 year old female had been depressed for 16 weeks. She had experienced two other episodes of depression in the previous 10 years and had been treated with mianserin and maprotiline; neither gave a satisfactory response. For the current episode of depression she had received alprazolam 1.5mg daily for 3 weeks, clomipramine 300mg daily and thioridazine 150mg daily for one week, and she had been taking diazepam 15mg daily for 12 months. She also took oxazepam (dose unspecified) from day -3 to day -2 and chloral hydrate from day -3 to day 8.

She experienced mild hyperkinesia from day 6 which the investigator considered to be unrelated to therapy.

On day 10 the patient committed suicide by overdosing with doxepin. The relationship of this event to paroxetine therapy was unknown.

Patient 057.012.1217

Study Medication: Placebo

Cause of Death: Suicide

This 32 year old male attempted suicide by taking 60 x 10mg temazepam capsules on day 29. Later in the study he ate toxic plants as a suicidal gesture (Day 57); he suffered from abdominal pain, nausea and headache (no doubt as a result of this). On Days 106 and 113, more than 14 days after the last dose of study medication, the patient made further attempts (toxic seeds and intoxication by motor car gas). Finally, 33 days after completion of the study, he died. His death was considered to be unrelated to trial therapy.

Patient 627.605.01012

Study Medication: Placebo

Cause of Death: Suicide

Case reference number 1999005430-1, is a clinical trial report from blinded study 29060/627 for post-traumatic stress disorder. This report refers to a 39 year old male (patient identification number 627.605.01012).

The patient's medical history includes major depression, social phobia, panic disorder, agoraphobia, obsessive compulsive disorder and suicidal ideation (since 1996). Concomitant medications include gliclazide, metformin hydrochloride and captopril.

The patient received oral study medication (placebo dose level 1) from 13 February 1999. On 19 February 1999, some 7 days after the first dose, the patient experienced severe depressive symptoms which worsened over the next 2-3 weeks. During this time, the patient experienced extreme post-traumatic stress disorder symptoms, including strong feelings of agitation, social withdrawal and suicidal ideation. (The patient was advised at last visit to seek extensive help, primarily electroconvulsive therapy). The patient was diagnosed as having acute depression. The patient was treated for the event with clotiapine, oxazepam and fluoxetine.

Treatment with study medication was stopped due to the depression on 01 March 1999 and the patient was withdrawn from the study. The patient reported to be feeling better and denied having any thoughts of suicide, however, at times, he appeared to be agitated. He was discharged from hospital on 12 March 1999. On 15 March 1999, the patient underwent electroconvulsive therapy as an out-patient (last treatment of 6) and his condition was reported as much improved. A follow-up visit was scheduled for 19 March 1999. The investigator considered this to be a serious event because it was life threatening, disabling, incapacitating and required hospitalisation.

The investigator reported the acute depression to be unrelated to treatment with study medication. The investigator reported that the event could be associated with the patient's primary condition.

On 18 March 1999, some 17 days after the last dose of study medication, the patient committed suicide by shooting himself. An autopsy was performed by the State Pathologist, but the report was unavailable.

The investigator reported the patient's suicide as unrelated to treatment with study medication. The investigator reported the event could be associated with the patient's primary condition and major depression.

Patient 785.721.00716

Study Medication: Placebo

Cause of Death: Suicide

This report refers to a 31 year old male (patient identification number 785.721.00716) who participated in double-blind study 29060/785 for the treatment of major depressive disorder with anxiety.

The patient's medical history included a hemangioma left facial distribution, allergy to pollen, and hayfever. The patient had no concomitant medication use.

The patient received study medication from 31 May 2001 to 10 Jul 2001. On 29 Jul 2001, 19 days after completing the study and the last dose of study medication, the patient's brother called to report the patient passed away. A second call from the patient's brother confirmed the patient committed suicide.

The investigator reported the suicide as not related to treatment with study medication and probably associated with major depressive disorder.

Patient 197.045.0322

Study Medication: Imipramine

Cause of Death: Suicide

On entry to the study (a comparison of paroxetine and imipramine in the treatment of depression and behavioural disturbance associated with dementia), this 70 year old Caucasian male had a history of headache and neck rigidity. He was stable on oxazepam on entry to the study. The present episode of depression had lasted for more than 1 year and had been treated with bi/tri/tetracyclic antidepressants and oral neuroleptics. He received imipramine in the study.

On day 13 the patient experienced severe restlessness lasting one day but recovered without sequelae. On day 22 the patient committed suicide (severe adverse experience of emotional lability) and was considered to have been withdrawn from the study. The investigator considered both events to be unrelated to study medication.
