

Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name: Extracorporeal Shock Wave Therapy Device

Device Trade Name: Dornier Epos? Ultra

Applicant's Name and Address: Dornier Medical Systems, Inc.
1155 Roberts Boulevard
Kennesaw, Georgia 30144

PMA Number: P000048

Date of Notice of Approval to Applicant: January 15, 2002

II. Indications for Use

The Dornier Epos Ultra is a non-surgical alternative for the treatment of chronic plantar fasciitis for patients with symptoms of plantar fasciitis for 6 months or more and a history of unsuccessful conservative therapy. Plantar fasciitis is defined as the traction degeneration of the plantar fascial band at its origin on the medial tubercle of the calcaneus.

III. Contraindications

None known.

IV. Warnings and Precautions

The warnings and precautions can be found in the device labeling.

V. Device Description

The Dornier Epos™ Ultra is an extracorporeal shock wave therapy (ESWT) system. The Epos Ultra consists of a transportable cart housing the electromagnetic shock wave circuit, the hand held control unit, the CPU, a water circuit and the ultrasound subsystem. A therapy head mounted to the articulated arm, the hand control unit and the power cable are attached to the exterior of the cart. An ultrasound imaging system with a 7.5 MHz transducer is located on top of the cart. An isocentric locating arm fixed to the therapy head is used for positioning the therapy focus into the treatment area. In addition, the ultrasound is used to observe and monitor the shock wave treatment.

The shock wave source of the Epos™ Ultra uses electromagnetic technology to generate shock waves. Shock waves are acoustic waves that are characterized by a quick rise time of a few nanoseconds to a high maximum positive pressure (amplitude) of more than 80 Mpa (1 Mpa=10 bar). A pulse of electrical energy flowing through a disc coil at the base of the therapy head induces strong magnetic fields, which produce forces that propel the membrane producing a plane pressure wave. The shock waves travel through the water filled coupling cushion mounted to the therapy head, where they are precisely focused by an acoustic lens to the target tissue.

Figure 1 gives a pictorial view of the Dornier Epos™ Ultra System.

Figure 1: Dornier Epos™ Ultra



Chronic plantar fasciitis is a common cause of heel pain. It is the most common diagnosis for pain in the inferior aspect of the heel.

Current conservative treatments for plantar fasciitis include:

- Rest
- Physical therapy
- Heel cushions
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroid injections
- Taping
- Orthotics
- Shoe modifications
- Nightsplinting
- Casting

Current non-conservative treatments for plantar fasciitis include:

- Surgery

VII. Marketing History

Epos™ Ultra devices have been marketed in Europe, Russia, Africa, Middle East, Asia, Japan, Australia, Canada and South America. The Epos™ Ultra devices received a CE mark and were first distributed in November 1996. The Epos™ Ultra has not been withdrawn from marketing for any reason relating to its safety or effectiveness.

VIII. Adverse events of the Device on Health

The adverse events that occurred during the clinical study are listed under Tables 6 8 7. The adverse events observed during treatment with the Dornier Epos™ Ultra include:

- Pain and/or discomfort during treatment
- Pain or swelling for a brief period following treatment
- Localized numbness, tingling or decreased sensation in the foot or at the site of shock wave delivery; and
- Local subcutaneous hematoma, minor bruising, or petechial bleeding in the foot or at the treatment site

Other potential adverse events may include:

- Rupture of the plantar fascia
- Possible bleeding and/or infection at the injection site related to injection of local anesthetic

Temporary or permanent nerve damage associated with the injection or shock wave treatment
Misdirection of extracorporeal shock wave energy to a major nerve or blood vessel, resulting
in injury; and/or
Anesthesia complication, including allergic reactions to local anesthetic agents

IX. Summary of Non-clinical Studies

Shock Wave Characterization Produced by the Epos™ Ultra

The Dornier Epos™ Ultra's therapy head with the 14Qmm diameter EMSE 0-80 is designed as a standard lithotripsy therapy head for orthopedic shock wave applications. The 140mm diameter EMSE, which produces the shock waves, was previously approved for use in the Dornier Compact S Lithotripter in P840008, Supplement 62. Shock wave measurements produced by the EMSE 0-80 shock wave emitter were characterized and documented in accordance with the parameters defined in the FDA *Draft of Suggested Information for Reporting Extracorporeal Shock Wave Lithotripsy Device Shock Wave Measurements* and IEC 1846. Measurements were recorded using a fiber optic hydrophone.

Measurements of the shock wave field of the EMSE 0-80 were recorded at the minimal, typical and maximum energy settings as defined in the study protocol. Calculations of focal energy per pulse are based upon equation (4) in section 2.3, Beam Energy, of the draft guidance. The values were calculated including positive and rarefaction portions of the waves. Completion of calculations determined minimal shock-to-shock variation over the minimum, typical and maximum intensity settings for 5mm, 10mm and 12mm diameters of the pulse frequency ranges, demonstrating the accuracy of the EMSE pressure pulse generator.

The testing also included measurements of pulse intensity integral and effective energy as defined in the guidance. Both parameter values for positive signal and for the complete signal including rarefaction were measured and documented.

EMI / EMC Testing

Testing was conducted on the Epos™ Ultra without ultrasound to demonstrate compliance with EN 60601-1-2. This standard regulates the EMI/EMC of medical equipment that includes compliance with EN 55011 for radio frequency emissions, IEC 801-2, IEC 801-3, IEC 801-4, and IEC 801-5 represent immunity to electrostatic discharge (ESD), immunity to radio frequency electromagnetic fields, immunity to fast transients (bursts), and immunity to surges.

Testing was conducted on the ultrasound unit used in this study to demonstrate compliance with IEC 60601-1-2 (for EMC) and IEC 950 (for external TV monitors and other peripherals).

Other Testing

Testing was conducted with the Epos™ Ultra in accordance with 21 CFR 1010, *Performance Standards for Electronic Products: General*.

In Vitro and Animal Studies

In vitro or animal experiments were not conducted with the Dornier Epos™ Ultra. Previous studies with similar Dornier lithotripters were used to support safety of the Epos Ultra because shock waves are produced similarly.

X. Clinical Studies

Study Design and Objectives

The study was designed as a multicenter, randomized, placebo-controlled, prospective, double masked clinical study of patients with plantar fasciitis with at least moderate pain for at least six months and a history of prior conservative therapy with two groups: a group receiving ESWT with the Epos™ Ultra and a control group receiving a sham treatment. A total of 150 patients were enrolled at six clinical centers. The original randomization provided allocation for 75 Active and 75 Sham patients, i.e., one Active patient to one Sham patient; however, one patient in the Sham group erroneously received an Active treatment making the allocation 76 in the Active group and 74 in the Sham group. The study was conducted to determine whether a single, outpatient extracorporeal shock wave treatment can safely and effectively relieve the pain associated with plantar fasciitis. The follow-up visits occurred at 3-5 days, 6 weeks, 3 months, 6 months, and 12 months after treatment. After 3 months, patients who were treated with Sham treatment were offered an Active unmasked treatment in the open label extension study if they still met inclusion criteria. This was done after the masked 3 month safety and effectiveness outcome assessments were collected.

The primary efficacy endpoint was the difference between the active Epos™ Ultra treatment and the sham Epos™ Ultra treatment at 3 months post-treatment in the improvement from baseline in the VAS score for pain while walking for the first few minutes in the morning using a repeated measures analysis with covariates. In addition to evaluating the actual changes in pain score, the proportion of patients achieving at least **60%** improvement in pain while walking for the first few minutes in the morning was compared between treatment groups at 3 months.

The secondary efficacy endpoints were the difference between groups in the improvement from baseline at 3 months post-treatment of the pain evaluation from the AOFAS Ankle-Hindfoot Scale Score, the Roles and Maudsley Score, the SF-12 health status questionnaire, pain measurement on palpation with a pressure threshold meter, and the ROM Assessment from the AOFAS Ankle-Hindfoot Scale Score. Safety was assessed as the number of adverse events and severity of complications that were related to extracorporeal shock wave therapy.

Subject Inclusion and Exclusion The principal inclusion criteria were:

- Greater than 18 years old
- Symptoms present for greater than 6 months as assessed by patient history
- Visual Analog Scale (VAS) score of >5 for pain during the first few minutes of walking in the morning
- History of 6 months of unsuccessful conservative therapy to include any NSAIDS and two other conservative therapies
- Roles and Maudsley Score of 3 or 4
- Signed informed consent
- Single site of tenderness with local pressure over the medial calcaneal tuberosity on passive dorsiflexion of the foot

The principal exclusion criteria were:

- Previous treatment with any other conservative therapies within two weeks of treatment;
corticosteroid injection within one month of treatment
- Previous surgery for plantar fasciitis
- History or documented evidence of autoimmune disease
- History or documented evidence of peripheral vascular disease
- History or documented evidence of Type I or Type II diabetes mellitus
- History or documented evidence of peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome, etc.
- History or documented evidence of systemic inflammatory disease such as rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, etc.
- History or documented evidence of a bleeding disorder or hemophilia

Study Methodology

At screening and follow up, data collection included: history and physical exam, pain measurement on palpation with pressure threshold meter, VAS pain score questionnaires, SF- 12 health status questionnaire, AOFAS Ankle-Hindfoot Scoring System questionnaire, and Roles and Maudsley questionnaire. Patients were asked which treatment they believed they received as an assessment of masking.

Study Enrollment

A total of three patients from the Active group and one patient from the Sham group discontinued prior to the 3 month follow up visit. Enrolled patients underwent a single, outpatient ESWT session after being randomized to an active (76 patients) or sham (74 patients) treatment. Follow up compliance at 3 months was **96.1%** in the Active group and **98.6%** in the Sham group. Two females and one male in the Active group and 1 female in the Sham group discontinued prior to the 3 month follow-up visit. Table 1 provides a summary of patients enrolled and treated.

Table 1: Patient Accounting up to 3 month follow-up visit

Reason	Active Treatment Pts (N = 76)	Sham Treatment Pts (N = 74)
Patient lost to follow-up	1	0
Adverse event ¹	1	0
Lack of effectiveness of treatment	1	1
Follow-up frequency	73 (96.1%)	73 (98.6%)

1. This event was reported as severe pain during treatment despite local anesthesia use

Baseline Characteristics

There were differences between treatment groups in gender (p=0.02), height (p=0.01), and the use of taping as a pre-treatment conservative therapy (p=0.02) of baseline characteristics. No significant differences were found between treatment groups in any of the other characteristics which included age, weight, affected foot, participation in a weekly exercise program, duration of plantar fasciitis symptoms, and the requirement of standing while at work. Table 2 below provides patient demographics for both active and sham treatment groups. Table 3 provides baseline values for the primary and secondary endpoints.

Table 2: Patient Demographics

Characteristic		Active Treatment Patients (n =76)	Sham Treatment Patients (n = 74)	p-value ¹
Age (years)	Mean	50	53	NS
	Range	26-69	31-72	
Gender	Male	14 (18.0%)	27 (36.5%)	NS
	Female	62 (81.6)%	47 (63.5%)	
Height (inches)	Mean	66	68	0.0131
	Range	60.4-77.0	56.0-79.5	
Weight (lbs)	Mean	180	186	NS
	Range	120.0-294.0	115.0-390.0	
Affected Foot	Right	46%	55%	NS
	Left	54%	45%	NS
Required to Stand		55%	68%	NS
Participation in weekly exercise		55%	60%	NS
Duration of symptoms (months)	Mean	22	24.1	NS
	Range	6-120	3.0-99.0	

1. p-value associated with 2-way ANOVA for continuous parameters, & Cochran-Mantel Haenszel for categorical variables.

Table 3: Baseline Values for Primary and Secondary Endpoints

Parameter	Active Treatment Patients (n = 76)	Sham Treatment Patients (n = 74)	p-value (n = 150)
VAS Pain 1° Endpoint (0-10) Mean Range	7.7 5.0-10.0	7.7 4.7-10.0	.9644
Mean AOFAS Pain Severe = 0 Moderate = 20 Mild = 30 None = 40	13.4	12.2	.4746
Mean Roles & Maudsley Score Excellent = 1 Good = 2 Fair = 3 Poor = 4	3.8	3.8	.3217
Mean SF-12 (Mental)	53	52	.2410
Mean SF-12 (Physical)	39	38	.4733
Mean AOFAS ROM-Saggital Normal/Mild = 8 Moderate = 4 Severe = 0	7.4	7.0	.0710
Mean AOFAS ROM-Hindfoot Normal/Mild = 6 Moderate = 3 Marked = 0	5.5	5.5	.6954
Pain on Palpation (kg) Mean Range	5.8 1.1-15.9	5.6 1.3-13.3	0.4533

Treatment Characteristics

The procedure for active and sham treatments was performed identically except that for patients randomized to sham, a thin air cushion was placed on the therapy head prior to the patients arrival to the treatment room. The treatment was administered by a physician who did not perform follow-up evaluations. All patients received an injection of 5ml of 1% Xylocaine into the medial calcaneal branch of the tibial nerve. Eleven percent (**10.5%**, 8/76) of patients in the Active group and **4.1%** (3/74) of patients in the Sham group received additional anesthesia during treatment.

The average treatment time was 21 minutes in the Active group and 19.8 minutes in the Sham group. The therapy was delivered by administering a total of 3800 shock waves to reach an approximated total energy delivery of 1300 mJ/mm. The mean number of shocks delivered was 3742 in the Active group and 3744 in the Sham group. Patients were not informed of their randomization until after 3 months.

In the Active group, 45/76 patients (**59.2%**) correctly guessed that they received an Active treatment and 31/76 believed they received a Sham treatment or were not sure. Eighty-four percent (**84.4%**, 38/45) of patients who believed they received an Active treatment also experienced pain during treatment. Of the 31 patients who guessed that they received a Sham treatment or were not sure, 17/31 (**54.8%**) experienced pain during treatment. Although Active patients who reported pain during treatment were more likely to have reported active therapy in the blinding verification, there was no difference at any follow-up visit in the change from baseline in the VAS score as assessed by the patient for pain with the first few steps in the morning between active patients who believed they received an active treatment and those who believed they received a sham treatment ($p>0.51$).

In the Sham group, 11/74 (**14.9%**) patients correctly guessed that they received the Sham treatment and 63/74 (**85.1%**) believed they received an Active treatment or were not sure. No patient who correctly guessed they received a Sham treatment experienced pain during treatment. Five patients who believed they received an Active treatment experienced pain during treatment. Sixty-nine patients (**93.2%**) in the Sham group did not experience pain during treatment.

The incidences of device malfunctions were also recorded during the clinical trial. Table 4 summarizes the device malfunctions that occurred for both Active and Sham patients. A total of eight device malfunctions occurred during the clinical study, four in the Active group and four in the Sham group. Two malfunctions, one in the Active group and one in the Sham group, were related to the printer, which is used in conjunction with the ultrasound to print images from the ultrasound screen. The malfunction in the Sham group occurred prior to treatment when the printer would not print. After adjusting the printer cable, the video printer functioned as intended and treatment began. The malfunction in the Active group occurred during treatment. The printer cable had to be adjusted in order to obtain an image of the patient's foot. Treatment continued and was completed according to protocol.

One device malfunction occurring in the Active group during treatment was related to a drop in the frequency of the shock wave delivery. It was determined that this occurred due to overheating of the device. The treatment continued with the patient receiving the appropriate amount of shocks at a reduced intensity level.

One device malfunction occurring in the Sham group was related to an intermittent display problem with the hand control unit which did not affect the delivery of shock waves. Treatment was completed according to protocol.

Four malfunctions, two in the Active group and two in the Sham group, occurred during treatment when the machine would not deliver shocks. These malfunctions were determined to be related to a connection problem with the hand switch, which allows the delivery of shock waves.

No patient in either group experienced any adverse events as a result of the device malfunction, and all patients remained blinded to their treatment randomization.

Table 4: Device Malfunctions

	Active Treatment Patients (n = 76)	Sham Treatment Patients (n = 74)	Total (n = 150)
Total Malfunctions	4 (5.3%)	4 (5.4%)	8 (5.3%)
Before Treatment	0 (0.0%)	1 (25.0%)	1 (12.5%)
During Treatment	4 (100%)	3 (75.0%)	7 (87.5%)

Primary Endpoint

In the Active group, the mean pain score decreased from 7.7 +1.4 at baseline to 3.4 + 2.8 at 3 months post-treatment, a mean percent improvement of **56.5%**. In the Sham group, the mean score decreased from 7.7 + 1.5 at baseline to 4.1 t 3.1 at 3 months post-treatment, a mean percent improvement of **46.6%**. The change from baseline to 3 months in VAS pain due to treatment was statistically significant using a repeated measures analysis (p=0.0149), with covariate analysis and without imputing missing data (3 active patients and 1 sham patient) as summarized in Table 5.

The proportion of patients achieving at least **60%** improvement in pain during the first few minutes of walking in the morning was compared between treatment groups at 3 months. Fifty- six percent (**56.2%**) of the Active group demonstrated **60%** improvement from baseline in their VAS scores or greater reduction in their pain, compared to **45.2%** of the patients in the Sham group. This was not statistically significant.

Table 5: VAS Scores for Active and Sham Patients Baseline Through 3 months Post

		Baseline	3-5 days	6 weeks	3 months	Change from baseline
Active Treatment Patients	N	76	74	72	73	--
	Mean	7.7	5.0	4.6	3.4	-4.4
	SD	1.4	2.8	3.1	2.7	2.8
Sham Treatment Patients	N	74	74	71	73	--
	Mean	7.7	5.7	5.0	4.1	-3.6
	SD	1.5	2.8	3.0	3.1	3.1

The clinical data showed that on average, patients with a lower baseline VAS score, a shorter duration of symptoms, or a lower body mass index (BMI) had a higher improvement in VAS pain score.

Secondary Endpoint

The Roles and Maudsley pain score was used as a secondary endpoint. At 3 months post-treatment, the distribution of patients in the four categories, excellent, good, fair, and poor, was

found to be statistically significant between the treatment groups (p=0.03) with **61.6%** of Active patients having good to excellent results, compared to only **39.7%** of Sham patients.

The SOFAS Ankle-Hindfoot Scale and the SF12 Health Status Questionnaire, which did not show statistically significant change between active and sham patients, over time were also used as secondary endpoints.

Safety Results

Adverse events were evaluated by type, nature, severity and intensity during treatment and at each follow up visit. No study subject experienced an unanticipated serious device-related adverse event during the course of the study.

All but one complication resolved with little or no intervention. The most common complications were pain during treatment and pain 3-5 days post-treatment. Pain during treatment occurred in **72.4%** Active patient group and **6.8%** Sham patient group. Pain during treatment was recorded on a scale of 1-10 (mild-severe) with a mean score during treatment of 3.5 in the Active group and 0.2 in the Sham group. Pain post-treatment at 3-5 days was reported in **40.8%** of Active patients (31/76) and **35.1%** of Sham patients (26/74).

Table 6 summarizes the adverse events related to ESWT at treatment through 3 month follow up. Other than pain during treatment, there were no differences in the nature or type of adverse events reported between the Active and Sham groups. There were no serious unanticipated adverse device effects to report related to ESWT.

Table 6: Adverse events Treatment Through 3 Months Follow Up

Adverse Event	Active Treatment Patients (n = 76)			Sham Treatment Patients (n = 74)			p-value
	Number of Patients ¹	Number of Occurrences	% of Patients	Number of Patients ¹	Number of Occurrences	% of Patients	
Pain During Treatment ²	55	55	73%	5	5	7%	<0.001
Pain Post Treatment ³	28	31	37%	24	26	32%	1.0000
Edema	5	5	7%	6	7	8%	0.3655
Echymosis	5	5	7%	4	4	5%	1.0000
Petechiae	0	0	0%	1	1	1%	0.4933
Rash	1	1	1%	0	0	0%	1.0000
Hypesthesia	2	3	3%	6	6	8%	1.0000
Neuralgia	1	1	1%	0	0	0%	1.0000
Paresthesia	3	3	4%	3	4	4%	1.0000
Total Events	104			53			---

1. Number of patients experiencing at least one occurrence
2. Pain during shock wave application: statistical significance with p-value <0.0001 by Fischer's Exact Test
3. Pain experienced immediately after treatment through 3 month follow -up

but one adverse event was reported by the investigator as not serious: one patient reported strong pain at the 3 month follow-up visit. The event resolved without intervention before the patient was exited from the study.

All but one adverse event had resolved: one patient in the Active group reported paresthesia of the lateral distal part of the plantar surface at the 3-5 day follow-up visit. The ankle-foot sensation testing was abnormal for all four locations at the 3-5 day follow-up visit. The patient was prescribed ibuprofen, ice, and rest and was referred to a neurologist for further evaluation, with abnormal ankle/foot sensation testing at locations 1,2,3, but normal at location 4. The neurologist report noted irritation of the N. plantaris lateralis with no loss of muscle strength. This adverse event was reported as unresolved at the 3 month visit. The patient was seen at the 6 month follow-up visit and the adverse event was again reported as unresolved. The patient discontinued from the study before the 12 month follow-up.

Adverse events were evaluated through 12 months for Active and Sham patients. No adverse events were reported in the Active group after the 3 month follow-up visit. Adverse events for patients who originally received Sham treatment who elected Active unmasked treatment were also evaluated. The events, which are summarized in Table 7 below, were evaluated through 12 months after initiating Active unmasked treatment. Of the 73 Sham patients remaining at the 3 month follow-up visit, 51 elected to receive the unmasked Active treatment. Adverse events reported through 12 months for these patients are presented in Table 7 below.

Table 7: Adverse Events for Open Label Active Treatment of Patients Originally Randomized to Sham Treatment Through 12 Months Follow Up

Adverse event	X-over Treatment (n = 51)		3-5 day		6 weeks		3 months		6 months		12 months	
	pts ¹	occur	pts ¹	Occur	pts ¹	occur	pts ¹	occur	pts ¹	occur	pts ¹	occur
Pain during Treatment	26	26	--	--	--	--	--	--	--	--	--	--
Pain post Treatment	--	--	11	11	3	3	3	4	2	2	0	0
Edema	--	--	7	7	0	0	0	0	0	0	0	0
Ecchymosis	--	--	1	1	0	0	0	0	0	0	0	0
Petechiae	--	--	1	1	0	0	0	0	0	0	0	0
Paresthesia	--	--	1	1	1	1	0	0	0	0	0	0
Infection	--	--	0	0	0	0	1	1	0	0	0	0
Injection Site Hemorrhage	--	--	1	1	0	0	0	0	0	0	0	0

1. Patients experiencing at least one occurrence within each interval

Conclusions drawn from the Studies

The preclinical and clinical data provide reasonable assurance that the Dornier Epos™ Ultra device is safe and effective when used in accordance with the device labeling.

XI. CDRH Decision:

Approval for this PMA was issued on January 15, 2002. FDA inspection of the manufacturing facility determined that the applicant was in compliance with the Quality Systems Regulation (21 CFR 820).

XII. Approval Specifications:

Directions for use: See the Labeling.

Hazard to health from the use of the device: See the Warnings, Precautions, and Adverse effects section in the Labeling.

Postapproval Requirements and Restrictions: See Approval order.