

P970062



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

JUN 24 1998

Mr. David R. Balzer, Jr.  
Official Correspondent  
BMT, Inc.  
660 Main Street South, Suite 7  
Woodbury, Connecticut 06798

Re: P970062  
Genestone 190 Lithotripter  
Filed: December 23, 1997  
Amended: February 17, March 30, and April 3, 1998

Dear Mr. Balzer:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Genestone 190 Lithotripter. This device is indicated for use in the non-invasive fragmentation of kidney (renal pelvic and renal calyceal) and upper ureteral stones between 5 and 20mm in size. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the following information:

Valid scientific evidence which evaluates the long-term effects of the Genestone 190 Lithotripter on hypertension.

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

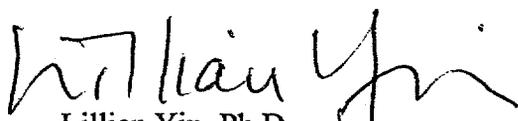
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Blvd.  
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Nicole L. Wolanski at (301) 594-2194.

Sincerely yours,



Lillian Yin, Ph.D.  
Director, Division of Reproductive,  
Abdominal, Ear, Nose and Throat,  
and Radiological Devices  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

Issued: 3-4-98

#### CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effectuated" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effectuated" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effectuated." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mix-up of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and.....

(a) has not been addressed by the device's labeling or.....

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc. Any written report is to be submitted to:

Food and Drug Administration  
Center for Devices and Radiological Health  
Medical Device Reporting  
PO Box 3002  
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at

800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

**SUMMARY OF SAFETY AND EFFECTIVENESS DATA:  
GENESTONE 190 LITHOTRIPTER**

**I. GENERAL INFORMATION**

DEVICE GENERIC NAME: Extracorporeal Shock Wave Lithotripter

DEVICE TRADE NAME: Genestone 190 Lithotripter

APPLICANT: BMT, Inc.  
660 Main Street, South  
Suite 7  
Woodbury, CT 06798

PREMARKET APPROVAL APPLICATION (PMA) NUMBER: P970062

DATE OF NOTICE OF APPROVAL TO THE APPLICANT: JUN 24 1998

**II. INDICATIONS FOR USE**

The BMT Genestone 190 Extracorporeal Shock Wave Lithotripter is indicated for use in the non-invasive fragmentation of kidney (renal pelvic and renal calyceal) and upper ureteral stones between 5 and 20mm in size.

**III. DEVICE DESCRIPTION**

The Genestone 190 is an extracorporeal shock wave lithotripter (ESWL) device which includes a (i) spark gap electrode powered by a high voltage generator, (ii) ellipsoidal stainless steel focusing reflector, (iii) water cushion with coupling membrane, (iv) motorized treatment table (3-D positioning capability), (v) remote controller, and (vi) accessories for stone focusing and patient positioning. The system does not include the C-arm X-ray unit, ECG monitor, respiration monitor (optional), and anesthesia apparatus (optional), all of which must be supplied by the user. Ultrasound imaging may be used only for the monitoring of fragmentation during treatment, however, only X-ray imaging was used in the clinical investigation of safety and effectiveness. Although the device is provided with casters on its legs (to facilitate installation in an institution) the device is **not** intended to be mobile. The casters should always be in the locked position once the device is delivered to the site and installed in its treatment location.

### Shock Wave Generator

The shock wave generator consists of the spark gap electrode which is powered by a high voltage generator (adjustable between 10 and 22 kV). The spark gap electrode is located at the end of the focusing reflector and produces short sparks between the two electrode points. The disturbances created by these sparks travel through the water, producing shock waves. The intensity of the shock wave is determined by the voltage supplied (16 kV is the recommended starting voltage). The generator control mechanism (i.e., remote controller/control box) is coupled to an ECG monitor to synchronize the shock wave to the patient's cardiac cycle, i.e., firing on the R-wave. If desired, the shocks may also be limited to the exhalation phase of the patient's respiratory cycle using an external respiration monitor.

### Water Chamber

Components in the water chamber include: the focusing reflector, rubber latex membrane (patient contact), membrane clamp, focus pointer, and water inlet pipe. Water enters the chamber from a reservoir tank which automatically fills when the key-switch is activated. The shock wave generated at one focus of the ellipsoid reflector will propagate through the water and be refocused at the second focal point, which is directed at the stone.

### Treatment Table

The treatment table is motorized and able to move in the x, y, and z-axis planes. Table movements are regulated by the controller. Mattresses (urethane/vinyl) to be placed on top of the treatment table are also supplied.

### Accessories for Stone Focusing and Patient Positioning

The system has been designed to operate in conjunction with certain items (not included in the system) which must be supplied by the user, e.g., C-arm X-ray imaging system, ECG monitor, respiration monitor, and anesthesia apparatus. The C-arm X-ray imaging system locates the stones and permits proper shock wave focusing. Although the selection of the imaging system is at the discretion of the user, the sponsor recommends a 6" or 9" C-arm X-ray system with CRT and memory. The respiration monitor is optional and may be used to synchronize firing of the shock wave with the exhalation phase of the patient's breathing cycle, when the patient's movement (due to breathing) is at a minimum. Accessories for patient positioning (also supplied by the user) include pillows to prop the patient and restraints to minimize patient movement during the procedure.

## **IV. CONTRAINDICATIONS, WARNINGS, PRECAUTIONS**

The labeling for the Genestone 190 Lithotripter contains the following contraindications, warnings, and precautions:

Contraindications for the Genestone 190 Lithotripter are:

1. Patients with a coagulation abnormality as indicated by abnormal prothrombin

time (PT), partial thromboplastin time (PTT), or bleeding time, including patients receiving an anticoagulant (including aspirin).

2. Patients with urinary tract obstructions distal to the target stone.
3. Patients in whom pregnancy is known or suspected.
4. Patients whose anatomy precludes focusing of the device in the area of the target stone, including obesity or severe curvature of the spine.
5. Patients with arterial calcification or vascular aneurysms in the lithotripter shock wave path.
6. Patients with a history of chronic or acute pancreatitis or gall bladder disease.
7. Patients whose weight exceeds the weight limit of the table (286 lbs).
8. Patients in whom epidural or general anesthesia, IV or oral analgesia, and IV sedation are contraindicated.
9. Patients in whom the use of x-ray is contraindicated.

Warnings for the Genestone 190 Lithotripter are:

1. A C-arm X-ray imaging system is required in conjunction with the Genestone 190 Lithotripter to locate the stone and to focus the shock wave on it. Do not operate the Genestone 190 Lithotripter without a C-arm X-ray imaging system.
2. Although patients with infected stones and/or acute urinary tract infections have been successfully treated with shock wave therapy, the experience with the Genestone 190 Lithotripter in such cases is limited. Therefore, the safety and effectiveness of treatment of infected stones with the Genestone 190 Lithotripter have not been demonstrated. Due to the possibility of systemic infection from pathogen-bearing calculus debris, use of prophylactic antibiotics should be considered whenever the possibility of stone infection exists.
3. Bilateral treatment of renal stones should not be performed in a single treatment session because total urinary tract obstruction by stone fragments may result. Patients with bilateral renal stones should be treated using a separate treatment session for each side. In the event of total urinary obstruction, corrective procedures may be needed to assure drainage of urine from the kidney.
4. Care should be taken to ensure that shock waves are not applied to air-filled areas, i.e., intestines or lungs. Shock waves are rapidly dispersed by passage through an

air-filled interface which can cause harmful side effects.

5. Although children have been treated with shock wave therapy for upper urinary tract stones, experience with the Genestone 190 Lithotripter in such cases is limited. Therefore, the safety and effectiveness of the Genestone 190 Lithotripter in the treatment of urolithiasis in children have not been demonstrated. Studies indicate that there are growth plate disturbances in the epiphyses of developing long bones in rats subjected to shock waves. The significance of this finding in humans, however, is unknown.
6. The safety and effectiveness of using the Genestone 190 in the treatment of middle and lower ureteral stones is currently unknown. The treatment of lower ureteral stones should specifically be avoided in women of childbearing age because treatment of this patient population could possibly result in irreversible damage to the female reproductive system and to the unborn fetus in an undiagnosed pregnancy.

Precautions for the Genestone 190 Lithotripter are:

1. Cardiac monitoring should be performed during treatment. This is especially important for patients who may be at risk for cardiac arrhythmia due to a history of cardiac irregularities, because the use of extracorporeal shock wave lithotripsy is known to cause ventricular cardiac arrhythmias in some patients and limited information is available on the effect of the Genestone 190 Lithotripter on cardiac rhythm.
2. Extreme caution must be used in the treatment of patients at high risk for heart failure, those with cardiac pacemakers or pneumonia, and patients with very low diaphragms. Although patients with implanted pacemakers have been treated with extracorporeal shock wave lithotripters<sup>1</sup>, the safety of using the Genestone 190 Lithotripter to treat patients with cardiac pacemakers and other implanted devices, whose function could be affected by shock waves, has not been studied.
3. Extracorporeal shock wave lithotripsy procedures have been known to cause damage to the treated kidney. The potential for injury, its long-term significance, and its duration are unknown. However, lithotripsy is believed to be less damaging than the persistence of the disease or alternative methods of treatment.
4. Treated patients should be followed radiographically until the patient is stone-free or there are no remaining stone fragments which are likely to cause a silent obstruction and loss of renal function.
5. While fluoroscopy must be used during the procedure, caution should be taken to minimize the exposure.

6. No safety and effectiveness information is available regarding the treatment of patients with staghorn calculi.
7. Experience treating impacted or embedded stones with the Genestone 190 Lithotripter is limited and safety and effectiveness cannot be assured. Experience reported by other manufacturers and investigators using extracorporeal shock wave lithotripters for impacted stones has shown limited success. Alternative procedures are recommended.
8. It is recommended that there be no less than a 1 month interval between treatments of the same kidney or focal area, and no more than three treatments to the same kidney. The number of shock waves should be minimized and limited to 2,500 in a single treatment session.
9. Due to noise associated with shock wave generation, both the patients and staff should wear ear protection during treatment.
10. The Genestone 190 water cushion contains a natural rubber latex membrane which may cause allergic reactions.

## **V. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Adverse effects reported in association with the use of extracorporeal shock wave lithotripters include: skin bruising/redness at the treatment site, gross hematuria, renal colic/flank pain, nausea/vomiting, general/muscle pain, dysuria, elevated pancreatic amylase, infection, urosepsis, obstruction, renal hematomas, hypertension, hydronephrosis, and cardiac events. More detailed information on these events can be found on page 10 of this document.

## **VI. ALTERNATE PRACTICES AND PROCEDURES**

Urinary tract stone treatment has been based predominantly on the symptomatology and location of the stone. Treatment varies with the type and size of stone and the condition of the patient. The most common treatment for kidney stones is dietary restriction and consumption of large amounts of fluid. Soft ammonium-magnesium phosphate and uric-acid calculi may be dissolved in some instances by irrigation through ureteral catheters. Calculi of small size may be removed from the lower ureter by means of instruments passed through the urethra into the ureter to snare the stone.

Patients with stones in the kidney and the upper ureter with persistent and significant symptoms have historically been treated with open surgery. Surgical techniques to remove kidney stones include: pyelolithotomy, nephrolithotomy, partial nephrectomy, Gil-Vernet operation, and

ureterolithotomy. The use of open surgery carries the following risks: bleeding and hematuria, infection, persistent urinary drainage, urinoma, and the potential loss of a kidney after multiple surgeries.

In recent years, percutaneous stone removal techniques have been developed for use on patients who were poor surgical candidates or had undergone open surgery in the past. Percutaneous stone removal is now being used on patients who have not had previous operations because it is felt to be less invasive than open surgery and, in general, requires shorter hospitalization. This procedure involves the placement of a needle and guidewire into the renal pelvis through a small puncture wound in the flank, under the guidance of ultrasound or x-ray. The needle tract is dilated to admit surgical instruments and the stone can be removed or, if too large, the stone can be fragmented (using either mechanical, ultrasonic, or electrohydraulic lithotripsy techniques). The resulting fragments can then be removed. Complications reported with this procedure include: hematuria, infection, bleeding, pneumothorax, need for open surgery, and loss of a kidney.

Most kidney stones can be treated without surgery. For small kidney stones there are few complications other than discomfort to the patient. In some cases, however, the stone may cause severe pain or damage the kidney or urinary tract.

Other currently marketed extracorporeal shock wave lithotripters that have the same or broader indications for use offer another alternative.

## **VII. MARKETING HISTORY**

Since August 1991, approximately 90 devices have been in use internationally. The device has not been withdrawn from marketing for any reason related to safety or effectiveness of the device.

## **VIII. SUMMARY OF STUDIES**

### **1. NON-CLINICAL STUDIES**

#### **a. Evaluation of Shock Wave Pressure**

Testing was conducted to characterize the shock wave generated by the Genestone 190 Lithotripter.

A polyvinylidene fluoride (PVDF) reference hydrophone integrally connected to a preamplifier system (time base accuracy of  $\pm 10$ ns) was used. The particular hydrophones used for this survey had sensitivities of 0.030 and 0.040 MPa/mV. The following data were collected.

Pressure Measurement Data		
Power Setting	Peak Positive Pressure (MPa)	Peak Negative Pressure (MPa)
16 kV	51.4	-4.5
20 kV	66	-6.31

In addition, integration of the energy per pulse was performed over the annular area within the -6 dB region around the point of peak pressure. The average beam energy was calculated to be 23.48 mJ at 14 kV and 35.21 mJ at 22 kV.

**b. Animal Study**

Animal testing was not conducted due to the human treatment data available, i.e., over 5 years of device use on at least 10,000 subjects. There have been no reports of unanticipated reactions.

**2. CLINICAL INVESTIGATIONS**

The supporting clinical study was performed at three investigational sites. The purpose of this investigation was to demonstrate the safety and effectiveness of the Genestone 190 Lithotripter in the fragmentation of upper urinary tract calculi. A total of 214 treatments were administered to 180 patients.

The 180 patients were treated for a total of 217 different stones. Safety data are reported on 180 patients in the total cohort. An evaluable cohort of 164 patients (201 stones) with 3-month data is reported on for effectiveness. This cohort appropriately excludes 10 patients with distal and middle ureteral stones since safety and effectiveness could not be evaluated for those two stone locations. Six patients were considered to have dropped out of the study for reasons unrelated to the treatment.

The design of the clinical investigation of the Genestone 190 Lithotripter is consistent with the recommendations that were made by the Gastroenterology and Urology Devices Panel members at their October 20, 1989, meeting. Specifically, the panel recommended that PMAs for renal extracorporeal shock wave lithotripters be based on a clinical study involving at least three investigational sites and 150 patients.

A list of the sites and investigators are presented in the following table.

<b>Investigational Site</b>	<b>Investigator</b>	<b>Patients</b>
St. Elisabeth Hospital Turnout, Belgium	Dr. Koenraad S. Ackaert Chief of Urology	61
Keio University School of Medicine Tokyo, Japan	Dr. Hiroshi Tazaki Professor of Urology	58
Franciscus Hospital Rosendahl, Netherlands	Dr. Johann Plasmin	61

In all of the following discussions, the data are pooled and not separated into cohorts by investigational site. This was justified by a series of analyses that indicated that there were no major differences in the results from the three sites.

**a. Subject Selection and Exclusion Criteria**

Patients eligible for inclusion in this study were adults who had an upper urinary tract stone(s), in anesthesia risk group I-IV, whose anatomy permitted focusing of the device, whose renal function was in satisfactory condition, and who was competent to understand the risks associated with and freely agrees to undergo treatment. There was no limit on the number of stones.

Patients were excluded from the study for any of the following reasons: an untreated or active urinary tract infection; renal arterial calcification near the area to be treated; calcified kidney; unable to receive epidural or general anesthesia were contraindicated; could not be properly placed on the table; pregnancy; heart problems, including a cardiac pacemaker; or health problems serious enough to prohibit ESWL.

Before enrollment in the study, patients were evaluated for suitability for lithotripsy. Information used in the evaluation included medical history and physical examination, laboratory work-up, and kidney-ureter-bladder (KUB) X-rays. Those patients who met the entrance criteria and signed an informed consent form were enrolled in the study.

**b. Study Population**

Of the 180 patients enrolled in the study, 118 (66%) were males and 62 (34%) were females. The mean age was 47.5 years (range 20 to 86 years) and the mean weight was 68.8 kg (range 36 to 102 kg).

The ratio of men to women in this study is similar to the ratios reported in similar studies. The general patient population in this study is also comparable to the populations reported in other studies, with similar demographic data reported for mean age, weight, etc.

**c. Stone Characteristics**

Of the 180 patients treated, 170 had stones located in the kidney and upper ureter. Six of these patients are considered to have dropped out by the final 3-month follow-up visit and the remaining 164 patients (201 stones) account for the 197 treatments in the total cohort. The mean largest stone size was 11.5 mm. The location of the primary stones were: 67 (39.4%) in the calices, 55 (32.4%) in the renal pelvis, and 48 (28.2%) in the upper ureter.

**d. Treatment Characteristics**

The 180 patients treated received 214 procedures with an average number of shocks per treatment equal to 2219, with an average treatment time of 43.7 minutes. The types of anesthesia/analgesia administered varied widely and the selection depended mainly investigator/site preferences and practices. Most patients received some type of anesthesia/analgesia/sedation, either epidural anesthesia (34%), IV analgesia (28%), oral analgesia (21%), general anesthesia (15%), or IV sedation (1%); while only three patients (2%) received nothing at all.

**Retreatments**

The main criterion for retreatment was the presence of stones or fragments equal to or greater than 5mm in size. Of the 186 targeted stones, 34 were treated twice and no patient received three treatments. The recommended retreatment schedule calls for a maximum of three treatments at a minimum interval of 1 month.

**Ancillary Treatments**

Stents were placed in approximately 35% (60) of the 170 patients before treatment. The placing of stents is standard medical practice; therefore, stenting is not considered a true ancillary treatment. Other procedures such as percutaneous nephrostomy (7 patients, 4.1%), laser lithotripsy (5 patients, 2.9%), ureteral manipulation (4 patients, 2.4%), and ureterolithotomy (1 patient, 0.6%) were performed on study patients. These patients are considered lithotripsy failures.

**e. Results**

The effectiveness of treatment with the Genestone 190 Lithotripter was evaluated by X-ray (KUB) to determine the presence and dimensions of remaining kidney stones or stone fragments after treatment. KUBs were performed immediately post-treatment and at subsequent follow-up visits. Successful cases consisted of those patients who were stone free or had stone fragments less than 5 mm in size at follow-up. Clinical success in the evaluable cohort was demonstrated to be 74% (122/164) by 3 months.

The effects of selected patient characteristics on treatment outcome, including body-mass index, age, sex, stone size, stone location, number of treatments, total stone burden, and site were analyzed to determine if these characteristics could be used to predict which patients benefited from treatment. Treatment parameters such as number of shock waves delivered, duration, energy setting, and various types of anesthesia/analgesia/sedative administered were also assessed to determine whether or not these could be used to predict which patients would benefit from the treatment. Of all the patient

characteristics and treatment parameters analyzed, only stone burden demonstrated correlation to outcome. As expected, the smaller the stone burden, the greater the likelihood of treatment success.

**f. Adverse Reactions and Complications**

Adverse effects reported in the study are similar to those reported for other lithotripters and are described below. The events are reported for 177 patients in the total cohort at the 1 to 3 day visit following their last treatment and for 174 patients seen at 1 to 3 months post-procedure.

<b>Adverse Event</b>	<b>1-3 Days n=177</b>	<b>1-3 Months n=174</b>
Gross Hematuria	75 (42%)	0
Skin Effect/Bruising	58 (33%)	0
Pain		
Slight	44 (25%)	5 (3%)
Moderate	26 (15%)	5 (3%)
Severe (Renal Colic)	0	4 (2%)
Ureteral Obstruction	5 (3%)	0
UTI	1 (1%)	1 (1%)
Fever	2 (1%)	0

Hematuria, bruising, and pain were shown by most patients immediately following treatment. The severity of these complications varied from slight to moderate, but resolved spontaneously in every case without intervention by the investigator or attending clinician. Also, renal colic is considered secondary to the passage of stone fragments and typically resolves with the elimination of the fragments. Arrhythmia was not reported in any of the treatments, most likely because ECG triggering was required. Other complications of ESWL that were not reported in this study include intrarenal and perirenal hematoma and hypertension. The relationship between hypertension and ESWL is not fully understood and continues to undergo investigation.

**g. Laboratory Values**

The blood pressure and laboratory values from the three sites were combined and compared. There were no statistical differences between the measurements taken at the pre-treatment and follow-up visits at 1-3 months for systolic and diastolic blood pressures, hematocrit, creatinine, or BUN. Amylase, LDH, and SGOT demonstrated statistically significant, but clinically insignificant changes from pre-treatment to 1-3 month follow-up. The Japanese site did not report amylase values for any of their patients.

**h. Renal Scan**

Dr. Ackaert performed nuclear renal scans (DMSA) on 40 patients from the Belgium site. Scans were first made at pre-treatment and then repeated at the 3-month follow-up. A statistical comparison using P-values based on paired t-test of the laboratory values of the renal scan patients showed no difference between the baseline measurements and final follow-up. Only SGOT showed a statistically significant change from baseline at 1-3 months, however, a mean change of 1.6 is not considered clinically significant.

**i. Device Failures**

No system failures were reported during the clinical studies.

**j. Training**

A training regimen has been developed by the company and will be required prior to use of the device.

**IX. CONCLUSIONS FROM THE STUDIES**

The laboratory, animal, and clinical data provide reasonable assurance of the safety and effectiveness of the Genestone 190 Lithotripter for the non-invasive fragmentation of kidney (renal pelvic and renal calyceal) and upper ureteral stones between 5 and 20mm in size.

**X. PANEL RECOMMENDATION**

Pursuant to section 515(c)(2) of the Food, Drug, and Cosmetic Act (the act) as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

**XI. CDRH DECISION**

An FDA inspection of manufacturing facility was completed, and determined that the manufacturer was in compliance with the device Good Manufacturing Practices (GMP) Regulation. The date of GMP clearance was June 23, 1998.

Based upon a review of the data contained in the PMA, CDRH determined that the Genestone 190 Lithotripter is safe and effective for the indication of the non-invasive fragmentation of kidney and upper ureteral between 5 and 20mm in size. Furthermore, the applicant agreed to the postapproval requirement that they develop a plan to collect valid scientific evidence to evaluate the long-term effect of their device on hypertension and submit this plan for FDA approval.

CDRH issued an approval order for the stated indication for the applicant's PMA for the Genestone 190 Lithotripter on JUN 24 1998.

## **XII. REFERENCES**

1. Goldsmith M.F., "ESWL Now Possible for Patients with Pacemakers", JAMA, 258: pg. 1284, September 11, 1987.
2. Jameson R.M., Burrows K., Large B., Management of the Urological Patient, Churchill Livingstone, New York: pp. 142-145, 1976.
3. Segura J.W, Patterson D.A., LeRoy A.J., May G.R., Smith L.H., "Percutaneous Lithotripsy," J. Urol., 130: pp. 1051-1054, 1983.

## **XIII. Approval Specifications**

1. Instructions for Use: See labeling;
2. Hazards to Health from Use: See indications, contraindications, warnings, precautions, and adverse events sections of labeling;
3. Postapproval Requirements and Restrictions: See approval order.

## INDICATIONS FOR USE

The Genestone 190 Extracorporeal Shock Wave Lithotripter is indicated for use in the non-invasive fragmentation of kidney (renal pelvic and renal calyceal) and upper ureteral stones between 5 and 20mm in size.

## CONTRAINDICATIONS

1. Patients with a coagulation abnormality as indicated by abnormal prothrombin time (PT), partial thromboplastin time (PTT), or bleeding time, including patients receiving an anticoagulant (including aspirin).
2. Patients with urinary tract obstructions distal to the target stone.
3. Patients in whom pregnancy is known or suspected.
4. Patients whose anatomy precludes focusing of the device in the area of the target stone, including obesity or severe curvature of the spine.
5. Patients with arterial calcification or vascular aneurysms in the lithotripter shock wave path.
6. Patients with a history of chronic or acute pancreatitis or gall bladder disease.
7. Patients whose weight exceeds the weight limit of the table (286 lbs).
8. Patients in whom epidural or general anesthesia, IV or oral analgesia, and IV sedation are contraindicated.
9. Patients in whom the use of x-ray is contraindicated.

## WARNINGS

1. A C-arm X-ray imaging system is required in conjunction with the Genestone 190 Lithotripter to locate the stone and to focus the shock wave on it. Do not operate the Genestone 190 Lithotripter without a C-arm X-ray imaging system.
2. Although patients with infected stones and/or acute urinary tract infections have been successfully treated with shock wave therapy, the experience with the Genestone 190 Lithotripter in such cases is limited. Therefore, the safety and effectiveness of treatment of infected stones with the Genestone 190 Lithotripter have not been demonstrated. Due to the possibility of systemic infection from pathogen-bearing calculus debris, use of prophylactic antibiotics should be considered whenever the possibility of stone infection exists.
3. Bilateral treatment of renal stones should not be performed in a single treatment session because total urinary tract obstruction by stone fragments may result. Patients with bilateral renal stones should be treated using a separate treatment session for each side. In the event of total urinary obstruction, corrective procedures may be needed to assure drainage of urine from the kidney.
4. Care should be taken to ensure that shock waves are not applied to air-filled areas, i.e., intestines or lungs. Shock waves are rapidly dispersed by passage through an air-filled interface which can cause harmful side effects.
5. Although children have been treated with shock wave therapy for upper urinary tract stones, experience with the Genestone 190 Lithotripter in such cases is limited. Therefore, the safety and effectiveness of the Genestone 190 Lithotripter in the treatment of urolithiasis in children have not been demonstrated. Studies indicate that there are growth plate disturbances in the epiphyses of developing long bones in rats subjected

to shock waves. The significance of this finding in humans, however, is unknown.

6. The safety and effectiveness of using the Genestone 190 in the treatment of middle and lower ureteral stones is currently unknown. The treatment of lower ureteral stones should specifically be avoided in women of childbearing age because treatment of this patient population could possibly result in irreversible damage to the female reproductive system and to the unborn fetus in an undiagnosed pregnancy.

## PRECAUTIONS

1. Cardiac monitoring should be performed during treatment. This is especially important for patients who may be at risk for cardiac arrhythmia due to a history of cardiac irregularities, because the use of extracorporeal shock wave lithotripsy is known to cause ventricular cardiac arrhythmias in some patients and limited information is available on the effect of the Genestone 190 Lithotripter on cardiac rhythm.
2. Extreme caution must be used in the treatment of patients at high risk for heart failure, those with cardiac pacemakers or pneumonia, and patients with very low diaphragms. Although patients with implanted pacemakers have been treated with extracorporeal shock wave lithotripters<sup>1</sup>, the safety of using the Genestone 190 Lithotripter to treat patients with cardiac pacemakers and other implanted devices, whose function could be affected by shock waves, has not been studied.
3. Extracorporeal shock wave lithotripsy procedures have been known to cause damage to the treated kidney. The potential for injury, its long-term significance, and its duration are unknown. However, lithotripsy is believed to be less damaging than the persistence of the disease or alternative methods of treatment.
4. Treated patients should be followed radiographically until the patient is stone-free or there are no remaining stone fragments which are likely to cause a silent obstruction and loss of renal function.
5. While fluoroscopy must be used during the procedure, caution should be taken to minimize the exposure.
6. No safety and effectiveness information is available regarding the treatment of patients with staghorn calculi.
7. Experience treating impacted or embedded stones with the Genestone 190 Lithotripter is limited and safety and effectiveness cannot be assured. Experience reported by other manufacturers and investigators using extracorporeal shock wave lithotripters for impacted stones has shown limited success. Alternative procedures are recommended.
8. It is recommended that there be no less than a 1 month interval between treatments of the same kidney or focal area, and no more than three treatments to the same kidney. The number of shock waves should be minimized and limited to 2,500 in a single treatment session.
9. Due to noise associated with shock wave generation, both the patients and staff should wear ear protection during treatment.
10. The Genestone 190 water cushion contains a natural rubber latex membrane which may cause allergic reactions.

## Clinical Study Summary

### Objective

This clinical trial was designed to demonstrate that the Genestone 190 Lithotripter is safe and effective for the treatment of kidney (renal pelvic and renal calyceal) and upper ureteral stones.

### Subject Selection and Exclusion Criteria

Adult men and women with upper urinary tract stone(s), with satisfactory renal function, in anesthesia risk groups I-IV, and whose anatomy permitted focusing of the device were considered eligible for study enrollment. Patients were excluded from the study for any of the following reasons: untreated urinary tract infection, renal arterial calcification of the treatment area, calcified kidney, unable to receive general or epidural anesthesia, could not be properly positioned on the treatment table, pregnancy, heart problems including pacemaker, or any health problem considered serious enough to prohibit the safe application of ESWL.

### Study Design

The 180 patients were treated for a total of 217 different stones. Safety data are reported on 180 patients in the total cohort. An evaluable cohort of 164 patients (201 stones) with 3-month data is reported on for effectiveness. This cohort appropriately excludes 10 patients with distal and middle ureteral stones since too few patients were enrolled to evaluate the safety and effectiveness of these stone locations. Also, six patients were considered to have dropped out of the study for reasons unrelated to the treatment and, therefore, were not included in the effectiveness analysis.

Patients were evaluated 1-3 days and 1-3 months following. Treatment success is defined as the ability to fragment urinary stones resulting in either stone free status or fragments less than 5 mm in size, which is considered small enough for spontaneous passage.

### Patient Demographics

Of the 180 patients enrolled in the study, 118 (66%) were males and 62 (34%) were females. The mean age was 47.5 years (range 20 to 86 years) and the mean weight was 68.8 kg (range 36 to 102 kg).

### Stone Characteristics

The 164 patients in the evaluable cohort had an average largest stone size of 11.5 mm. The location of the primary stones were: 67 (39.4%) in the calices, 55 (32.4%) in the renal pelvis, and 48 (28.2%) in the upper ureter.

### Treatment Characteristics

The 180 patients treated received 214 procedures with an average number of shocks per treatment equal to 2219 and an average treatment time of 43.7 minutes. The types of anesthesia/analgesia administered varied widely and the selection depended mainly on investigator/site preferences and practices. A number of patients received either an epidural anesthesia (34%), IV analgesia (28%), oral analgesia (21%), general anesthesia (15%), or IV sedation (1%); while only a few patients (2%) received nothing at all.

### Retreatments

The main criterion for retreatment was the presence of stones or fragments greater than or equal to 5 mm in size. Of the 186 targeted stones, 34 were treated twice and no patient received three treatments. The recommended retreatment schedule calls for a maximum of three treatments at a minimum interval of 1 month.

### Safety

There were no unanticipated adverse events reported during the course of the study, nor did any subject require prolonged follow-up due to a complication. Adverse effects reported in the study are similar to those reported for other lithotripters and are described below. The events are reported for 177 patients in the total cohort at the 1 to 3 day visit following their last treatment and for 174 patients seen at 1 to 3 months post-procedure.

Adverse Event	1-3 Days n=177	1-3 Months n=174
Hematuria	75 (42%)	0
Skin Effect/Bruising	58 (33%)	0
Pain		
Slight	44 (25%)	5 (3%)
Moderate	26 (15%)	5 (3%)
Severe (Renal Colic)	0	4 (2%)
Ureteral Obstruction	5 (3%)	0
UTI	1 (1%)	1 (1%)
Fever	2 (1%)	0

Hematuria, bruising, and pain were shown by most patients immediately following treatment. The severity of these complications varied from slight to moderate, but resolved spontaneously in every case without intervention by the investigator or attending clinician. Also, renal colic is considered secondary to the passage of stone fragments and typically resolves with the elimination of the fragments. Arrhythmia was not reported in any of the treatments, most likely because ECG triggering was required. Other complications of ESWL which were not observed in this study include intrarenal and perirenal hematoma and hypertension. The relationship between hypertension and ESWL is not fully understood and continues to undergo investigation.

#### Effectiveness

The effectiveness of treatment with the Genestone 190 Lithotripter was evaluated by X-ray (KUB) to determine the presence and dimensions of remaining kidney stones or stone fragments after treatment. KUBs were performed immediately post-treatment and at subsequent follow-up visits. Successful cases consisted of those patients who were stone free or had stone fragments less than 5 mm in size at follow-up. Clinical success in the evaluable cohort was demonstrated to be 74% (122/164) by 3 months.

The effects of selected patient characteristics on treatment outcome, including body-mass index, age, sex, stone size, stone location, number of treatments, total stone burden, and site were analyzed to determine if these characteristics could be used to predict which patients benefited from treatment. Treatment parameters such as number of shock waves delivered, duration, energy setting, and various types of anesthesia/analgesia/sedative administered were also assessed to determine whether or not these could be used to predict which patients would benefit from the treatment. Of all the patient characteristics and treatment parameters analyzed, only stone burden demonstrated correlation to outcome. As expected, the smaller the stone burden, the greater the likelihood of treatment success.