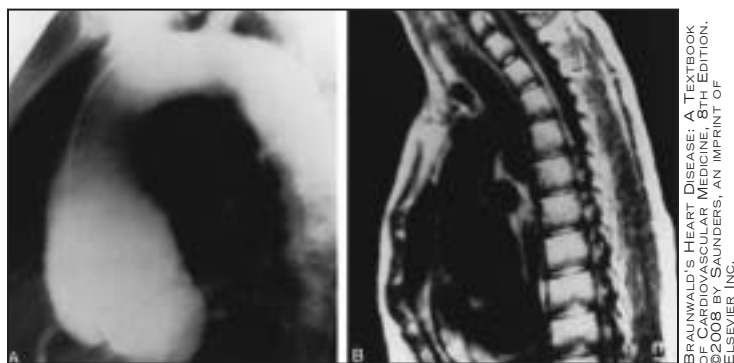


Aortic Surgery in Marfan Predisposes to Migraine

Left: Lateral angiogram of the ascending aorta shows dilation of the sinuses of Valsalva and proximal ascending aorta and normal ascending aorta. **Right:** Lateral MRI of the same patient.



BY BRUCE JANCIN
Denver Bureau

MUNICH — Patients who have Marfan syndrome also experience a sharply increased prevalence of migraine, especially migraine with aura, according to a group of Dutch investigators.

Moreover, those Marfan syndrome patients who undergo aortic root surgery have an independent further

increase in the risk of migraine, Dr. Jeroen C. Vis reported at the annual congress of the European Society of Cardiology.

The explanation for the association between aortic root surgery and a high rate of migraine in Marfan syndrome patients is unclear.

One possibility mentioned by the researchers is that the aortic graft throws off microemboli, which trigger headache attacks, according to Dr. Vis of Academic Medical Centre, Amsterdam.

Dr. Vis reported on 97 adults with Marfan syndrome and who had a mean age of 39 years, plus an additional 80 age- and gender-matched controls.

All of the patients underwent a clinical interview in which diagnosis of migraine was based on International Headache Society criteria.

Migraine was diagnosed in a total of

44% of the patients with Marfan syndrome, compared with 28% of the control patients.

Thirty-seven percent of Marfan syndrome patients had migraine with aura, as did 10% of the controls.

Interestingly, the prevalence

of migraine among the controls was higher than usual, Dr. Vis reported.

This observation is most likely due to the influence of familial migraine; 16 of the 80 controls were first-degree relatives of participating Marfan syndrome patients, he commented.

Marfan syndrome was an independent risk factor for migraine overall, and conferred an adjusted 2.4-fold increased risk, along with a 6.2-fold increased risk for migraine with aura.

Thirty-five percent of the Marfan syndrome patients underwent aortic root surgery.

Having a history of the aortic root surgery was independently associated with a 3.9-fold increased risk of migraine, as well as a 4.5-fold greater risk of migraine with aura.

The study investigators also looked at other cardiovascular features of Marfan syndrome.

Neither mitral valve surgery, aortic dilatation, aortic dissection, mitral valve prolapse, nor mitral regurgitation was showed to be independently associated with an increase in migraine.

Aortic root surgery was therefore unique in this regard.

Dr. Vis said he and his colleagues are planning, as a next step, to observe the headache patterns in patients who do not have Marfan syndrome but who have undergone aortic root surgery.

The goal of that research will be to determine whether a history of the surgery is a risk factor for migraine and migraine with aura in those patients, too. ■



UNIQUE NATIONAL
HCPCS CODE
J7323

BRIEF SUMMARY

Please consult package insert for full Prescribing Information.

INDICATION

EUFLEXXA® (1% sodium hyaluronate) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen).

CONTRAINDICATIONS

- Do not use EUFLEXXA® to treat patients who have a known hypersensitivity to hyaluronan preparations
- Do not use EUFLEXXA® to treat patients with knee joint infections, infections or skin disease in the area of the injection site

WARNINGS

- Mixing of quaternary ammonium salts such as benzalkonium chloride with hyaluronan solutions results in formation of a precipitate. EUFLEXXA® should not be administered through a needle previously used with medical solutions containing benzalkonium chloride. Do not use disinfectants for skin preparation that contain quaternary ammonium salts
- Do not inject intravascularly because intravascular injection may cause systemic adverse events

PRECAUTIONS

General

- Patients having repeated exposure to EUFLEXXA® have the potential for an immune response; however, this has not been assessed in humans
- Safety and effectiveness of injection in conjunction with other intra-articular injectables, or into joints other than the knee has not been studied
- Remove any joint effusion before injecting
- Transient pain or swelling of the injected joint may occur after intra-articular injection with EUFLEXXA®
- Do not use after expiration date
- Protect from light
- Do not re-use—dispose of the syringe after use
- Do not use if the blister package is opened or damaged

Information for Patients

- Transient pain and/or swelling of the injected joint may occur after intra-articular injection of EUFLEXXA®
- As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged (i.e., more than 1 hour) weight-bearing activities such as jogging or tennis within 48 hours following intra-articular injection
- The safety and effectiveness of repeated treatment cycles of EUFLEXXA® have not been established

ADVERSE EVENTS

Adverse event information regarding the use of EUFLEXXA® as a treatment for pain in OA of the knee was available from two sources; a multicenter clinical trial conducted in Germany and a single center clinical trial that was conducted in Israel.

Multicenter Clinical Investigation

This clinical investigation was a prospective randomized, double blinded, active control (commercially available hyaluronan product) study conducted at 10 centers. Three hundred twenty-one patients were randomized into groups of equal size to receive either EUFLEXXA® (n=160) or the active control (n=161). A total of 119 patients reported 196 adverse events; this number represents 54 (33.8%) of the EUFLEXXA® group and 65 (44.4%) of the active control group. There were no deaths reported during the study.

Incidences of each event were similar for both groups, except for knee joint effusion, which was reported by 9 patients in the active control group and one patient in the EUFLEXXA® treatment group. A total of 160 patients received 478 injections of EUFLEXXA®. There were 27 reported adverse

events considered to be related to EUFLEXXA® injections: arthralgia – 11 (6.9%); back pain – 1 (0.63%); blood pressure increase – 3 (1.88%); joint effusion – 1 (0.63%); joint swelling – 3 (1.88%); nausea – 1 (0.63%); paresthesia – 2 (1.25%); feeling of sickness of injection – 3 (1.88%); skin irritation – 1 (0.63%); tenderness in study knee – 1 (0.63%). Four adverse events were reported for the EUFLEXXA® group that the relationship to treatment was considered to be unknown: fatigue – 3 (1.88%); nausea – 1 (0.63%).

Single Center Study

In a single-center, single-blinded, placebo controlled, prospective, two parallel treatment arm clinical trial a total of 49 (25 EUFLEXXA®, 24 placebo) patients were randomized into two treatment groups in a ratio of 1:1 EUFLEXXA® or placebo. A total of 65 adverse events were reported by 17 (68%) of the patients in the EUFLEXXA® group and 15 (63%) in the placebo group. Of the 65 total events reported, 20 were regarded as treatment related. Knee pain, hypokinesia of the knee, knee swelling, and rash were considered to be treatment related adverse events.

DETAILED DEVICE DESCRIPTION

Each syringe of EUFLEXXA® contains:

Sodium hyaluronate	20 mg
Sodium chloride	17 mg
Disodium hydrogen phosphate dodecahydrate	1.12 mg
Sodium dihydrogen phosphate dihydrate	0.1 mg
Water for injection	q.s.

HOW SUPPLIED

EUFLEXXA® is supplied in 2.25 ml nominal volume, disposable, pre-filled glass syringes containing 2 ml of EUFLEXXA®. Only the contents of the syringe are sterile. EUFLEXXA® is nonpyrogenic. 3 disposable syringes per carton.

This product is latex-free.

DIRECTIONS FOR USE

- Do not use EUFLEXXA® if the package is open or damaged. Store in the original package below 77°F (25°C). Do not freeze. Protect from light.
- EUFLEXXA® is administered by intra-articular injection into the knee synovial capsule using strict aseptic injection procedures. The full content of the syringe is injected into the affected knee at weekly intervals for 3 weeks, for a total of 3 injections.

Toll free number for providers and patients to call with questions: 1-(888)-FERRING (1-(888)-337-7464).

MANUFACTURED FOR:

FERRING
PHARMACEUTICALS

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MANUFACTURED BY:

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