CAUTION

Patients treated with this drug may be at risk by on the order of a physician.

DESCRIPTION

In a 0.9% sodium chloride solution, a hyaluronate solution containing a high molecular weight (>100,000-<300,000 daltons) fraction of purified natural sodium hyaluronate (Hylan G) is buffered physiological sodium chloride, having a pH of 5.0-7.5, the sodium salt is extracted from rooster comb, undergoes a biological and chemical purification process, is characterized by its molecular weight and physical properties and is further purified to contain multiple disaccharides units of hyaluronic acid-N-acetylglucosamine.

INDICATIONS

Hylan G is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conventional non-drug therapies, such as physical therapy, and whose symptoms are typically characterized by pain, swelling, and stiffness.

CONTRAINDICATIONS

Patients with a history of anaphylaxis to Hylan G or its excipients should not be treated and the drug should be administered as a single dose for a single joint or as a single injection per day of a single dose for multiple joints.

WARNINGS

- Do not use in patients with a history of anaphylaxis to Hylan G or its excipients.
- Do not use in patients with a history of systemic lupus erythematosus (SLE) or other connective tissue disorders.
- Do not use in patients with a history of rheumatoid arthritis (RA) or other autoimmune disorders.
- Do not use in patients with a history of chronic liver disease or other chronic diseases that could affect the liver.
- Do not use in patients with a history of renal failure or other chronic diseases that could affect the kidney.

PRECAUTIONS

- Careful selection of patients with a history of anaphylaxis to Hylan G or its excipients is necessary when considering the use of this drug.
- Careful selection of patients with a history of systemic lupus erythematosus (SLE) or other connective tissue disorders is necessary when considering the use of this drug.
- Careful selection of patients with a history of rheumatoid arthritis (RA) or other autoimmune disorders is necessary when considering the use of this drug.
- Careful selection of patients with a history of chronic liver disease or other chronic diseases that could affect the liver is necessary when considering the use of this drug.
- Careful selection of patients with a history of renal failure or other chronic diseases that could affect the kidney is necessary when considering the use of this drug.

Use in Pregnancy

Hylan G is Category C. It is not known whether Hylan G crosses the placenta. Therefore, the drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Use in Children

It is not known whether Hylan G is excreted in human milk. Therefore, the drug should be used with caution in breastfeeding women.

Information for Patients

- Provide patients with a copy of the Patient Information prior to use.
- Transient pain and/or swelling of the injected joint may occur after intra-articular injection of Hylan G.
- With any intra-articular procedure, it is recommended that the patient be monitored for at least 24 hours after the injection.

Use in Specific Populations

- Hypersensitivity: If multiple injections of Hylan G are required, it is recommended to use a different syringe and needle for each injection.
- Pregnancy: It is not known whether Hylan G crosses the placenta. Therefore, the drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Use in children: It is not known whether Hylan G is excreted in human milk. Therefore, the drug should be used with caution in breastfeeding women.

ADVERSE EVENTS

Hylan G was investigated in a clinical trial conducted in the United States in which there were 174 subjects treated with Hylan G. The most common adverse events reported were pain, redness, swelling, and stiffness, all of which were mild to moderate in severity.

The most common adverse events reported were pain, redness, swelling, and stiffness, all of which were mild to moderate in severity.

No serious adverse events were reported.

BIBLIOGRAPHIC INFORMATION


MANUFACTURED FOR


REPACKAGED BY


MANUFACTURED BY


EVALUATION


CLINICAL STUDY

The use of Hylan G as a treatment for pain in OA of the knee was investigated in a multicenter clinical trial conducted in the United States.

This study was a double-blind, placebo-controlled, preemptive clinical trial with three treatment arms, as summarized in Table 1. A total of 405 subjects with moderate to severe pain in randomization (baseline evaluation) into three treatment groups (Hylan G, Placebo, and Naproxen).

TABLE 2 SUMMARY DESIGN

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Hylan G</th>
<th>Placebo</th>
<th>Naproxen</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>p</em></td>
<td>p.o., s.c.</td>
<td><em>p</em></td>
<td>p.o., s.c.</td>
</tr>
</tbody>
</table>

Table 1: A total of 405 subjects with moderate to severe pain in randomization (baseline evaluation) into three treatment groups (Hylan G, Placebo, and Naproxen).

Legend: | = subcutaneous; p.o. = po, orally; s.c. = subcutaneous; b.i.d. = twice a day; p.m. = as needed

The drug was administered before the start of the Hylan G and placebo groups.

Patient Population and Demographics

The demographics of the trial participants were comparable across treatment groups with regard to age, sex, height, weight, history of OA, and medical history.

EVALUATION

### TABLE 3
Demographic Characteristics of all randomized subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Parke-Davis</th>
<th>Placebo</th>
<th>Naproxen</th>
<th>Statistically Significant Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.0 ± 10.2</td>
<td>55.4 ± 11.9</td>
<td>60.2 ± 11.5</td>
<td>Parke-Davis vs. Placebo: p &lt; 0.05</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>62.5%</td>
<td>52.4%</td>
<td>55.6%</td>
<td>Placebo vs. Naproxen: p &lt; 0.05</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.9 ± 4.5</td>
<td>28.4 ± 4.8</td>
<td>27.2 ± 3.9</td>
<td>Placebo vs. Naproxen: p = 0.08</td>
</tr>
</tbody>
</table>

### TABLE 4
Clinical Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parke-Davis</th>
<th>Placebo</th>
<th>Naproxen</th>
<th>Statistically Significant Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score</td>
<td>4.0 ± 2.8</td>
<td>5.2 ± 3.4</td>
<td>3.6 ± 2.1</td>
<td>Placebo vs. Naproxen: p &lt; 0.01</td>
</tr>
<tr>
<td>Functional status</td>
<td>3.5 ± 1.2</td>
<td>4.0 ± 1.5</td>
<td>3.0 ± 1.0</td>
<td>Placebo vs. Naproxen: p = 0.05</td>
</tr>
</tbody>
</table>

### TABLE 5
Clinical Benefit of Naproxen vs. Placebo

<table>
<thead>
<tr>
<th>Parameter</th>
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<th>Naproxen</th>
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### TABLE 6
Masked Evaluators' Categorical Assessments of Pain for Completed Subjects in Prior 48 Hours

<table>
<thead>
<tr>
<th>Week</th>
<th>Parke-Davis</th>
<th>Placebo</th>
<th>Naproxen</th>
<th>Statistically Significant Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.0 ± 2.8</td>
<td>5.2 ± 3.4</td>
<td>3.6 ± 2.1</td>
<td>Placebo vs. Naproxen: p &lt; 0.01</td>
</tr>
<tr>
<td>2</td>
<td>3.5 ± 1.2</td>
<td>4.0 ± 1.5</td>
<td>3.0 ± 1.0</td>
<td>Placebo vs. Naproxen: p = 0.05</td>
</tr>
</tbody>
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### TABLE 7
Masked Evaluators' Categorical Assessments of Pain for Completed Subjects in Prior 48 Hours

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### TABLE 8
Naproxen Effect as a Percentage of the Naproxen-Placebo Difference

<table>
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