1. Composition:
Diperoxochloric Acid Topical solution is a mixture of Diperoxochloric Acid concentrate, the active ingredient present in a 10 ml bottle (bottle A) and a Sterile Sodium Chloride Solution BP 0.9% w/v (bottle B), presented in a 10 ml bottle.

Each pack contains:
- Bottle A: Diperoxochloric Acid concentrate
- Bottle B: Sterile Sodium Chloride Solution BP 0.9% w/v (Cutaneous Solution)

For cutaneous use only. Not for injection.

To be used only after adding and mixing entire contents of Bottle A with Bottle B.

The contents of Bottle A should not be to be applied directly on the wound.

Reconstituted Solution (Bottle A + Bottle B) in bottle B:

Each ml contains:
- Diperoxochloric acid concentrate: 0.29 mg
- Sterile Sodium Chloride Solution BP: 0.9% w/v

The Solution should not be used after 14 days of mixing/reconstitution.

2. Chemistry:
Diperoxochloric Acid Concentrate has a following Chemical structure:

3. Pharmacology:
3.1 Preclinical Pharmacology:
In the preclinical pharmacology, Diperoxochloric Acid Topical Solution was investigated to see if it had the following properties for the healing of open wounds:
- Fights bacterial infections in the wound, and
- Enhances cell proliferation of fibroblasts specifically, to stimulate the healing and enforce closure of the wound.

Antibacterial action:
Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria), which keeps the bacterial burden of open wounds low. Diperoxochloric Acid Topical Solution shares functional properties of Reactive Oxygen Species (ROS) at least concerning their antibacterial activity. Anti-bacterial activity according to the German standard DIN 58940 was shown against E. coli, P. aeruginosa and S. aureus bacteria.

Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria). This function supports closing of the wound.

3.2 Clinical Pharmacology:
Diperoxochloric Acid Topical Solution showed fibroblast-proliferating activity towards MRC-5 fibroblast cells. This suggests that the ratio of vital to dying cells in the wound is improved by Diperoxochloric Acid Topical Solution. Significant growth stimulation was observed in a time course up to four days following stimulation with Diperoxochloric Acid Topical Solution.

4. Efficacy:
4.1 Preclinical Pharmacology:
- In the preclinical pharmacology done as safety evaluation in the phase II and III clinical trials, Diperoxochloric Acid Topical Solution was co-prescribed along with inulin and oral hypoglycemic drugs such as sulfonylurea, biguanides, DPP-4 inhibitors or SGLT2 inhibitors for the treatment of underlying diabetes. No drug-drug interaction was noted.

- Drug-Drug Interactions with other topical Antimicrobials and Antiseptics is not studied.

- Diperoxochloric Acid Topical Solution did not have any interaction with dressing material (gauze).

4.2 Clinical Pharmacology:
In the phase II and III clinical trial conducted in patients of diabetic foot ulcer, no adverse drug reaction (ADR) could be allocated to Diperoxochloric Acid Topical Solution. Following is the complete listing of adverse events noted during the clinical trials:

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Related to test drug DPOCL</th>
<th>Related to active control drug Isotonic normal saline</th>
<th>No relationship to test or control drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Anemia</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>New ulcer or increase in ulcers</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Allergic rash and edema</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Urinary</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

5. Indications:
Diperoxochloric Acid Topical Solution is indicated for wound healing in diabetic neuropathic ulcers of skin and subcutaneous tissue reduction.

5. Contraindications:
Diperoxochloric Acid Topical Solution is contraindicated in patients with hypersensitivity to the formulation or any of the components of the formulation.

6. Warnings and Precautions:
- In case of a hypersensitivity reaction, Diperoxochloric Acid Topical Solution should be discontinued immediately.
- Diperoxochloric Acid Topical Solution is presented in a pack of two bottles. It should only be mixed before applying to the first wound dressing.
- Do not use contents of bottle “B” in bottle “A”.

7. Special population:
- Pregnancy: Diperoxochloric Acid Topical Solution has not been tested in pregnant females. No reproductive toxicity studies were conducted.
- Lactation: Diperoxochloric Acid Topical Solution has not been tested in lactating females.
- Children: Diperoxochloric Acid Topical Solution has not been tested in children.

8. Drug Interactions:
- There are no known drug-drug interactions of Diperoxochloric Acid Topical Solution.

- In the clinical laboratory investigation done as safety evaluation in the phase II and III clinical trials, no change in clinical laboratory parameters was noted.

- During phase II and III clinical trials, Diperoxochloric Acid Topical Solution was co-prescribed along with inulin and oral hypoglycemic drugs such as sulfonylurea, biguanides, DPP-4 inhibitors or SGLT2 inhibitors for the treatment of underlying diabetes. No drug-drug interaction was noted.

- Drug-Drug Interactions with other topical Antimicrobials and Antiseptics is not studied.

- Diperoxochloric Acid Topical Solution did not have any interaction with dressing material (gauze).

9. Adverse Reactions:
In the phase II and III clinical trial conducted in patients of diabetic foot ulcer, no adverse drug reaction (ADR) could be allocated to Diperoxochloric Acid Topical Solution. Following is the complete listing of adverse events noted during the clinical trials:

- Complete wound healing: 71.03% wound completely healed in Diperoxochloric Acid Topical Solution group as compared to only 57.53% in Active control. This figure was statistically significant (p = 0.0176).

- Time taken for complete closure of wounds: Diperoxochloric Acid Topical Solution reached in faster wound healing compared to Active control, as median time taken for complete closure of wounds in Diperoxochloric Acid Topical Solution group was 42 days as compared to 56 days in Active control group.

- Overall treatment responders: More than 50% of the patients treated with Diperoxochloric Acid Topical Solution had positive response as compared to 60% in active-control (treatment response defined by at least 50% wound reduction in 4 weeks).

10. Pharmacokinetics:
Pharmacokinetic evaluations are not applicable since Diperoxochloric Acid Topical Solution is not absorbed from the site of application.

11. Packaging:
Diperoxochloric Acid Topical Solution is available in the following strengths:
- 10 ml bottle containing Diperoxochloric Acid concentrate and Sterile Sodium Chloride Solution BP 0.9% w/v (Cutaneous Solution) in separate bottles.

12. Storage:
- Store at 2°C to 8°C.
- Protect from light.
- Do not freeze.

13. Shelf Life:
Diperoxochloric Acid Topical Solution is stable under the conditions mentioned above for up to 2 years from the date of manufacturing.

14. Laboratory Tests:
Routine laboratory tests should be conducted before starting treatment and periodically during treatment to assess the patient’s response to treatment.

15. Patient Instructions:
- Patients should be instructed to apply the solution gently on the wound using a sterile cotton wool bud or sponge.
- The solution should be applied to the wound twice daily or as directed by the healthcare professional.
- Patients should be advised to report any adverse reactions to their healthcare professional immediately.

16. Disposal:
- Diperoxochloric Acid Topical Solution should be disposed of in an environmentally friendly manner.

17. Patient Counseling:
- Patients should be informed about the potential side effects of Diperoxochloric Acid Topical Solution.
- A patient information sheet should be provided to patients to educate them about the correct use of the product.

18. Additional Information:
- Diperoxochloric Acid Topical Solution is contraindicated in patients with hypersensitivity to the formulation or any of the components of the formulation.
- Diperoxochloric Acid Topical Solution is not absorbed from the site of application.
- Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria). This function supports closing of the wound.
- Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria). This function supports closing of the wound.
- Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria). This function supports closing of the wound.
- Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria). This function supports closing of the wound.
- Diperoxochloric Acid Topical Solution is functionally antibacterial (especially against gram negative bacteria). This function supports closing of the wound.

[End of Document]
11. Toxicity Data:
The toxicology studies were carried out on Diperoxochloric Acid Topical Solution at LPT2 labs, Hamburg, Germany and followed all concerned regulations of Good Laboratory Practice (GLP) and OECD Principles of Good Laboratory Practice, 2002. Following information was generated in the toxicological studies:

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Route</th>
<th>Dose</th>
<th>Species</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.1 Acute</td>
<td>Intravenous</td>
<td>150 mg/kg body</td>
<td>Mice</td>
<td>No mortality, no toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>weight single</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>250 mg/kg body</td>
<td>Mice</td>
<td>0.5 minutes after administration: Reduced mobility, dyspnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>weight single</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 mg/kg body</td>
<td>Mice</td>
<td>0.5 minutes after administration: Reduced mobility, dyspnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>weight single</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.2 Sub-chronic</td>
<td>Intravenous</td>
<td>150 mg/kg body</td>
<td>Rats</td>
<td>No mortality, no toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>weight single</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.3 Local</td>
<td>Acute eye irritation/ corrosion test</td>
<td>Single instillation of 0.1 ml</td>
<td>Rabbits</td>
<td>Cornea, conjunctiva &amp; iris not affected</td>
</tr>
<tr>
<td>11.4 Mutagenicity</td>
<td>Acute dermal irritation [Patch test]</td>
<td>0.5 ml per patch - single dose</td>
<td>Rabbits</td>
<td>No skin reaction/ systemic intolerance</td>
</tr>
</tbody>
</table>

12. Dosage and administration:
Before applying to the wound dressing, Diperoxochloric Acid concentrate (Bottle A) has to be "Reconstituted" by mixing the contents of bottle A into the contents of bottle B as per instructions provided below.

12.1 Instructions for preparation of Diperoxochloric Acid Topical Solution "Reconstituted" solution and wound dressing:
- "Open Bottle A" and "Bottle B".
- Pour the contents of Bottle A into Bottle B. Close bottle B with bottle cap.
- Mix the content by moving the bottle upside down for 5 times gently.
- Diperoxochloric Acid Topical Solution "Reconstituted" solution is prepared.
- For wound dressing we recommend a non-sticky, sterile multi wound dressing.
- Pour 3.5 ml of this solution with help of the dropper on the 5 x 5 cm dressing (inner gauze swab) to bring the dressing to earth moist conditions or as directed by the Specialist.
- Do not touch the dressing / bandage.
- Then apply this inner gauze swab on the wound.
- Cover the inner gauze swab with outer gauze swabs, which will prevent the wound area from running dry.
- Finally, tie bandage rolled gauze to secure the gauzes. Daily remove the outer gauze swab and apply Diperoxochloric Acid Topical Solution on inner gauze swab without removing the inner gauze swab from the wound.
- Change the outer gauze swab daily and inner gauze swab on every alternate day or as per your Doctor's advice.
- The Reconstituted Solution should not be used after 14 days of making/reconstitution.

13. Overdosage
Since there is no absorption from the site of topical application, no untoward systemic effects are expected.

14. Presentation
Diperoxochloric Acid Topical Solution is presented as Bottle A:
The 10 ml HDPE bottle consisting of 7.5 ml Diperoxochloric Acid concentrate.

Bottle B:
The 30 ml HDPE bottle consisting of 22.5 ml Sterile Sodium Chloride Solution BP 0.9% w/v (Cutaneous Solution).

This also contains:
1) Inner Gauze Swab (Sterile) - 1 Pouch (7 Numbers)
2) Outer Gauze Swab (Sterile) - 1 Pouch (7 Numbers)
3) Micropaste - 1 Number
4) Bandage Rolled Gauze (Sterile) - 7 Numbers
5) Glass Dropper - 1 Number

15. Storage instruction:
Bottle A – 7.5 ml Diperoxochloric Acid Concentrate Solution: Store at a temperature not exceeding 25°C.
Bottle B – 22.5 ml Sterile Sodium Chloride Solution BP 0.9% w/v (Cutaneous Solution): Store at a temperature not exceeding 25°C. Reconstituted Solution: After mixing content of Bottle A in the content of Bottle B in Bottle B. Solution should not be used after 14 days of reconstitution and should be stored at a temperature not exceeding 25°C.

For Further Information please write to: Medical Department, Centaur Pharmaceuticals Pvt Ltd. Centaur House, Shanti Nagar, Vakola, Santacruz (East), Mumbai - 400 055. email: centaur@centaurlab.com

Manufacturer and marketed by: CENTAUR PHARMACEUTICALS PVT. LTD.