- Metabolism Activator -

**ADETPHOS KOWA Enteric Coated Tablet 20**

**ADETPHOS KOWA Enteric Coated Tablet 60**

**ADETPHOS KOWA Granule 10%**

< ATP Product >

### DESCRIPTION

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Adenosine triphosphate disodium hydrate</th>
<th>Adenosine triphosphate disodium hydrate</th>
<th>Adenosine triphosphate disodium hydrate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADETPHOS KOWA Enteric Coated Tablet 20</strong></td>
<td>20.0 mg in each tablet</td>
<td>60.0 mg in each tablet</td>
<td>100 mg in each gram</td>
</tr>
<tr>
<td><strong>Ingredients</strong></td>
<td>Cellulose, hydroxypropyl cellulose, talc, triethyl citrate, titanium oxide</td>
<td>Cellulose, hydroxypropyl cellulose, talc, triethyl citrate, titanium oxide</td>
<td>Cellulose, hydroxypropyl cellulose, talc, triethyl citrate, titanium oxide</td>
</tr>
<tr>
<td><strong>Inactive ingredients</strong></td>
<td>Carmellose calcium, magnesium stearate, methacrylic acid copolymer LD, sodium lauryl sulfate, polysorbate 80, carnauba wax</td>
<td>Corn starch, hydrogenerated oil, sugar, hydroxypropyl methylcellulose acetate succinate, sorbitan sesquioleate, gelatin</td>
<td>Corn starch, hydrogenerated oil, sugar, hydroxypropyl methylcellulose acetate succinate, sorbitan sesquioleate, gelatin</td>
</tr>
</tbody>
</table>

**Color/dosage form**

- White Enteric film-coated tablets (Diameter: approximately 8.3 mm; thickness: approximately 4.4 mm; weight: approximately 0.22 g)
- White Enteric granules

**Description**

- Odorless, sweet taste

**Identification code**

<table>
<thead>
<tr>
<th>Enteric Coated Tablet 20</th>
<th>Enteric Coated Tablet 60</th>
<th>Granule 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval No.</td>
<td>(45AM)2758</td>
<td>(45AM)2934</td>
</tr>
<tr>
<td>Date of listing in the NHI reimbursement price</td>
<td>February 1972</td>
<td>February 1972</td>
</tr>
<tr>
<td>Date of initial marketing in Japan</td>
<td>February 1972</td>
<td>February 1972</td>
</tr>
<tr>
<td>Date of latest reevaluation</td>
<td>June 1999</td>
<td></td>
</tr>
<tr>
<td>Date of latest approval of indications</td>
<td></td>
<td>May 1988</td>
</tr>
</tbody>
</table>

### INDICATIONS

<table>
<thead>
<tr>
<th>ADETPHOS KOWA Enteric Coated Tablet 20,60</th>
<th>ADETPHOS KOWA Granule 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Improvement of symptoms resulting from the following disease:</td>
<td>● Improvement of symptoms resulting from the following disease:</td>
</tr>
</tbody>
</table>

**Sequeleaes of head injury**

- Cardiac failure
- Stabilization of accommodative function in accommodative asthenopia
- Chronic gastritis accompanied with decreased gastrointestinal function
- Dizziness associated with Meniere's disease or inner ear disorder

**Dosage and Administration**

For oral use, dosage is 40 mg to 60 mg of adenosine triphosphate disodium hydrate, three times daily.

For oral use, dosage is 100 mg of adenosine triphosphate disodium hydrate three times daily when used for dizziness associated with Meniere's disease or inner ear disorder.

In addition, the dosage may be adjusted according to the patient’s condition.

### Precautions

1. Drug Interactions

   **Precautions for co-administration** (ADETPHOS KOWA Enteric Coated Tablet 20,60, Granule 10% should be administered with care when co-administered with the following drugs.)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Signs, Symptoms, and Treatment</th>
<th>Mechanism and Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipyridamole</td>
<td>Dipyridamole reportedly increases blood concentrations of adenosine, an ATP degradation product, and enhances</td>
<td>Due to the inhibitory effects of dipyridamole on adenosine up-</td>
</tr>
</tbody>
</table>
2. Adverse Reactions
In accumulated data on oral preparations (tablets/granules), adverse reactions were reported in 35 (1.82%) of 1920 patients. The major symptoms were gastrointestinal disorders, nausea and pruritus, etc. No significant abnormalities in laboratory data have been observed. (Accumulated data for re-evaluation and application on new indications for Adetphos Granule 10%)

<table>
<thead>
<tr>
<th>Incidence</th>
<th>&lt;1.0%</th>
<th>Incidence unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, anorexia, gastrointestinal disorders, constipation tendency, stomatitis</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>General throbbing</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Pruritus, Rash</td>
<td></td>
</tr>
<tr>
<td>Psychoneurologic</td>
<td>Headache, sleepiness, restless feeling</td>
<td></td>
</tr>
<tr>
<td>Sensory</td>
<td>Tinnitus</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>Feelings of weakness</td>
<td></td>
</tr>
</tbody>
</table>

3. Use in the Elderly
Since elderly patients often have reduced physiological function, careful supervision and measures such as reducing the dose are recommended.

4. Use during Pregnancy, Delivery or Lactation
Use of this drug in pregnant women or in women who may possibly be pregnant is not recommended (safety of this product in pregnant women has not been established.)

5. Pediatric Use
The safety of this drug in children has not been established.

6. Precautions concerning Use
(1) Precautions regarding dispensing (tablets only)
   In the case of press-through packages (PTP), instruct the patient to remove the drug from the package prior to use (if the PTP sheet is swallowed, the sharp corners may penetrate the esophageal mucosa, leading to severe complications such as mediastinitis).
(2) Precautions during preparation
   Do not grind with a mortar, etc., to use this drug.

7. CLINICAL STUDIES
The results of double-blind comparative studies showed that this drug was effective for cardiac failure, sequelae of head injury, chronic gastritis associated with gastropitosis, asthenopia, and dizziness associated with Meniere’s disease or inner ear disorder (granules only).1-5)

PHARMACOLOGY
1. Increases blood flow of various organ tissues by vasodilatory actions.

   Increases blood flow in the brain (dog, cat, adult male)6-8), heart (dog)9,10), stomach (dog)11) and inner ear (guinea pig)12,13).

2. Increases intravital metabolic activity.
   Increases metabolic activity in the brain (guinea pig, in vitro)14,15), heart (dog, rabbit)16,17), and inner ear (guinea pig, in vitro), etc.18,19).

3. Increases the contractile strength of muscles.
   Enhances myocardial contractile strength (frog, in vitro)20), and the contractile strength of gastrointestinal smooth muscle (rat, healthy adult humans)21,22).

4. Enhances neurotransmission efficiency.
   Enhances neurotransmission efficiency (bullfrog, in vitro)23).

5. Improves impaired function of inner ear.
   Prevents vestibular function disorder caused by streptomycin (guinea pig)24).

PHYSICOCHEMISTRY
Nonproprietary name:
Adenosine Triphosphate Disodium Hydrate
Chemical name:
Disodium adenosine-5'-triphosphate (ATP-2Na)
Structural formula:

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\[
\text{Na}_2\text{H}_8\text{N}_2\text{O}_9\text{P}_3 \cdot 3\text{H}_2\text{O}
\]
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Molecular formula: C_{10}H_{14}N_{5}Na_{2}O_{13}P_{3} \cdot 3H_{2}O
Molecular weight: 605.19
Description:
Adenosine triphosphate disodium hydrate occurs as white crystals or a crystalline powder, odorless with a slight acidic taste. It is freely soluble in water, and practically insoluble in ethanol (95%) or diethyl ether.

PACKAGING
ADETPHOS KOWA Enteric Coated Tablet 20
PTP: 100 tablets, 500 tablets, 1000 tablets, 2100 tablets
Bottle: 1000 tablets
ADETPHOS KOWA Enteric Coated Tablet 60
PTP: 100 tablets, 1000 tablets, 2100 tablets
Bottle: 1000 tablets
ADETPHOS KOWA Granule 10%
100 g, 500 g, 1 kg, 0.5 g × 1050 packets
1.0 g × 600 packets, 1.0 g × 1050 packets, 1.0 g × 1200 packets

REFERENCES
1) Takasaki, H. et al. : Rinsho to Kenkyu,55.207(1978)
5) Watanabe, I. et al. : Practica Oto-Rhino-Laryngologica,
75.393(1982)
6) Matsumoto, H. et al.: Rinsho to Kenkyu,50.1510 (1973)
10) Oshima, K. et al.: Kokyu to Junkan,7.115(1959)
16) Ito, T.: Vitamin,17.319(1959)
19) Koide, Y. et al.: Practica Oto-Rhino-Laryngologica, 57.149(1964)
22) Yamagata, K. et al.: ATP no Kiso to Rinsho

REQUEST FOR LITERATURE SHOULD BE MADE TO:
Ethical Drug Information Department, Pharmaceutical Division
KOWA COMPANY, LTD.
3-4-14, Nihonbashi-Honcho, Chuo-ku, Tokyo, Japan 103-8433

Contact for Product Information:
Pharmaceutical Information Services Center, Pharmaceutical Division
KOWA COMPANY, LTD.
Telephone: 0120-508-514
03-3279-7587
Hours: 09:00 to 17:00 (except for Saturdays, Sundays, and national holidays)

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KOWA COMPANY, LTD.
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