

- ANTI-GASTRITIS AND ANTI-GASTRIC ULCER DRUG –

MUCOSTA® Tablets 100mg


< Rebamipide >

DESCRIPTION

1. Composition

Each MUCOSTA Tablet contains 100 mg of rebamipide.

2. Product Description

| | | | | |
|---|---------------------------|---------------------------|------------------------|-------------|
| Brand name | MUCOSTA Tablets 100 mg | | | |
| Description | White film-coated tablets | | | |
| Appearance | Diameter (mm) | Thickness (mm) | Weight (mg) | Code |
|  | 8.1 | 3.4 | Approx. 175 | OG 33 |

INDICATIONS

- Gastric ulcers
In combination with offensive factor inhibitors (Proton Pump Inhibitors, Anticholinergic, H2-antagonist).
- Gastritis

CONTRAINDICATIONS (MUCOSTA Tablets are contraindicated in the following patients)

Patients with a history of hypersensitivity to any ingredient of this drug.

DOSAGE AND ADMINISTRATION

- Gastric ulcers: In combination with offensive factor inhibitors the usual adult dosage of rebamipide is 100 mg (1 tablet of **MUCOSTA Tablets 100 mg**) taken by the oral route three times daily, in the morning, in the evening, and before at bedtime.
- Gastritis: The usual adult dosage of rebamipide is 100 mg (1 tablet of **MUCOSTA Tablets 100 mg**) three times daily taken by the oral route.

PHARMACOLOGY

1. Preventive or healing effects in gastric ulcer models

Rebamipide inhibited gastric mucosal injury in various experimental rat models of ulcers, including ulcers induced by water-immersion restraint stress, aspirin, indomethacin, histamine, serotonin, and pyloric ligation. The drug also protected the mucosa from injury caused by other ulcerogenic

conditions that presumably yield reactive oxygen species, including mucosal ischemia-reperfusion, administration of platelet activating factor (PAF) or diethyldithiocarbamate (DDC), and administration of indomethacin under stressed conditions.

In a rat acetic acid-induced ulcer model, the drug promoted healing of gastric ulcers and was seen to suppress the recurrence and relapse of ulcers 120-140 days after ulcer induction.

2. Preventive or healing effects in gastritis models

Rebamipide inhibited the development of taurocholic acid (one of the main ingredients of bile acid)-induced gastritis and promoted healing of the mucosal inflammation associated with gastritis in rat experiments.

3. Prostaglandin-increasing effect

Rebamipide increased the generation of prostaglandin E2 (PGE2) in the gastric mucosa in rats. The drug also increased the contents of PGE2, 15-keto-13,14-dihydro-PGE2 (a metabolite of PGE2) and PGI2 in the gastric juice. In healthy male subjects, the drug again revealed the increasing effect on the PGE2 content in the gastric mucosa and protected the gastric mucosa from injury caused by ethanol loading.

4. Cytoprotective effect

Rebamipide exhibited a gastric cytoprotective effect to inhibit the mucosal injury induced by ethanol, strong acid, or strong base in rats. In *in vitro* studies, the drug also protected cultured gastric epithelial cells obtained from rabbit fetuses against aspirin- or taurocholic acid (one of the main ingredients of bile acid) -induced injury.

In healthy male subjects, the drug inhibited gastric mucosal injury induced by aspirin, ethanol, or HCl-ethanol loading.

5. Mucus-increasing effect

Rebamipide promoted gastric enzyme activity to synthesize high molecular weight glycoproteins, thickened the superficial mucous layer of gastric mucosa, and increased the amount of gastric soluble mucus in rats. Endogenous PGs were not involved in the increase in soluble mucus.

6. Mucosal blood flow-increasing effect

Rebamipide increased gastric mucosal blood flow and improved impaired hemodynamics after blood loss in rats.

7. Effect on mucosal barrier

Rebamipide did not ordinarily affect the gastric transmucosal potential difference in rats, but did inhibit lowering of the potential difference by ethanol.

8. Effect on gastric alkaline secretion

Rebamipide promoted gastric alkaline secretion in rats.

9. Effect on mucosal cell turnover

Rebamipide activated gastric mucosal cell proliferation and increased the number of covering epithelial cells in rats.

10. Effect on gastric mucosal repair

Rebamipide restored the bile acid- or hydrogen peroxide-induced retardation of artificial wound-repair in cultured rabbit gastric epithelial cells.

11. Effect on gastric secretion

Rebamipide did not alter either basal secretion of gastric juice or secretagogue-stimulated acid secretion.

12. Effects on reactive oxygen species

Rebamipide scavenged hydroxyl radicals directly and suppressed superoxide production by polymorphonuclear leukocytes. The drug inhibited the gastric mucosal cell injury caused by reactive oxygen species released from neutrophils stimulated by *Helicobacter pylori* *in vitro*. The drug reduced the content of lipid peroxide in the gastric mucosa of rats treated with indomethacin under stressed conditions and inhibited the mucosal injury.

13. Effect on inflammatory cell infiltration in the gastric mucosa

Rebamipide prevented inflammatory cell infiltration in rat models of taurocholic acid (one of the main ingredients of bile acid)- induced gastritis and NSAID-induced or ischemia-reperfusion-induced gastric mucosal damage.

14. Effect on inflammatory cytokine release (interleukin-8) in the gastric mucosa

Rebamipide, taken by the oral route, suppressed the increased production of interleukin-8 in the mucosa of patients with *Helicobacter pylori*. The drug also inhibited the activation of NF-κB, the expression of interleukin-8 mRNA, and the production of interleukin-8 in epithelial cells cocultured with *Helicobacter pylori*.

PHARMACOKINETICS

1. Plasma Concentrations

The table below shows the pharmacokinetic parameters of rebamipide following single oral administration of **MUCOSTA Tablets 100 mg** at a dose of 100 mg to 27 healthy male subjects in a fasted state. Repeated administration studies have shown that the drug does not accumulate in humans.

Pharmacokinetic Parameters of Rebamipide

| | t_{max} (hr) | C_{max} (µg/L) | t_{1/2} (hr) | AUC_{24h} (µg/L.hr) |
|---------------------------|---------------------------------------|---|---------------------------------------|--|
| MUCOSTA Tablets 100 mg | 2.4±1.2 | 216±79 | 1.9±0.7 | 874±209 |

Mean value±SD, n=27, t_{1/2} calculated from values up to 12 hr

The absorption rate of rebamipide following single oral administration at a dose of 150 mg to 6 healthy male subjects in a fed state tended to be slower than that in a fasted state. However, food did not affect bioavailability of the drug in humans.

Pharmacokinetic parameters obtained from patients with renal impairment after single oral administration of rebamipide at 100 mg revealed higher plasma concentrations and a longer elimination half-life compared with those in healthy subjects. At steady-state, rebamipide plasma concentrations observed in dialyzed renal patients following repeated administration were very close to the values simulated from single administration. Therefore, the drug was not considered to accumulate.

2. Metabolism

Rebamipide was primarily excreted as the unchanged compound in the urine after single oral administration to healthy adult males at a dose of 600 mg. A metabolite with a hydroxyl group at the 8th position was identified in the urine. However, the excretion of this metabolite was only 0.03% of the administered dose. The enzyme involved in the formation of the metabolite was CYP3A4.

(Note) The usual dosage in adults is 100 mg three times

Daily

3. Excretion

Approximately 10% of the administered dose was excreted in the urine when rebamipide was administered as a single oral dose to healthy adult males at 100 mg.

4. Protein Binding

Rebamipide at 0.05 – 5 µg/mL was added to human plasma *in vitro*, and 98.4% – 98.6% of the drug was bound to plasma proteins.

CLINICAL STUDIES

1. Clinical Efficacy in Gastric Ulcer

MUCOSTA Tablets were studied in patients with gastric ulcer, using endoscopy for objective drug evaluation. In the final endoscopic assessment, the drug achieved complete healing in 60% (200/335) of the patients studied and near-complete healing in 67% (224/335). The clinical usefulness of this drug, based on efficacy and safety was demonstrated in a double-blind study. Six-month follow-up of 67 patients who showed healing at a daily dose of 300 mg revealed that recurrence occurred in only 4 patients (approx. 6%).

2. Clinical Efficacy in Acute Gastritis and Acute Exacerbation of Chronic Gastritis

MUCOSTA Tablets were studied in patients with acute gastritis or acute exacerbation of chronic gastritis. The drug achieved an 80% (370/461) global efficacy rate in the patients evaluated, with 76% (351/461) showing moderate or marked improvement. The drug's clinical usefulness was found to be reproducible in a double-blind study.

PRECAUTIONS

1. Use in the Elderly

Special care is required in elderly patients to minimize the risk of gastrointestinal disorders, because these patients may be physiologically more sensitive to this drug than younger patients.

2. Use during Pregnancy, Delivery, or Lactation

(1) This drug should be administered to pregnant or possibly pregnant women only if the anticipated therapeutic benefit is thought to outweigh any potential risk. (The safety of this drug in pregnant women has not been established.)

(2) Nursing should be interrupted when this drug is administered to. (Rat studies have shown that rebamipide is excreted in the breast milk.)

3. Pediatric Use

The safety of this drug in low birth weight infants, newborns, suckling infants, infants and children has not been established. (Clinical experience is insufficient.)

4. Precautions for Use

MUCOSTA Tablets 100 mg

Patient's Instructions for Use:

Patients should be instructed not to ingest any portion of the press-through package (PTP). (There have been reports that the sharp edges of the sheet can cut or penetrate the esophageal mucosa if accidentally ingested, resulting in mediastinitis or other serious complications.)

Effects on ability to drive and use machines

No data available.

ADVERSE REACTIONS

Of 10,047 patients treated, adverse reactions, including abnormal laboratory findings, were reported in 54 patients (0.54%). Of 3,035 patients aged over 65 years, adverse reactions were noted in 18 patients (0.59%). The nature and incidence of adverse reactions showed no differences between elderly and younger patients. The following summary of data includes adverse reactions voluntarily reported after marketing (Figures are total cases reported at the time of approval and at the completion of reexamination of **MUCOSTA Tablets 100**).

(1) Clinically significant adverse reactions

1) **Shock, anaphylactoid reactions** (incidence unknown*): Shock or anaphylactoid reactions may occur. Patients should therefore be closely monitored. If abnormal findings are observed, the drug should be discontinued and appropriate measures taken.

2) **Leukopenia** (incidence <0.1%) and **thrombocytopenia** (incidence unknown*): Leukopenia and thrombocytopenia may occur. Patient should therefore be closely monitored. If abnormal findings are observed, the drug should be discontinued and appropriate measures taken.

3) **Hepatic dysfunction** (incidence <0.1%) and **jaundice** (incidence unknown*): Hepatic dysfunction and jaundice, as indicated by increases in AST (GOT), ALT (GPT), γ -GTP, and alkaline phosphatase levels, have been reported in patients receiving **MUCOSTA Tablets**. Patient should therefore be closely monitored. If abnormal laboratory findings are observed, the drug should be discontinued and appropriate measures taken.

(2) **Other adverse reactions**

| Body system/ frequency | Rare (< 0.1%) | *Incidence unknown |
|--|---|---|
| Hypersensitivity <small>(note 1)</small> | Rash, pruritus, drug-eruption-like eczema, other symptoms of hypersensitivity | Urticaria |
| Neuro- psychiatric | | Numbness, dizziness, sleepiness |
| Gastro- intestinal | Constipation, feeling of abdomen enlarged, diarrhea, nausea, vomiting, heartburn, abdominal pain, belching, taste abnormality, etc. | Dry mouth |
| Hepatic <small>(note 2)</small> | Increased AST (GOT), ALT (GPT), γ -GTP, alkaline phosphatase levels | |
| Hematologic | Leukopenia, granulocytopenia, etc. | Thrombocytopenia |
| Other | Menstrual disorders, increased BUN levels, edema, feeling of a foreign body in the pharynx | Breast swelling and pain, gynecomastia, induction of lactation, palpitations, fever, facial flushing, numbness of tongue, cough, respiratory distress, alopecia |

Note 1) If such symptoms of hypersensitivity occur, the drug should be discontinued.

Note 2) If transaminase levels are markedly increased or fever and rash develop, the drug should be discontinued and appropriate measures should be taken.

*The incidence rates of voluntarily reported adverse reactions are not known.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal products. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional

Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif

Badan Pengawas Obat dan Makanan

Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560

Email: pv-center@pom.go.id

Phone: +62-21-4244691 Ext. 1079

Website: <https://e-meso.pom.go.id/ADR>

DRUG INTERACTION

No study was done to evaluate drug interaction.

Overdosage

No data available.

PHYSICOCHEMISTRY

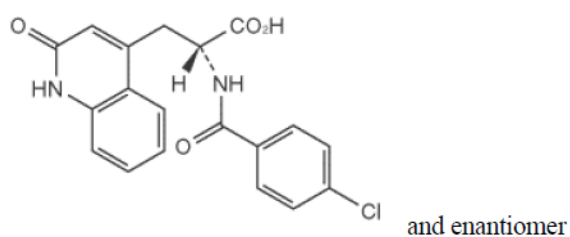
Nonproprietary name:

Rebamipide (JAN)

Chemical name:

(2*RS*)-2-(4-Chlorobenzoylamino)-3-(2-oxo-1,2-dihydroquinolin-4-yl) propionic acid

Structural formula:



Molecular formula:

C₁₉H₁₅ClN₂O₄

Molecular weight:

370.79

Description:

Rebamipide occurs as a white crystalline powder. It has a bitter taste. It is soluble in *N,N*-dimethylformamide, very slightly soluble in methanol and ethanol (99.5), and practically insoluble in water. Its *N,N*-dimethylformamide solution (1→20) shows no optical rotation.

Melting point: About 291°C (decomposition)

Inactive ingredients:

Magnesium stearate, Hypromellose, Macrogol 6000, Titanium dioxide, Hyprolose, Microcrystalline cellulose, and Purified water

STORAGE

Store below 30 °C

SHELF LIFE

Mucosta tablet 100 mg: 36 months

PACKAGING**MUCOSTA Tablets 100 mg:**

Boxes of 10 blister of 10 tablets

REG No DKL0518707017A1

HARUS DENGAN RESEP DOKTER

**MUCOSTA TABLET**

Manufactured by:

PT Otsuka Indonesia

Jl Sumber Waras No 25

Lawang, Malang 65216, Indonesia



Under License of:

Otsuka Pharmaceutical Co., Ltd., Japan

INFORMASI PRODUK UNTUK PASIEN

MUCOSTA® Tablets 100mg

< Rebamipide >

| | |
|-----------------------|--|
| Nama Obat | : MUCOSTA |
| Bentuk Sediaan | : Tablet |
| Deskripsi | : Tablet salut selaput berwarna putih |
| Komposisi | : Tiap tablet mengandung rebamipide 100 mg |

Baca seluruh isi leaflet ini secara saksama sebelum Anda memulai penggunaan obat karena leaflet ini berisi informasi yang penting bagi Anda.

- Simpan leaflet ini. Anda mungkin perlu untuk membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker Anda.
- Obat ini hanya diresepkan untuk Anda. Jangan berikan kepada orang lain. Hal ini dapat membahayakan mereka, meskipun gejala penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping, konsultasikan dengan dokter atau apoteker Anda. Ini termasuk efek samping yang mungkin terjadi yang tidak tercantum dalam *leaflet* ini. Lihat bagian 5.

Apa yang terdapat dalam *leaflet* ini

1. Apa itu MUCOSTA dan apa kegunaannya?
2. Apa yang perlu Anda ketahui sebelum mengonsumsi MUCOSTA?
3. Bagaimana cara mengonsumsi MUCOSTA?
4. Siapa yang tidak boleh mengonsumsi MUCOSTA?
5. Apa kemungkinan efek samping dari MUCOSTA?
6. Apakah ada efek pada saat mengendarai kendaraan dan menjalankan mesin selama mengonsumsi MUCOSTA?
7. Overdosis
8. Penggunaan pada anak-anak
9. Bagaimana cara menyimpan MUCOSTA?
10. Apa komposisi MUCOSTA?

1. Apa itu MUCOSTA dan apa kegunaannya?

MUCOSTA adalah obat perlindungan jaringan lambung. Obat ini digunakan untuk mengobati tukak lambung (luka pada lambung) dan gastritis (peradangan pada lambung) dengan membantu menekan peradangan dan memperbaiki mukosa gaster / selaput lendir dinding lambung.

2. Apa yang perlu Anda ketahui sebelum mengonsumsi MUCOSTA?

Pastikan untuk memberi tahu dokter dan apoteker Anda jika Anda dalam kondisi berikut ini:

- Jika Anda sebelumnya pernah mengalami reaksi alergi (gatal, ruam kemerahan, dll.) terhadap obat atau makanan.
- Jika Anda sedang hamil atau menyusui.
- Jika Anda sedang mengonsumsi obat-obatan lain. (Beberapa obat dapat berinteraksi untuk meningkatkan atau mengurangi efek obat. Berhati-hatilah terhadap obat bebas dan suplemen makanan serta obat resep lainnya.)

3. Bagaimana cara mengonsumsi MUCOSTA?

- Selalu konsumsi obat ini sesuai dengan petunjuk dokter. Konsultasikan dengan dokter atau apoteker Anda jika Anda tidak yakin.
- Untuk tukak lambung : secara umum untuk dewasa, minum 1 tablet (100 mg rebamipide) 3 kali sehari pada pagi, siang dan sebelum tidur.
Untuk gastritis : secara umum untuk dewasa, minum 1 tablet (100 mg rebamipide) 3 kali sehari. Ikuti instruksi dengan ketat.
- Jika Anda lupa mengonsumsi satu dosis, konsumsi obat yang terlewat segera setelah Anda mengingatnya. Jika sudah mendekati waktu untuk mengonsumsi dosis berikutnya, lewatkan saja dosis yang terlupa dan konsumsi dosis sesuai jadwal selanjutnya. Jangan mengonsumsi dua dosis MUCOSTA sekaligus.
- Jangan berhenti mengonsumsi obat kecuali atas instruksi dokter Anda.

4. Siapa yang tidak boleh menggunakan MUCOSTA?

Jika Anda memiliki reaksi alergi (gatal, ruam kemerahan, dll) terhadap salah satu bahan yang terkandung dalam obat ini (lihat *Bagian 10. Apa komposisi MUCOSTA?*)

5. Apa kemungkinan efek samping dari MUCOSTA?

Gejala – gejala di bawah ini jarang terlihat sebagai gejala awal dari reaksi yang tidak diinginkan. Jika salah satu dari gejala ini terjadi, hentikan mengonsumsi obat ini dan segera konsultasikan dengan dokter Anda.

- wajah pucat, keringat dingin, pusing saat berdiri [syok / renjatan].
- pembengkakan di sekitar mata atau mulut, gatal-gatal, gangguan pernapasan [anafilaksis].
- nyeri tenggorokan, demam, *malaise* [penurunan jumlah sel darah putih].
- mimisan, gusi berdarah, perdarahan subkutan di anggota tubuh [penurunan jumlah trombosit].
- *malaise* umum, kehilangan nafsu makan, menguningnya kulit dan mukosa [disfungsi hati, penyakit kuning (*jaundice*)].

Reaksi yang tidak diinginkan yang jarang dilaporkan meliputi hal-hal di bawah ini. Jika salah satu dari gejala ini terjadi, konsultasikan dengan dokter atau apoteker Anda.

- ruam, gatal, eksim yang dipicu oleh penggunaan obat (*drug-eruption-like eczema*), gejala alergi/hipersensitivitas lainnya
- sembelit, perut terasa membesar (kembung), diare, mual, muntah, nyeri ulu hati, nyeri perut, bersendawa, gangguan pencernaan, dll.
- peningkatan kadar enzim hati di dalam darah seperti AST (*Aspartate Aminotransferase*) (*GOT/Glutamic-Oxaloacetic Transaminase*), ALT (*Alanine Aminotransferase*) (*GPT/Glutamic-Pyruvic Transaminase*), γ -GTP (*Gamma-Glutamyl Transpeptidase*), alkali fosfatase
- rendahnya jumlah sel darah putih dalam darah (*leukopenia*), rendahnya jumlah granulosit dalam darah (*granulositopenia*), dll.
- gangguan menstruasi, peningkatan kadar Nitrogen Urea Darah (*Blood Urea Nitrogen / BUN*), edema, sensasi benda asing pada tenggorokan

Gejala-gejala di bawah ini merupakan kejadian reaksi yang tidak diinginkan yang dilaporkan secara sukarela dan tidak diketahui.

- Biduran (*urtikaria*)
- Kebas, pusing, mengantuk
- Mulut kering
- Rendahnya jumlah trombosit dalam darah (*trombositopenia*)
- Pembengkakan dan nyeri pada payudara, ginekomastia, induksi laktasi, berdebar-debar (*palpitasi*), demam, kemerahan pada wajah, kebas pada lidah, batuk, gangguan pernapasan, alopesia (*kebotakan*)

6. Apakah ada efek pada saat mengendarai kendaraan dan menjalankan mesin selama mengonsumsi MUCOSTA?

Tidak ada data tersedia yang berkaitan dengan efek pada saat mengendarai kendaraan dan menjalankan mesin selama mengonsumsi MUCOSTA.

7. Overdosis

Tidak ada data tersedia yang berkaitan dengan efek overdosis dari obat ini. Jika Anda mengonsumsi MUCOSTA terlalu banyak, hubungi tenaga kesehatan atau kunjungi instalasi gawat darurat rumah sakit terdekat.

8. Penggunaan pada anak-anak

Keamanan penggunaan MUCOSTA pada pasien anak-anak belum tersedia.

Gejala-gejala di atas tidak menggambarkan semua reaksi yang tidak diinginkan dari obat ini. Jika Anda melihat atau merasakan gejala-gejala yang mengkhawatirkan seperti yang tercantum atau tidak tercantum di atas, Anda dapat melaporkan keluhan efek samping atau kondisi yang tidak nyaman secara langsung ke:

PT Otsuka Indonesia

Pondok Indah Office Tower 1 Lantai 8

Jl. Sultan Iskandar Muda Kav. V-TA, Jakarta Selatan 12310

Tel. +62-21-7654466

Email: otsuka.pv@ho.otsuka.co.id

Website: <https://www.otsuka.co.id/id/sideeffect>

Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

Pelaporan efek samping yang Anda lakukan tidak dapat menggantikan konsultasi medis.

Konsultasikan dengan dokter atau apoteker Anda jika Anda melihat atau merasakan gejala-gejala yang mengkhawatirkan seperti yang tercantum atau tidak tercantum di atas.

9. Bagaimana cara menyimpan MUCOSTA?

Simpan di bawah suhu 30°C. Jauhkan dari jangkauan anak-anak.

Buang obat yang tidak terpakai. Jangan menyimpannya.

10. Apa komposisi MUCOSTA?

Zat aktif : Rebamipide

Bahan tambahan : *Magnesium stearate, Hypromellose, Macrogol 6000, Titanium dioxide, Hyprolose, Microcrystalline cellulose, dan Purified water*

HARUS DENGAN RESEP DOKTER

KEMASAN

Tablet MUCOSTA 100 mg:

Dus 10 blister @ 10 tablet

REG. No.: DKL0518707017A1



Diproduksi oleh:
PT Otsuka Indonesia
Jl. Sumber Waras No 25
Lawang, Malang 65216, Indonesia



Dibawah lisensi dari:
Otsuka Pharmaceutical Co., Ltd., Japan