SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PRODUCT

Hovid Alendronate 70 mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ACTIVE INGREDIENTS	PER TABLET (MG)
Alendronate Sodium Trihydrate (equivalent to Alendronic Acid 70 mg)	91.40

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

To treat or prevent postmenopausal osteoporosis, corticosteroid-induced osteoporosis and reduces the risk of vertebral and hip fractures.

To treat Paget's disease of bone, bone metastases and hypercalcaemia of malignancy.

Posology and Method of administration

The recommended dosage is one 70 mg tablet once weekly.

To permit adequate absorption of alendronate

- Hovid Alendronate 70 mg Tablet must be taken at least 30 minutes before the first food, beverage, or medicinal product of the day with plain water only. Other beverages (including mineral water), food and some medicinal products are likely to reduce the absorption of alendronate.

To facilitate delivery to the stomach and thus reduce the potential for local and oesophageal irritation or adverse experiences:

- Hovid Alendronate 70 mg Tablet should only be swallowed upon arising for the day with a full glass of water (not less than 200 ml or 7 fl.oz.).
- Patients should only swallow Hovid Alendronate 70 mg Tablet whole. Patients should not crush or chew the tablet or allow the tablet to dissolve in their mouths because of a potential for oropharyngeal ulceration.
- Patients should not lie down until after their first food of the day which should be at least 30 minutes after taking the tablet.

- Patients should not lie down for at least 30 minutes after taking Hovid Alendronate 70 mg Tablet.
- Hovid Alendronate 70 mg Tablet should not be taken at bedtime or before arising for the day.

Patients should receive supplemental calcium and vitamin D if dietary intake is inadequate.

Use in the elderly
No dosage adjustment is necessary for the elderly.

Use in renal impairment
No dosage adjustment is necessary for patients with GFR greater than 35 ml/min. Alendronate is not recommended for patients with renal impairment where GFR is less than 35 ml/min, due to lack of experience.

Use in children (under 18 years)
There is insufficiency of data for use in children.

Contraindication

- Abnormalities of the oesophagus and other factors which delay oesophageal emptying such as stricture or achalasia.
- Inability to stand or sit upright for at least 30 minutes.
- Hypersensitivity to alendronate or to any of the excipients.
- Hypocalcaemia.

Warnings and precautions

Alendronate can cause local irritation of the upper gastro-intestinal mucosa. Because there is a potential for worsening of the underlying disease, caution should be used when alendronate is given to patients with active upper gastro-intestinal problems, such as dysphagia, oesophageal disease, gastritis, duodenitis, ulcers, or with a recent history (within the previous year) of major gastro-intestinal disease such as peptic ulcer, or active gastro-intestinal bleeding, or surgery of the upper gastro-intestinal tract other than pyloroplasty.

In patients with known Barrett's oesophagus, prescribers should consider the benefits and potential risks of alendronate on an individual patient basis.

Oesophageal reactions (sometimes severe and requiring hospitalisation), such as oesophagitis, oesophageal ulcers and oesophageal erosions, rarely followed by oesophageal stricture, have been reported in patients receiving alendronate. Physicians should therefore be alert to any signs or symptoms signalling a possible oesophageal reaction and patients should be instructed to discontinue alendronate and seek medical attention if they develop symptoms of oesophageal irritation such as dysphagia, pain on swallowing or retrosternal pain, new or worsening heartburn.

The risk of severe oesophageal adverse experiences appears to be greater in patients who fail to take alendronate properly and/or who continue to take alendronate after developing symptoms suggestive of oesophageal irritation. It is very important that the full dosing instructions are provided to, and understood by the patient. Patients should be informed that failure to follow these instructions may increase their risk of oesophageal problems.

Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis), has been reported in patients with cancer receiving treatment regimens including primarily intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates.

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene, periodontal disease).

While on treatment, these patients should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

Bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates. In post-marketing experience, these symptoms have rarely been severe and/or incapacitating. The time to onset of symptoms varied from one day to several months after starting treatment. Most patients had relief of symptoms after stopping. A subset had recurrence of symptoms when rechallenged with the same drug or another bisphosphonate.

Stress fractures (also known as insufficiency fractures) of the proximal femoral shaft have been reported in patients treated long-term with alendronic acid (time to onset in the majority of cases ranged from 18 months to 10 years). The fractures occurred after minimal or no trauma and some patients experienced thigh pain, often associated with imaging features of stress fractures, weeks to months before presenting with a completed femoral fracture. Fractures were often bilateral; therefore the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture. Poor healing of these fractures was also reported. Discontinuation of bisphosphonate therapy in patients with stress fracture is advisable pending evaluation of the patient, based on an individual benefit risk assessment.

Patients should be instructed that if they miss a dose of Hovid Alendronate 70mg Tablet, they should take one tablet on the morning after they remember. They should not take two tablets on the same day but should return to taking one tablet once a week, as originally scheduled on their chosen day.

Alendronate is not recommended for patients with renal impairment where GFR is less than 35 ml/min.

Causes of osteoporosis other than oestrogen deficiency and ageing should be considered.

Hypocalcaemia must be corrected before initiating therapy with alendronate. Other disorders affecting mineral metabolism (such as vitamin D deficiency and hypoparathyroidism) should also be effectively treated. In patients with these conditions, serum calcium and symptoms of hypocalcaemia should be monitored during therapy with Hovid Alendronate 70mg Tablet.

Due to the positive effects of alendronate in increasing bone mineral, decreases in serum calcium and phosphate may occur especially in patients taking glucocorticoids in whom calcium absorption may be decreased. These are usually small and asymptomatic. However, there have been rare reports of symptomatic hypocalcaemia, which have occasionally been severe and often occurred in patients with predisposing conditions (e.g. hypoparathyroidism, vitamin D deficiency and calcium malabsorption).

Ensuring adequate calcium and vitamin D intake is particularly important in patients receiving glucocorticoids.

Drug Interactions

If taken at the same time, it is likely that food and beverages (including mineral water), calcium supplements, antacids, and some oral medicinal products will interfere with absorption of alendronate. Therefore, patients must wait at least 30 minutes after taking alendronate before taking any other oral medicinal product.

No other interactions with medicinal products of clinical significance are anticipated. A number of patients in the clinical trials received oestrogen (intravaginal, transdermal, or oral) while taking alendronate. No adverse experiences attributable to their concomitant use were identified.

Since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with alendronate.

Although specific interaction studies were not performed, in clinical studies alendronate was used concomitantly with a wide range of commonly prescribed medicinal products without evidence of clinical adverse interactions.

Pregnancy and lactation
Pregnancy
Alendronate should not be used during pregnancy. There are no adequate data from the use of alendronate in pregnant women.

Lactation
It is not known whether alendronate is excreted into human breast milk. Alendronate should not be used by breast-feeding women.

Effects on ability to drive and use machines

NOT APPLICABLE

Main Side/ Adverse Effects

Adverse experiences reported by the investigators as possibly, probably or definitely drug-related are presented below if they occurred in ≥ 1% in either treatment group in the one-year study, or in ≥ 1% of patients treated with alendronate 10 mg/day and at a greater incidence than in patients given placebo in the three-year studies:

Common adverse effects: Headache, Abdominal pain, Dyspepsia, Constipation, Diarrhoea, Flatulence, Oesophageal ulcer, dysphagia, Abdominal distension, Acid regurgitation, Musculoskeletal (bone, muscle or joint) pain, Erosions, Retrosternal pain, Peptic ulceration, Renal failure, Hepatitis and hepatocellular damage with raised liver enzyme concentrations, Auditory hallucinations and red-coloured visual disturbances.

Uncommon adverse effects: Nausea, Vomiting, Gastritis, Oesophagitis, Oesophageal erosions, Melena, Rash, Pruritus, Erythema.

Rare adverse effects: Hypersensitivity reactions including urticaria and angioedema, Symptomatic hypocalcaemia, Uveitis, Scleritis, Episcleritis, Oesophageal stricture, Oropharyngeal ulceration, Upper gastrointestinal PUBs (perforation, ulcers, bleeding), Rash with photosensitivity, Osteonecrosis of the jaw, Myalgia, Malaise, Fever.

Very rare adverse effects and isolated cases: Severe skin reactions including Stevens-Johnson syndrome, Toxic epidermal necrolysis

Unknown adverse effects: Dizziness, Dysgeusia, Vertigo, Alopecia, Joint swelling, Stress fractures of the proximal femoral shaft, Asthenia, Peripheral oedema.

Overdose

Symptoms

Hypocalcaemia, hypophosphataemia and upper gastro-intestinal adverse events, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdosage.

Treatment

No specific information is available on the treatment of overdosage with alendronate. Milk or antacids should be given to bind alendronate. Owing to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain fully upright.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The active ingredient of Hovid Alendronate 70 mg Tablet, alendronate sodium trihydrate, is a bisphosphonate that inhibits osteoclastic bone resorption with no direct effect on bone formation. Preclinical studies have shown preferential localisation of alendronate to sites of active resorption. Activity of osteoclasts is inhibited, but recruitment or attachment of osteoclasts is not affected. The bone formed during treatment with alendronate is of normal quality.

Alendronate is given in the management of osteoporosis either alone or with Vitamin D.

Pharmacokinetic properties

Absorption

Alendronate is poorly absorbed after oral doses. Absorption is decreased by food, especially by products containing calcium or other polyvalent cations.

Relative to an intravenous reference dose, the oral mean bioavailability of alendronate in women was 0.64% for doses ranging from 5 to 70 mg when administered after an overnight fast and two hours before a standardised breakfast. Bioavailability was decreased similarly to an estimated 0.46% and 0.39% when alendronate was administered one hour or half an hour before a standardised breakfast. In osteoporosis studies, alendronate was effective when administered at least 30 minutes before the first food or beverage of the day.

Bioavailability was negligible whether alendronate was administered with, or up to two hours after, a standardised breakfast. Concomitant administration of alendronate with coffee or orange juice reduced bioavailability by approximately 60%.

In healthy subjects, oral prednisone (20 mg three times daily for five days) did not produce a clinically meaningful change in oral bioavailability of alendronate (a mean increase ranging from 20% to 44%).

Distribution

The mean steady-state volume of distribution, exclusive of bone, is at least 28 litres in humans. Concentrations of drug in plasma following therapeutic oral doses are too low for analytical detection (<5 ng/ml). Protein binding in human plasma is approximately 78%.

Metabolism

There is no evidence that alendronate is metabolised in humans.

Elimination

Following a single intravenous dose of [^{14}C] alendronate, approximately 50% of the radioactivity was excreted in the urine within 72 hours and little or no radioactivity was recovered in the faeces. Following a single 10 mg intravenous dose, the renal clearance of alendronate was 71 ml/min, and systemic clearance did not exceed 200 ml/min. Plasma concentrations fell by more than 95% within six hours following intravenous administration. The terminal half-life in humans is estimated to exceed ten years, reflecting release of alendronate from the skeleton.

Preclinical Safety Data

NOT APPLICABLE

6. PHARMACEUTICAL PARTICULARS

List of excipeints

Excipients

Microcrystalline Cellulose
Pregelatinised Starch
Lactose Monohydrate
Sodium Starch Glycolate
Magnesium Stearate

Incompatibilities

NOT APPLICABLE

Shelf life

3 years from date of manufacture

Special precaution for storage

Store below 30˚C. Protect from moisture and light.

Nature and contents of container

Blister Pack

Type	:	Push-through Aluminium-Aluminium blister pack; the package consists of cold form blister foil material and a heat-sealed, lacquered backing material.
Material	:	Cold Form Blister Foil Backing Material : Aluminium Foil

Instructions for use and handling <and disposal>

NOT APPLICABLE

7. MARKETING AUTHORISATION HOLDER

Name: HOVID Bhd.
Address : 121, Jalan Tunku Abdul Rahman,
(Jalan Kuala Kangsar)
30010 Ipoh, Perak, Malaysia

Manufacturer Name :

Name	:	HOVID Bhd.
Address	:	Lot 56442, 7 ½ Miles, Jalan Ipoh / Chemor, 31200 Chemor, Perak., Malaysia.

8. NUMBER (S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

HOV/MAL/0029

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

May 2017

10. DATE OF REVISION OF THE TEXT

Dec 2020