8030250-9093

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Tacrotor®

(Tacrolimus Ointment)

COMPOSITION

Tacrotor® 0.1%

Each gm of ointment contains :

Tacrolimus	1 mg
Ointment base	q.s.

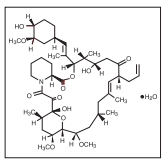
Tacrotor® 0.03%

Each gm of ointment contains :

Tacrolimus	0.3 mg
Ointment base	q.s.

DESCRIPTION

Tacrotor® 0.1 % and 0.03 %, contains the immunosuppressant agent, Tacrolimus. It is a macrolide lactone produced by *Streptomyces tsukubaensis*. It is for topical dermatologic use only. Its chemical structure is as follows:



MECHANISM OF ACTION

The exact mechanism of action of Tacrolimus in atopic dermatitis is not known. However, it has been demonstrated that Tacrolimus inhibits T-lymphocyte activation by first binding to an intracellular protein, FKBP-12. A complex of tacrolimus-FKBP-12, calcium, calmodulin, and calcineurin is then formed and the phosphatase activity of calcineurin is inhibited. This effect has been shown to prevent the dephosphorylation and translocation of nuclear factor of activated T-cells (NF-AT), a nuclear component thought to initiate gene transcription for the formation of lymphokines (such as interleukin-2, gamma interferon). Tacrolimus also inhibits the transcription for genes which encode IL-3, IL-4, IL-5, GM-CSF, and TNF, all of which are involved in the early stages of T-cell activation. Additionally, downregulation of the expression of the high-affinity IgE receptor in Langerhans cells and inhibition of the release of inflammatory mediators from mast cells and basophils by Tacrolimus may also serve as targets in the immune therapy of atopic dermatitis.

PHARMACOKINETICS

Systemic absorption with topical Tacrolimus is minimal. After single or multiple doses of 0.1% Tacrolimus ointment, peak blood concentrations were in the range of 5-20 ng/mL. The results from a pharmacokinetic study of 0.1% Tacrolimus ointment in 20 paediatric atopic dermatitis patients (ages 6-13 years), show peak Tacrolimus blood concentrations below 1.6 ng/mL in all patients.

The absolute bioavailability of topical Tacrolimus is unknown. Using historical intravenous data for comparison, the bioavailability of Tacrolimus ointment in patients with atopic dermatitis is less than 0.5%. In adults with an average of 53% body surface area (BSA) treated, exposure or area under curve (AUC) of Tacrolimus is approximately 30-fold less than that seen with oral immunosuppressive doses in kidney and liver transplant patients. The lowest Tacrolimus blood level at which systemic effects can be observed is not known. There was no evidence based on blood concentrations that Tacrolimus accumulates systemically upon intermittent topical application for periods of up to 1 year.

Studies have shown that damaged skin has a 7-fold higher rate of absorption of Tacrolimus. Healed skin regains percutaneous barrier function, preventing the large molecule of Tacrolimus from being absorbed.

CLINICAL STUDIES

Studies in Adults

Several studies have examined the efficacy of topical Tacrolimus in adult patients. In a double-blind, placebo-controlled study conducted by the European Tacrolimus Multicenter Atopic Dermatitis Study Group, 215 patients with moderate to severe atopic dermatitis were randomized to receive 0.03, 0.1, or 0.3 % Tacrolimus, or vehicle, applied twice daily. The decrease in severity scores for the three groups at 3 weeks of treatment was 67, 83, and 75 % for the 0.03, 0.1, and 0.3 % ointments, respectively. The vehicle group showed a 22% decrease in severity scores. No statistical difference was found among the three Tacrolimus groups, which showed equal efficacy in face, neck, and trunk regions.

Two identically designed, randomized, double-blind, multicenter studies were conducted in parallel, and jointly reported. In total, 632 patients with moderate to severe atopic dermatitis, aged 15-79 years, were randomized to receive topical Tacrolimus (0.03% or 0.1%) or vehicle, to be applied twice daily for 12 weeks. Physician assessment at 12 weeks showed 90 % improvement in 6.6 % of the vehicle patients, 27.5 % of the 0.03 % Tacrolimus group, and 36.8 % of the patients using 0.1 % Tacrolimus ointment ($P < 0.001$). Both treatment groups were significantly better than the vehicle group. Greater than 50 % improvement occurred in 19.8 % of the vehicle group, compared with 62 and 73 % of the 0.03 and 0.1 % Tacrolimus groups, respectively. The differences between the two Tacrolimus groups were most evident in patients with more severe disease and disease involving a larger surface area.

Paediatric studies

Paediatric studies have also demonstrated the efficacy of Tacrolimus in atopic dermatitis. In a randomized, double-blind, vehicle-controlled study, 0.03 %, 0.1 %, and 0.3 % Tacrolimus were compared with vehicle therapy in 180 children, 7 to 16 years of age, over 23 days, with twice-daily treatment. Physician assessment showed that 67 to 70 % of patients in the three treatment groups and 38 % in the vehicle group had greater than 75 % improvement in their atopic dermatitis.

In another multicenter, phase III, double-blind, randomized, vehicle-controlled study, 351 children, 2 to 15 years of age, with moderate to severe atopic dermatitis were treated for 12 weeks with 0.03 % or 0.1 % Tacrolimus ointment, or vehicle. At baseline, 58% of the patients had severe disease and the mean body surface area (BSA) affected was 46%. At baseline, 58% of the patients had severe disease and the mean body surface area (BSA) affected was 46%. By physician assessment, greater than 50 % improvement occurred in 73 and 78 % of the Tacrolimus groups, respectively, versus 27 % in the vehicle group.

A total of 571 patients applied Tacrolimus ointment 0.1% in long-term adult and paediatric safety studies for up to one year. In the adult study, 246 patients were evaluated for at least 6 months and 68 patients for 12 months. In the paediatric study, 219 patients were evaluated for at least 6 months and 180 patients for 12 months. On average, patients received treatment for 87% of study days. Tacrolimus ointment was found to be safe and effective in adult and paediatric patients with atopic dermatitis for upto 1 year.

Quality-of-life Study

A study of Dermatology Quality of Life Indexes performed on 985 adult and paediatric patients with moderate to severe atopic dermatitis showed significant improvement in all areas over 12 weeks in patients who used Tacrolimus. Patients were randomized to vehicle, 0.03 %, or 0.1 % Tacrolimus and evaluated at the end of 12 weeks. The surveys included such aspects as itchiness, self-consciousness, relationships, and dressing. Significant differences versus vehicle were seen in every category in adults. In children, the biggest quality-of-life differences were found in itchiness, sleeping, emotions, and activities. When patients were asked if they were "very likely to continue" using the medicine, those using both strengths of Tacrolimus were more likely to want to continue the medication than those who used the vehicle in all age groups.

CLINICAL INDICATION

Tacrotor® (0.03% and 0.1%) is indicated for short-term and intermittent long-term therapy in the treatment of patients with moderate to severe atopic dermatitis in whom the use of alternative, conventional therapies are not indicated because of potential risks, or in the treatment of patients who are not adequately responsive to or are intolerant of alternative, conventional therapies. Either strength (0.03% and 0.1%) of Tacrotor® can be used in adults, but only the 0.03% strength is indicated in children aged 2 to 15 years.

CONTRAINDICATIONS

Tacrotor® is contraindicated in patients with a history of hypersensitivity to Tacrolimus or any other component of the preparation.

WARNING

Tacrotor® (0.03% and 0.1%) is not for ophthalmic, oral or intravaginal use.

PRECAUTIONS

General

Studies have not evaluated the safety and efficacy of Tacrolimus ointment in the treatment of clinically infected atopic dermatitis. Before commencing treatment with Tacrotor®, clinical infections at treatment sites should be cleared.

While patients with atopic dermatitis are predisposed to superficial skin infections including eczema herpeticum (Kaposi's varicelliform eruption), treatment with Tacrotor® may be associated with an increased risk of varicella zoster virus infection (chicken pox or shingles), herpes simplex virus infection, or eczema herpeticum. In the presence of these infections, the balance of risks and benefits associated with Tacrotor ® use should be evaluated.

In clinical studies, 33 cases of lymphadenopathy (0.8%) were reported and were usually related to infections (particularly of the skin) and noted to resolve upon appropriate antibiotic therapy. Of these 33 cases, the majority had either a clear etiology or were known to resolve. Transplant patients receiving immunosuppressive regimens (e.g., systemic Tacrolimus) are at increased risk for developing lymphoma; therefore, patients who receive Tacrotor® and who develop lymphadenopathy should have the etiology of their lymphadenopathy investigated. In the absence of a clear etiology for the lymphadenopathy, or in the presence of acute infectious mononucleosis, discontinuation of Tacrotor® should be considered. Patients who develop lymphadenopathy should be monitored to ensure that the lymphadenopathy resolves.

The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Despite the absence of observed phototoxicity in humans (see ADVERSE REACTIONS), Tacrotor® shortened the time to skin tumor formation in an animal photocarcinogenicity study (see Carcinogenesis, Mutagenesis, Impairment of Fertility). Therefore, it is prudent for patients to minimize or avoid natural or artificial sunlight exposure.

The use of Tacrotor® may cause local symptoms such as skin burning (burning sensation, stinging, soreness) or pruritus. Localized symptoms are most common during the first few days of Tacrotor® application and typically improve as the lesions of atopic dermatitis heal. With Tacrotor® 0.1%, 90% of the skin burning events had a duration between 2 minutes and 3 hours (median 15 minutes). ninety % of the pruritus events had a duration between 3 minutes and 10 hours (median 20 minutes).

The use of Tacrotor® in patients with Netherton's Syndrome is not recommended due to the potential for increased systemic absorption of Tacrolimus. The safety of Tacrotor® has not been established in patients with generalized erythroderma.

VACCINATION

A potential interaction between vaccination and application of Tacrotor® has not been investigated. Because of the potential risk of vaccination failure, vaccination should be administered prior to commencement of treatment, or during a treatment-free interval with a period of 14 days between the last application of Tacrotor® and the vaccination. In case of live vaccination, this period should be extended to 28 days or the use of alternative vaccines should be considered.

Information for Patients

Patients using Tacrotor® should receive the following information and instructions:

- Patients should use Tacrotor® as directed by the physician. Tacrotor® is for external use only.
- As with any topical medication, patients or caregivers should wash hands after application if hands are not an area for treatment.
- Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using Tacrotor®.
- Patients should not use this medication for any disorder other than that for which it was prescribed.
- Patients should report any signs of adverse reactions to their physician.
- Before applying Tacrotor® after a bath or shower, be sure your skin is completely dry.

Drug Interactions

Formal topical drug interaction studies with Tacrotor® have not been conducted. Based on its minimal extent of absorption, interactions of Tacrotor® with systemically administered drugs are unlikely to occur but cannot be ruled out. The concomitant administration of known CYP3A4 inhibitors in patients with widespread and/or erythrodermic disease should be done with caution. Some examples of such drugs are erythromycin, itraconazole, ketoconazole, fluconazole, calcium channel blockers and cimetidine.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No evidence of genotoxicity was seen in bacterial or mammalian *in vitro* assays of mutagenicity, the *in vitro* CHO/HGPRT assay of mutagenicity, or *in vivo* clastogenicity assays performed in mice. Tacrolimus did not cause unscheduled DNA synthesis in rodent hepatocytes.

Oral (feed) carcinogenicity studies have been carried out with systemically administered Tacrolimus in male and female rats and mice. In the 80-week mouse study and in the 104-week rat study no relationship of tumor incidence to Tacrolimus dosage was found at daily doses up to 3 mg/kg [9X the Maximum Recommended Human Dose (MRHD) based on AUC comparisons] and 5 mg/kg (3X the MRHD based on AUC comparisons), respectively.

A 104 week dermal carcinogenicity study was performed in mice with Tacrotor® (0.03%-3%), equivalent to Tacrolimus doses of 1.1-118 mg/kg/day or 3.3-354 mg/m/day. In the study, the incidence of skin tumors was minimal and the topical application of Tacrolimus was not associated with skin tumor formation under ambient room lighting. However, a statistically significant elevation in the incidence of pleomorphic lymphoma in high dose male (25/50) and female animals (27/50) and in the incidence of undifferentiated lymphoma in high dose female animals (13/50) was noted in the mouse dermal carcinogenicity study. Lymphomas were noted in the mouse dermal carcinogenicity study at a daily dose of 3.5 mg/kg (0.1% Tacrotor®) (26X MRHD based on AUC comparisons). No drug-related tumors were noted in the mouse dermal carcinogenicity study at a daily dose of 1.1 mg/kg (0.03% Tacrotor®) (10X MRHD based on AUC comparisons).

In a 52-week photocarcinogenicity study, the median time to onset of skin tumor formation was decreased in hairless mice following chronic topical dosing with concurrent exposure to UV radiation (40 weeks of treatment followed by 12 weeks of observation) with Tacrotor® at ≥0.1% Tacrolimus.

Reproductive toxicology studies were not performed with topical Tacrolimus. In studies of oral Tacrolimus, no impairment of fertility was seen in male and female rats. Tacrolimus, given orally at 1.0 mg/kg (0.12X MRHD based on body surface area [BSA]) to male and female rats, prior to and during mating, as well as to dams during gestation and lactation, was associated with embryolethality and with adverse effects on female reproduction. Effects on female reproductive function (parturition) and embryolethal effects were indicated by a higher rate of pre-implantation loss and increased numbers of undelivered and nonviable pups. When given at 3.2 mg/kg (0.43X MRHD based on BSA), Tacrolimus was associated with maternal and paternal toxicity as well as reproductive toxicity including marked adverse effects on estrus cycles, parturition, pup viability, and pup malformations.

Pregnancy

Teratogenic Effects: Pregnancy Category C

There are no adequate and well-controlled studies of topically administered Tacrolimus in pregnant women. The experience with Tacrotor® when used by pregnant women is too limited to permit assessment of the safety of its use during pregnancy.

Reproduction studies were carried out with systemically administered Tacrolimus in rats and rabbits.

Adverse effects on the fetus were observed mainly at oral dose levels that were toxic to dams. Tacrolimus at oral doses of 0.32 and 1.0 mg/kg (0.04X-0.12X MRHD based on BSA) during organogenesis in rabbits was associated with maternal toxicity as well as an increase in incidence of abortions. At the higher dose only, an increased incidence of malformations and developmental variations was also seen. Tacrolimus, at oral doses of 3.2 mg/kg during organogenesis in rats, was associated with maternal toxicity and caused an increase in late resorptions, decreased numbers of live births, and decreased pup weight and viability. Tacrolimus, given orally at 1.0 and 3.2 mg/kg (0.04X-0.12X MRHD based on BSA) to pregnant rats after organogenesis and during lactation, was associated with reduced pup weights.

No reduction in male or female fertility was evident.

There are no adequate and well-controlled studies of systemically administered Tacrolimus in pregnant women. Tacrolimus is transferred across the placenta. The use of systemically administered Tacrolimus during pregnancy has been associated with neonatal hyperkalemia and renal dysfunction. Tacrotor® **should be used during pregnancy only if the potential benefit to the mother justifies a potential risk to the fetus.**

Nursing Mothers

Although systemic absorption of Tacrolimus following topical applications of Tacrotor® is minimal relative to systemic administration, it is known that Tacrolimus is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Tacrolimus, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Paediatric Use

Tacrotor® 0.03% may be used in paediatric patients 2 years of age and older. Two phase 3 paediatric studies were conducted involving 606 patients, 2-15 years of age: one 12-week randomized vehicle-controlled study and one open-label, 1 year, long-term safety study. Three hundred and thirty (330) of these patients were 2 to 6 years of age.

The most common adverse events associated with Tacrolimus ointment application in paediatric patients were skin burning and pruritus. In addition to skin burning and pruritus, the less common events (<5%) of varicella zoster (mostly chicken pox), and vesiculobullous rash were more frequent in patients treated with Tacrolimus ointment 0.03% compared to vehicle. In the long-term 1 year safety study involving 255 paediatric patients using Tacrolimus ointment, the incidence of adverse events, including infections, did not increase with increased duration of study drug exposure or amount of ointment used. In 491 paediatric patients treated with Tacrolimus ointment, 3 (0.6%) developed eczema herpeticum. Since the safety and efficacy of Tacrolimus ointment have not been established in paediatric patients below 2 years of age, its use in this age group is not recommended.

Geriatric Use

Twenty-five (25) patients ≥65 years old received Tacrolimus ointment in phase 3 studies. The adverse event profile for these patients was consistent with that for other adult patients.

ADVERSE REACTIONS

No phototoxicity and no photoallergenicity was detected in clinical studies of 12 and 216 normal volunteers, respectively. One out of 198 normal volunteers showed evidence of sensitization in a contact sensitization study.

The principal adverse events reported to date in clinical trials with topical Tacrolimus are primarily those of local application site reactions. The commonly reported adverse events in three randomized vehicle-controlled studies and two long-term safety studies involving 655 and 571 patients respectively, treated with Tacrolimus ointment, are presented in the following table.

Incidence of Treatment Emergent Adverse Events

	12-Week, Randomized, Double-Blind, Phase 3 Studies 12-Week Adjusted Incidence Rate (%)					Open-Label Studies (up to 3 years) 0.1% and 0.03% Tacrolimus Ointment Incidence Rate (%)		
	Adult			Pediatric		Adult	Pediatric	Total
	Vehicle (n=212) %	0.03% Tacrolimus Ointment (n=210) %	0.1% Tacrolimus Ointment (n=209) %	Vehicle (n=116) %	0.03% Tacrolimus Ointment (n=118) %	(n=4682) %	(n=4481) %	(n=9163) %
Skin Burning†	26	46	58	29	43	28	20	24
Pruritus†	37	46	46	27	41	25	19	22
Flu-like symptoms†	19	23	31	25	28	22	34	28
Allergic Reaction	8	12	6	8	4	9	13	11
Skin Erythema	20	25	28	13	12	12	7	9
Headache†	11	20	19	8	5	13	9	11
Skin Infection	11	12	5	14	10	9	16	12
Fever	4	4	1	13	21	2	14	8
Infection	1	1	2	9	7	6	10	8
Cough Increased	2	1	1	14	18	3	10	6
Asthma	4	6	4	6	6	4	13	8
Herpes Simplex	4	4	4	2	0	4	3	3
Eczema Herpeticum	0	1	1	0	2	0	0	0
Pharyngitis	3	3	4	11	6	4	12	8
Accidental Injury	4	3	6	3	6	6	8	7
Pustular Rash	2	3	4	3	2	2	7	5
Folliculitis†	1	6	4	0	2	4	2	3
Rhinitis	4	3	2	2	6	2	4	3
Otitis Media	4	0	1	6	12	2	11	6
Sinusitis†	1	4	2	8	3	6	7	6
Diarrhea	3	3	4	2	5	2	4	3
Urticaria	3	3	6	1	1	3	4	4
Lack of Drug Effect	1	1	0	1	1	6	6	6
Bronchitis	0	2	2	3	3	4	4	4
Vomiting	0	1	1	7	6	1	4	3
Maculopapular Rash	2	2	2	3	0	2	1	1
Rash†	1	5	2	4	2	2	3	3
Abdominal Pain	3	1	1	2	3	1	3	2
Fungal Dermatitis	0	2	1	3	0	2	4	3
Gastroenteritis	1	2	2	3	0	2	4	3
Alcohol Intolerance†	0	3	7	0	0	4	0	2
Acne†	2	4	7	1	0	3	2	3
Sunburn	1	2	1	0	0	2	1	1
Skin Disorder	2	2	1	1	4	2	2	2
Conjunctivitis	0	2	2	2	1	3	3	3
Pain	1	2	1	0	1	2	1	2
Vesiculobullous Rash†	3	3	2	0	4	2	1	1
Lymphadenopathy	2	2	1	0	3	1	2	1
Nausea	4	3	2	0	1	2	1	2
Skin Tingling†	2	3	8	1	2	2	1	1
Face Edema	2	2	1	2	1	1	1	1
Dyspepsia†	1	1	4	0	0	2	2	2
Dry Skin	7	3	3	0	1	1	1	1
Hyperesthesia†	1	3	7	0	0	2	0	1
Skin NeoplasmBenign‡‡	1	1	1	0	0	1	2	2
Back Pain†	0	2	2	1	1	3	0	2
Peripheral Edema	2	4	3	0	0	2	0	1
Varicella Zoster/Herpes Zoster† ‡⌀	0	1	0	0	5	1	2	2
Contact Dermatitis	1	3	3	3	4	2	2	2
Asthenia	1	2	3	0	0	1	0	1
Pneumonia	0	1	1	2	0	1	3	2
Eczema	2	2	2	0	0	1	0	1
Insomnia	3	4	3	1	1	2	0	1
Exfoliative Dermatitis	3	3	1	0	0	0	1	0
Dysmenorrhea	2	4	4	0	0	2	1	1
Periodontal Abscess	1	0	1	0	0	1	1	1
Myalgia†	0	3	2	0	0	2	1	1
Cyst†	0	1	3	0	0	1	0	1
Cellulitis	1	1	1	0	0	1	1	1
Exacerbation of Untreated Area	1	0	1	1	0	1	1	1
Procedural Complication	1	0	0	1	0	1	1	1
Hypertension	0	0	1	0	0	2	0	1
Tooth Disorder	0	1	1	1	0	2	1	1
Arthralgia	1	1	3	2	0	2	1	2
Depression	1	2	1	0	0	1	0	1
Paresthesia	1	3	3	0	0	2	1	2
Alopecia	0	1	1	0	0	1	1	1
Urinary Tract Infection	0	0	1	0	0	2	1	2
Ear Pain	1	0	1	0	1	0	1	1

† May be reasonably associated with the use of this drug product

† All the herpes zoster cases in the pediatric 12-week study and the majority of cases in the open-label pediatric studies were reported as chicken pox.

‡‡ Generally "warts".

Other adverse events which occurred at an incidence >1% in any clinical study include: alopecia, ALT or AST increased, anaphylactoid reaction, angina pectoris, angioedema, anorexia, anxiety, arrhythmia, arthralgia, arthritis, bilirubinemia, breast pain, cellulitis, cerebrovascular accident, cheilitis, chills, constipation, creatinine increased, dehydration, depression, dizziness, dyspnea, ear pain, ecchymosis, edema, epistaxis, exacerbation of untreated area, eye disorder, eye pain, furunculosis, gastritis, hernia, hyperglycemia, hypertension, hypoglycemia, hypoxia, laryngitis, leukocytosis, leukopenia, liver function tests abnormal, lung disorder, malaise, migraine, neck pain, neuritis, palpitations, paresthesia, peripheral vascular disorder, photosensitivity reaction, procedural complication, routine procedure, skin discoloration, sweating, taste perversion, tooth disorder, unintended pregnancy, vaginal moniliasis, vasodilatation, and vertigo.

OVERDOSAGE

Tacrotor® is not for oral use. Oral ingestion of Tacrotor® may lead to adverse effects associated with systemic administration of Tacrolimus. If oral ingestion occurs, medical advice should be sought.

DOSAGE AND ADMINISTRATION

Adults

Tacrotor® 0.03% and 0.1%

Apply a thin layer of Tacrotor® 0.03% or 0.1% to the affected skin areas twice daily and rub in gently and completely. Treatment should be continued for one week after clearing of signs and symptoms of atopic dermatitis.

The safety of Tacrotor® under occlusion which may promote systemic exposure has not been evaluated.

Tacrotor® 0.03% and 0.1% should not be used with occlusive dressings.

Paediatric patients

Tacrotor® 0.03%

Apply a thin layer of Tacrotor® 0.03% to the affected skin areas twice daily and rub in gently and completely. Treatment should be continued for one week after clearing of signs and symptoms of atopic dermatitis.

The safety of Tacrotor® under occlusion, which may promote systemic exposure, has not been evaluated.

Tacrotor® 0.03% should not be used with occlusive dressings.

EXPIRY DATE :

Do not use later than date of expiry.

STORAGE CONDITION:

STORE IN A COOL PLACE. DO NOT FREEZE. DO NOT STORE ABOVE 25ºC.

KEEP OUT OF REACH OF CHILDREN.

FOR EXTERNAL USE ONLY.

HOW SUPPLIED:

It is available as 10 gm lami tube.

® - Registered Trade Mark

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured in India by :
Glenmark Generics Ltd.
Glenmark House, 3rd Floor,
HDO Corporate Building, A Wing,
B.D. Sawant Road, Chakala, Andheri (E),
Mumbai 400 099, Maharashtra
At.: Vill. Malpur, P.O. Bhud Baddi,
Tehsil Nalagarh, Dist : Solan,
Himachal Pradesh-173 205

PD141190711-1

370 mm

370 mm

73 mm

73 mm