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

HAIRJOY M

1. Generic Name

Minoxidil Topical Solution U.S.P.

2. Qualitative and quantitative composition

HAIRJOY M 2%

Minoxidil I.P. ……2% w/v

Alcohol (Ethanol 95%) I.P.

Eq to Absolute alcohol ……..40% v/v

The excipients used are Propylene Glycol, Hydroxy Propyl Cellulose, Fragrance and Purified Water.

HAIRJOY M 5%

Minoxidil I.P. …….5% w/v

Alcohol (Ethanol 95%) I.P.

Eq to Absolute alcohol ……..40% v/v

The excipients used are Propylene Glycol, Hydroxy Propyl Cellulose, Fragrance and Purified Water.

3. Dosage form and strength

Dosage form: Topical Solution

Strength: 2% & 5% w/v

4. Clinical particulars

4.1 Therapeutic indication

HAIRJOY M 2% - It is indicated in treatment of male pattern baldness.

HAIRJOY M 5% - It is indicated in treatment of alopecia (male pattern baldness) in men.

4.2 Posology and method of administration

Men Aged 18-65:

Hair and scalp should be thoroughly dry prior to topical application of the medication. A dose of 1 ml solution should be applied to the total affected areas of the scalp twice daily or as directed by the Dermatologist, beginning at the center of the affected area. This dose should be used regardless of the size of the affected area. The total dosage should not exceed 2 ml. If fingertips are used to facilitate drug application, hands should be washed afterwards. If hair regrowth occurs, twice daily applications of the medication are necessary for continued hair growth. Anecdotal reports indicate that re-grown hair may disappear three to four months after stopping the topical solution application and the balding process will continue. Users should discontinue treatment if there is no improvement after one year.

Missed Dose: If a dose is missed, Minoxidil Topical Solution should be applied as soon as remembered, if within a few hours of the time usually applied. Do not apply if it is almost time

for the next dose. If a dose is missed, the amount used in the next regular dose should not be doubled.

Women, Children and the Elderly: Not recommended. The safety and effectiveness of Minoxidil Topical Solution in users aged under 18 or over 65 has not been established.

How to Use: It is important for the complete action of the drug that the medicine reaches the scalp skin, during the time of application. Due care should be taken to rub the medicine on the scalp along with application on hair.

4.3 Contraindications

- In users with a history of sensitivity to Minoxidil or any of its excipients.
- In users with treated or untreated hypertension.
- In users with any scalp abnormality (including psoriasis and sunburn).
- In users with a shaved scalp or whose scalp's skin is broken, inflamed, irritated, infected, or severely sunburned.
- If occlusive dressings or other topical medical preparations for treating disorders of the skin of the scalp are being used.
- During pregnancy or breastfeeding.
- In women
- Certain prescription and non-prescription medications, certain treatments, such as cancer chemotherapy, or certain diseases, such as iron deficiency, thyroid disorders or secondary syphilis, as well as severe nutritional problems and poor grooming habits, may also cause temporary hair loss which should not be treated with Minoxidil Topical Solution.

4.4 Special warnings and precautions for use

Before using of Minoxidil Topical Solution, the user should determine that the scalp is normal and healthy.

Minoxidil is only indicated for the treatment of alopecia androgenetica and should not be used in other types of hair loss for example when there is no family history of hair loss, hair loss is sudden and/or patchy, hair loss is due to childbirth or the reason for hair loss is unknown.

The patient should stop using of Minoxidil Topical Solution and see a doctor if hypotension is detected or if the patient is experiencing chest pain, rapid heartbeat, faintness or dizziness, sudden unexplained weight gain, swollen hands or feet or persistent redness. Patients with known cardiovascular disease or cardiac arrhythmia should contact a physician before using Minoxidil Topical Solution.

Minoxidil Topical Solution is for external use only. Do not apply to areas of the body other than the scalp. Hands should be washed thoroughly after applying the solution.

Minoxidil Topical Solution contains ethanol (alcohol), which will cause burning and irritation of the eye. In the event of accidental contact with sensitive surfaces (eye, abraded skin and mucous membranes) the area should be bathed with large amounts of cool tap water.

Minoxidil Topical Solution contains propylene glycol, which may cause skin irritation. Some patients have experienced changes in hair colour and/or texture with use of Topical Solution containing Minoxidil. Patients should be advised to consult their doctor or pharmacist if they are concerned at any time during treatment with Minoxidil Topical Solution.

Some consumers reported increased hair shedding upon initiation of therapy with of Topical Solution containing Minoxidil. This is most likely due to minoxidil's action of shifting hairs from the resting telogen phase to the growing anagen phase (old hairs fall out as new hairs grow in their place). This temporary increase in hair shedding generally occurs two to six weeks after beginning treatment and subsides within a couple of weeks. If shedding persists (>2 weeks), users should stop using Minoxidil Topical Solution and consult their doctor.

Users should be aware that, whilst extensive use of Topical Solution containing Minoxidil has not revealed evidence that sufficient Minoxidil is absorbed to have systemic effects, greater absorption because of misuse, individual variability, unusual sensitivity or decreased integrity of the epidermal barrier caused by inflammation or disease processes in the skin (e.g. excoriations of the scalp, or scalp psoriasis) could lead, at least theoretically, to systemic effects.

Monitoring and Laboratory Tests:

Patients should be monitored for signs of systemic effects of Minoxidil such as hypotension, chest pain, rapid heartbeat, faintness or dizziness, sudden unexplained weight gain, swollen hands or feet, persistent redness or irritation of the scalp. The use Minoxidil Topical Solution should be discontinued in the event of systemic effects and/or severe dermatologic reactions.

4.5 Drugs interactions

Absorption of topical minoxidil is controlled and rate-limited by the stratum corneum. Topical drugs, such as corticosteroids, tretinoin, dithranol or petrolatum, which alter the stratum corneum barrier, could result in increased absorption of minoxidil if applied concurrently. Although it has not been demonstrated clinically, there exists the theoretical possibility of absorbed minoxidil potentiating orthostatic hypotension caused by peripheral vasodilators.

4.6 Use in special population (such as pregnant women, lactating women, Pediatric patients, geriatric patients etc.)

Pregnancy and lactation

There are no adequate and well controlled studies in pregnant women. Animal studies have shown a risk to the foetus at exposure levels that are very high compared to those intended for human exposure. The potential risk in humans is unknown. Systemically absorbed Minoxidil is secreted in human milk. Minoxidil Topical Solution should not be used in women, especially during pregnancy or lactation.

Children and the Elderly

Not recommended. The safety and effectiveness of Minoxidil Topical Solution in users aged under 18 or over 65 has not been established. Effects on ability to drive and use machines. Based on the pharmacodynamic and overall safety profile of Minoxidil, it is not expected that Minoxidil Topical Solution would interfere with the ability to drive or operate machinery.

4.7 Effects on ability to drive and use machines

This product may cause dizziness or hypotension. If affected, patients should not drive or operate machinery**.**

4.8 Undesirable effects

In reported placebo controlled trials, the overall frequency of adverse events in females in all body system categories was approximately five times that of males. Data from reported placebo controlled trials on males and females treated with topical minoxidil solution (2% and 5%

combined) where adverse events were assessed. Additionally, adverse events reported in postmarketing are included. The frequency of adverse reactions to topical minoxidil solution is defined using the following convention: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data)

Body system	Incidence	Reported adverse event
Nervous system disorders	Common	Headache
Vascular disorders	Uncommon	Hypotension
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea
Skin and subcutaneous tissue disorders	Common	Hypertrichosis (unwanted non-scalp hair including facial hair growth in women) Pruritus (including rash pruritic generalised and eye pruritus) Rash (including pustular, popular, generalised, vestibular and macular rash) Dermatitis (including contact, allergic, atopic and seborrhoeic dermatitis)
	Uncommon	Temporary hair loss, changes in hair texture and hair colour, skin exfoliation (including application site, exfoliative rash and dermatitis exfoliative), rash (including application site, pustular, papular, generalized vestibular and macular rash), acne (dermatitis (including contact, application site, allergic, atopic and seborrhoeic dermatitis) and dry skin (including application site dryness)
General disorders and administration site conditions	Uncommon	Oedema peripheral Application site irritation (including skin irritation), site conditions application site erythema (including erythema and rash erythematous)

Users should stop using Minoxidil Topical Solution if they experience chest-pain, tachycardia, faintness, dizziness, sudden unexplained weight gain, swollen hands or feet or persistent redness or irritation of the scalp.

4.9 Overdose

Increased systemic absorption of minoxidil may potentially occur if higher-than-recommended doses of Minoxidil Topical Solution are applied to larger surface areas of the body or areas other than the scalp. Because of the concentration of minoxidil in Topical Solution accidental

ingestion has the potential of producing systemic effects related to the pharmacological action of the drug (5 ml of 2% minoxidil solution or 2 ml of 5% minoxidil contains 100 mg minoxidil; the maximum recommended adult dose for oral minoxidil administration in the treatment of hypertension). Signs and symptoms of minoxidil overdosage would primarily be cardiovascular effects associated with sodium and water retention, tachycardia and hypotension. Treatment of minoxidil overdosage should be symptomatic and supportive. If exaggerated hypotension is encountered, it is most likely to occur in association with residual sympathetic nervous system blockade from previous therapy (guanethidine -like effects or alpha-adrenergic blockade). The recommended treatment is intravenous administration of normal saline. Sympathomimetic drugs, such as norepinephrine or epinephrine, should be avoided because of their excessive cardiac-stimulating action. Phenylephrine, angiotensin II, vasopressin and dopamine, which reverse the effects of orally administered minoxidil, should only be used if inadequate perfusion of a vital organ is evident

5. Pharmacological properties

5.1 Mechanism of Action

When applied topically, it has been shown to stimulate hair growth in individual with alopecia androgenetica (male pattern baldness) and hair loss occurring on the crown of the scalp. The mechanism by which minoxidil stimulates hair growth is not fully understood, but minoxidil can reverse the hair loss process of androgenetic alopecia by the following means:

- increase the diameter of the hair shaft
- stimulate anagen growth
- prolong the anagen phase
- stimulate anagen recovery from the telogen phase

As a peripheral vasodilator minoxidil enhances microcirculation to hair follicles. The Vascular Endothelial Growth Factor (VEGF) is stimulated by minoxidil and VEGF is presumably responsible for the increased capillary fenestration, indicative of a high metabolic activity, observed during the anagen phase.

5.2 Pharmacodynamic properties

The hemodynamic effects of minoxidil do not correlate directly with serum levels. There is a delay in onset relative to observable serum concentrations, peak hemodynamic effects lag one hour behind peak serum concentrations, and hemodynamic effects persist long after nearly all the minoxidil has disappeared from the circulation. It appears that minoxidil requires bio activation before exerting its hemodynamic activity. The active metabolite is considered to be minoxidil sulphate. Sulfotransferase enzyme which converts minoxidil to minoxidil sulphate has been isolated from various human tissues including liver, platelets, scalp skin, hair follicles and epidermal keratinocytes. The effects of minoxidil on hair regrowth are possibly mediated by this active metabolite as well. In clinical studies, no correlation was established between serum or tissue minoxidil concentrations and hair regrowth.

5.3 Pharmacokinetic properties

Absorption

The failure to detect evidence of systemic effects during treatment with minoxidil solution reflects the poor absorption of topically applied minoxidil from normal intact skin. Systemic absorption of minoxidil from topically applied solution ranges between 1% and 2% of the total

applied dose. In a reported study in males, the minoxidil serum concentration time curve (AUC) for the 2% solution averaged 7.54 ng·h/ml compared to a mean AUC of 35.1 ng·h/ml for the 2.5 mg oral formulation. The mean peak plasma concentration (Cmax) for the topical solution was 1.25 ng/ml, compared to 18.5 ng/ml following the 2.5 mg oral dose. In another reported study in males, the mean steady state AUC (0-12 hr) and Cmax for 5% minoxidil solution were, respectively 18.71 ng·hr/mL and 2.13 ng/mL The time to maximum minoxidil concentration (Tmax) for the 5% solution, 5.79 hr, was similar to Tmax for the 5% foam, 5.42 hr. The three major factors by which topical minoxidil absorption is increased are: -increasing the magnitude of the dose applied; -increasing the frequency of dosing; and -decreasing the barrier function of the stratum corneum.

Distribution

There is some evidence from in vitro reported studies that minoxidil reversibly binds to human plasma proteins. However, since only 1-2% of topically applied minoxidil is absorbed, the extent of plasma protein binding occurring in vivo after topical application would be clinically insignificant. The volume of distribution of minoxidil after intravenous administration has been estimated at 70 litres. Renal clearance of Minoxidil corresponds to glomerular filtration rate and it does not cross the blood brain barrier. Minoxidil and its metabolites are hemodialyzable, although this does not rapidly reverse its pharmacological effect.

Metabolism & Excretion

Approximately 60% minoxidil absorbed after topical application is metabolised to minoxidil glucuronide, primarily in the liver. Minoxidil and its metabolites are excreted almost entirely in the urine, with a very minor degree of elimination via the faeces. Following cessation of dosing, approximately 95% of topically applied minoxidil will be eliminated within four days.

6. Nonclinical properties

Reportedly, preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or carcinogenic potential. Cardiac effects of minoxidil in dogs are species-specific in terms of the low doses that cause profound haemodynamic effects and associated changes in the heart. Available data indicate that similar cardiac effects do not occur in humans treated topically or orally with minoxidil.

Mutagenicity

Minoxidil showed no evidence of mutagenic/genotoxic potential in a number of *in vitro* and *in vivo* assays.

Teratogenicity

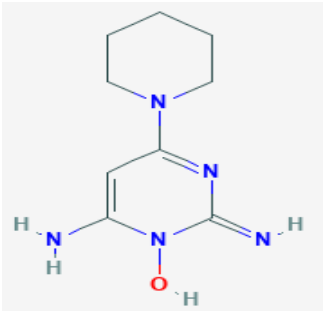
As per reported data, animal reproduction toxicity studies in rats and rabbits have shown signs of maternal toxicity and a risk to the foetus at exposure levels that are very high compared to those, intended for human exposure. A low, albeit remote, risk of foetal harm is possible in humans.

Fertility

Reported, preclinical fertility studies in rats have shown minoxidil doses equal to or greater than 3 mg/kg/day (at least 8-fold human exposure) when administered orally and greater than 9 mg/kg/day (at least 25-fold human exposure) when administered subcutaneously were associated with reduced conception and implantation rates as well as a reduction in the number of live pups**.**

7. Description

Minoxidil is 3-hydroxy-2-imino-6-piperidin-1-ylpyrimidin-4-amine having molecular weight of 209.25 and empirical formula of $C_9H_{15}N_5O$ and the chemical structure is:



Minoxidil Topical Solution is a colourless clear solution. The excipients used are Propylene Glycol, Hydroxy Propyl Cellulose, Fragrance and Purified Water.

8. Pharmaceutical particulars

8.1 Incompatibilities

None

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

HAIRJOY M is available in bottle pack of 60ml.

8.4 Storage and handing instructions

Store below 25°C. Protect from light

Keep out of reach of children.

Keep the bottle in the carton after every use & close the carton properly.

9. Patient counselling information

Package leaflet: Information for the user

HAIRJOY M

Minoxidil Topical Solution U.S.P.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- **This medicine has been prescribed for you only.** Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

9.2. What you need to know before you take HAIRJOY M

9.3. How to take HAIRJOY M

9.4. Possible side effects

9.5. How to store HAIRJOY M

9.6. Contents of the pack and other information

9.1 What HAIRJOY M is and what it is used for

HAIRJOY M contains Minoxidil. Minoxidil is thought to work by aiding the blood flow to the hair follicles on your scalp. It increases the circulation of blood to hair follicles which triggers an increase in hair growth and also prevents the hardening of hair shaft and the build-up of collagen around it.

HAIRJOY M is indicated in the topical treatment of alopecia androgenetica (Male Pattern Baldness) in males. Onset and degree of hair regrowth may be variable among users. Although trends in the data suggest that those users who are younger, who have been balding for a shorter period of time or who have a smaller area of baldness on the vertex are more likely to respond to Minoxidil topical solution, individual responses cannot be predicted.

- HAIRJOY M works best in men with hair loss or thinning at the top of the scalp.
- Those who are younger, have been losing hair for a short period of time or have a small area of baldness are likely to experience the best results.
- You are unlikely to benefit from HAIRJOY M if you have been bald, for many years or have a large area of hair loss.

Hereditary hair loss is recognizable because

- of the pattern of hair loss.
- It starts gradually and progresses.
- You have a family history of hair loss.
- No other symptoms are present with your hair loss

9.2 What you need to know before you take HAIRJOY M

This medicine is suitable for most people but a few people should not use it. If you are in any doubt, talk to your doctor.

Kindly note that this formulation is a drug and needs to be taken under dermatologist supervision.

Do not use HAIRJOY M if:

- If you are under the age of 18 or over the age of 65.
- If you have ever had a bad reaction to Minoxidil or any of the other ingredients.
- If you have hair loss caused by drug treatment.
- If you have total baldness or complete loss of all body hair.
- If the cause of your hair loss is unknown, or it is sudden and unexpected.
- If you have **high blood pressure**, even if it is not being treated.
- If you have any condition that affects your scalp, including sunburn and psoriasis.
- If you have **a shaved scalp**.
- If you are using creams, ointments or lotions used to treat scalp conditions, e.g.
  • Dithranol - used to treat psoriasis.

  - Tretinoin - used to treat acne or other skin disorders.
  - Corticosteroids - a type of anti-inflammatory.
  - Petrolatum - a common ingredient in hair wax or gel.
- If you have any kind of dressing or bandage on your scalp.
- Unless you know that your scalp is normal and healthy
- During pregnancy or breastfeeding.
- If patient taking treatment of cancer or other disease like iron deficiency
- Low nutrition and poor hygiene.

  If any of these bullet points apply to you now or in the past, **get advice from a doctor before using HAIRJOY M.**

Talk to your doctor

- If you are at all unsure whether your scalp is normal and healthy.
- If you suffer from heart disease, including abnormal heart rhythms or rates, angina or chest pains and/or circulation disorders.
- **If you are taking or using any other medicines** including:
- Certain blood pressure medicines called 'vasodilators' e.g. hydralazine. There is a potential risk that Minoxidil, the active ingredient in HAIRJOY M may interact with these medicines and increase their effect.

If you are not sure about the medicine you are taking or using, show the bottle or pack to your pharmacist.

If any of these bullet points apply now or in the past, **talk to a doctor.**

If you are pregnant or breast-feeding:

It should **NOT** be used if you are pregnant or breast-feeding.

Driving and using machines

 HAIRJOY M may cause dizziness or low blood pressure. If you experience these side effects do not drive or operate machinery.

Some of the ingredients can cause problems

 HAIRJOY M Solution contains ethanol (alcohol), which will cause burning and irritation if you get it in the eye. If you get HAIRJOY M in your eye, mouth or on a cut or damaged skin, wash the area well with lots of cool tap water.

Special warnings relating to HAIRJOY M Solution

- The patient should stop using of Minoxidil Topical Solution and see a doctor if hypotension is detected or if the patient is experiencing effects such as chest pain, rapid heartbeat, faintness, dizziness, swollen hands and feet, persistent redness or irritation of the scalp. If you experience any of these side-effects, stop using the medicine and tell your doctor.

  When is used as recommended, it is extremely unlikely that these effects will occur. However there is a chance the drug could get into the blood stream if it is over used or if there is a scalp condition such as psoriasis present. Therefore it is very important that you use your medicine as recommended and follow the instructions very carefully.

  Minoxidil Topical Solution is for external use only. Hands should be washed thoroughly after applying the solution.

- Avoid contact with the eyes, mouth, broken skin and sensitive areas.
- Do not apply to areas of the body other than the scalp.
- Contact your doctor if you experience change in hair color or Excessive hair shedding.
- Exceeding the recommended dose will **NOT** re-grow your hair any more quickly and you have an **increased likelihood of getting side-effects**.

9.3 How to take HAIRJOY M

HAIRJOY M is for topical and external use only. It should only be applied directly to the scalp area.

- Do not apply to areas of the body other than the scalp.
- Wash your hands thoroughly before and after applying the solution and rinse other areas that have come into contact with the solution.
- Make sure your hair and scalp are completely dry before applying the solution.
- Massage solution gently on affected areas of scalp.

Dose: A dose of 1 ml solution should be applied to the total affected areas of the scalp twice daily or as directed by the Dermatologist, beginning at the center of the affected area. This dose should be used regardless of the size of the affected area. The total dosage should not exceed 2 ml.

It may take twice daily applications for 4 months or more with minoxidil 2% solution and for 2 months or more with minoxidil 5% solution before evidence of hair growth can be expected.

If hair re-growth occurs, twice daily applications of the medication are necessary for continued hair growth. Users should discontinue treatment if there is no improvement after one year.

If anyone uses too much

Seek immediate medical advice if anyone, including a child, uses too much of HAIRJOY M. Take the container with you.

If you forget to apply a dose of the solution

If a dose is missed, Minoxidil Topical Solution should be applied as soon as remembered, if within a few hours of the time usually applied. Do not apply if it is almost time for the next dose. If a dose is missed, the amount used in the next regular dose should not be doubled.

Children and the Elderly

Not recommended. The safety and effectiveness of Minoxidil Topical Solution in users aged under 18 or over 65 has not been established.

HOW TO USE:

It is important for the complete action of the drug that the medicine reaches the scalp skin, during the time of application. Due care should be taken to rub the medicine on the scalp along with application on hair.

9.4 Possible side effects

Like all medicines, this medicine can cause side-effects, although not everybody gets them.

If you experience any of the following, stop using the medicine and seek immediate medical help:

- Chest pain.
- Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing.

If you experience any of the following, stop using the medicine and talk to your doctor:

- Allergic reactions including swollen face, skin redness or itching or throat tightness.
- Low blood pressure.
- Fast heart beat or an increased awareness of the heart beat (palpitations).
- Faintness or dizziness.
- Swollen hands or feet, shortness of breath.
- Sudden unexplained weight gain.
- Persistent local redness or rash.

Other effects which may occur, include

Common (may affect up to 1 in 10 people)

- Headache
- Itching or dermatitis.
- Unwanted non scalp hair has been reported (including facial hair growth in women). Always wash your hands, thoroughly after application and if you accidentally apply the Solution to parts of your body other than the scalp, rinse thoroughly with plenty of water.

Uncommon (may affect up to 1 in 100 people)

- Nausea
- Change in hair texture may occur. If this happens you should stop using HAIRJOY M.
- Decrease blood pressure
- Shortness of breath
- Scalp irritation such as local redness, dryness, flaky skin have all been reported. This is usually only a temporary effect, but if it is persistent you should stop using this product.
- Acne like rash, itchy rash, blistering, bleeding or ulceration.
- Temporary hair loss may occur during the first 2-6 weeks of use. This is likely to be as a result of a change within the growth cycle and it should stop within a couple of weeks. If this hair loss continues for longer than 2 weeks, stop using the product and talk to your doctor.
- Change in hair colour may occur. If this happens you should stop using HAIRJOY M.

If you experience any side-effects talk to your doctor. This includes any possible side effects not listed in this leaflet.

9.5 How to store HAIRJOY M

Store below 25°C. Protect from light

Keep out of reach of children.

Keep the bottle in the carton after every use & close the carton properly.

9.6 Contents of the pack and other information

The active substance in this product is Minoxidil.

Excipients used are Propylene Glycol, Hydroxy Propyl Cellulose, Fragrance and Purified Water.

10. Details of manufacturer

Manufactured by:
Nanz Med science pharma Pvt. Ltd
Village Rampur ghat, Paonta-Sahib, Distt. Sirmour, H.P. India.
Under technical collaboration with
Aurochem Laboratories (I) Pvt. Ltd.
8, Palghar Taluka Industrial Co-Operative Estate Ltd.,
Palghar- 401 404, Dist: Thane, Maharashtra, India.

11. Details of permission or licence number with date

Mfg Lic No S-MNB/09/41 issued on 29.04.2019

12. Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/HAIRJOY M 2% and 5% W/V/JUL -21/01/PI