SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Anabact 0.75% w/w Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Metronidazole 0.75% w/w

Excipients with known effect:
The preservative agent bronopol (2, bromo-2-nitro propan-1, 3-diol) and hydroxybenzoic acid esters, incorporated at a level of 0.06% w/w, and 0.13% respectively together with hydroxyethylcellulose, propylene glycol, and purified water.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel

A pale yellow water-based clear gel for topical application.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the treatment of acute inflammatory exacerbation of rosacea.

The deodorisation of malodorous fungating tumours, gravitational ulcers and decubitus ulcers.

4.2. Posology and method of administration

For topical administration only.

<u>For the treatment of rosacea:</u>

<u>Posology</u>

Adults: The average period of treatment is three to four months. The recommended duration of treatment should not be exceeded. However, if a clear benefit has been demonstrated, continued therapy for a further three to four months period may be considered by the prescribing physician depending on the severity of the condition. In clinical studies, topical metronidazole therapy for rosacea has been continued for up to 2 years. In the absence of a clear clinical improvement, therapy should be stopped.

Elderly: As detailed for other adults.

Children: Not recommended for children under 12 years of age.

Method of administration

Anabact should be applied in a thin layer to the affected areas of the skin twice daily, morning and evening. Areas to be treated should be washed with a mild cleanser before application. Patients may use non-comedogenic and non-astringent cosmetics after application of Anabact.

For deodorisation of malodorous fungating tumours, gravitations ulcers and decubitus ulcers:

Adults: Clean the wound thoroughly. Apply the gel over the complete area and cover with a non-adherent dressing. Use once or twice daily until the odour has been completely eradicated. Studies have shown that offensive odour is usually controlled with application of topical metronidazole gel 0.75% within two weeks.

Elderly: As detailed for other adults

Children: Not recommended for children under 12 years of age.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use

Contact with mucous membranes should be avoided.

Anabact has been reported to cause lacrimation of the eyes, therefore, contact with the eyes should be avoided. If a reaction suggesting local irritation occurs patients should be directed to use the medication less frequently or discontinue use temporarily and to seek medical advice if necessary. Metronidazole is a nitroimidazole and should be used with care in patients with evidence of, or history of, blood dyscrasia. Exposure of treated sites to ultraviolet (e.g. solarium, sun-lamp) or strong sunlight (including sun-bathing) should be avoided during use of metronidazole. Metronidazole transforms into inactive metabolite due to UV exposure, therefore its efficacy decreases significantly. Phototoxic side-effects haven't been reported in clinical trials in relation to metronidazole. Unnecessary and prolonged use of this medication should be avoided.

Evidence suggests that metronidazole is carcinogenic in certain animal species. There is no evidence to date of a carcinogenic effect in human (see section 5.3).

Anabact 0.75% w/w Gel contains bronopol which can cause local skin reactions such as contact dermatitis; propylene glycol which may cause skin irritation, and hydroxybenzoic acid esters that may cause allergic reactions (possibly delayed).

4.5. Interaction with other medicinal products and other forms of interaction

Interaction with systemic medication is unlikely because absorption of metronidazole following cutaneous application of Anabact is low. Nevertheless, it should be mentioned that disulfiram-like reactions have been reported in a small number of patients taking metronidazole and alcohol concomitantly. Oral metronidazole has been reported to potentiate the effect of warfarin and other coumarin anticoagulants, resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin is not known. However, very rare cases of modification of the INR

values have been reported with concomitant use of Anabact and coumarin anticoagulants.

4.6. Fertility, pregnancy and lactation

The safety of metronidazole in pregnancy and lactation has not been adequately established. The gel should not therefore be used in these circumstances unless the physician considers it essential. Medication should be stopped if pregnancy occurs.

Pregnancy

There has been no experience to date with the use of Anabact in pregnant patients. In case of oral administration, metronidazole crosses the placental barrier and enters foetal circulation rapidly. No foetotoxicity was observed after oral metronidazole in either rats or mice. However, because animal reproduction studies are not always predictive of human response and since oral metronidazole has been shown to be a carcinogen in some rodents this drug should be used in pregnancy only if clearly needed.

Breast-feeding

After oral administration metronidazole is secreted in breast milk in concentration similar to those found in plasma. Even though blood levels are significantly lower with cutaneous application of Anabact than those achieved after oral metronidazole in nursing mothers, 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.

4.7. Effects on ability to drive and use machines

Anabact has no influence on the ability to drive and use machines.

4.8. Undesirable effects

Because of the minimal absorption of metronidazole and consequently its insignificant plasma concentration after topical administration, the adverse experiences reported with the oral form of the drug have not been reported with Anabact. Adverse reactions reported with Anabact have been only local and mild.

System Organ Class	**Frequency**	**Adverse Drug Reaction**
Skin and subcutaneous tissue disorders	Common (≥ 1/100, < 1/10)	Dry skin, erythema, pruritus, skin discomfort (burning, pain of skin/stinging), skin irritation, worsening of rosacea
	Unknown frequency	Contact dermatitis, swelling face, skin exfoliation
Nervous system disorders	Uncommon (≥ 1/ 1,000, < 1/100)	Hypothesia, paraesthesia, dysgeusia (metallic taste)
Gastrointestinal disorders	Uncommon (≥ 1/ 1,000, < 1/100)	Nausea

Watery eyes have been reported if applied too closely to this area.

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

via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

No data exists about overdosage in humans. Acute oral toxicity studies with a topical gel formulation containing 0.75% w/w metronidazole in rats have shown no toxic action with doses of up to 5 g of finished product per kilogram body weight, the highest dose used. This dose is equivalent to the oral intake of 12 tubes of 30g packaging Anabact for an adult weighing 72 kg, and 2 tubes of Anabact for a child weighing 12 kg.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic Group: Chemotherapeutics for external use

ATC Code: D06B X01

Metronidazole is an antiprotozoal and antibacterial agent which is active against a wide range of pathogenic micro-organisms. The mechanisms of action of metronidazole in rosacea are unknown but available evidence suggests that the effects may be antibacterial and/or anti-inflammatory.

5.2. Pharmacokinetic properties

Absorption

Metronidazole is rapidly and nearly totally absorbed after oral administration. The drug is not significantly bound to serum proteins and distributes well to all body compartments with the lowest concentration found in the fat.

Distribution

The systemic concentration of metronidazole following the topical administration of 1 g of a 0.75% metronidazole gel to 10 patients with rosacea ranged from 25 ng/ml (limit of detection) to 66 ng/ml, with a mean c/max of 40.6 ng/ml. The corresponding mean c/max following oral administration of a solution containing 30 mg of metronidazole was 850 ng/ml (equivalent to 212 ng/ml if dose corrected). The mean Tmax for the topical formulation was 6.0 hours compared to 0.97 hours for the oral solution. The proposed formulation would be expected to afford minimal serum concentrations of metronidazole.

Elimination

Metronidazole is excreted primarily in the urine as parent drug, oxidative metabolites and conjugates.

5.3. Preclinical safety data

The toxicity studies conducted with the Metronidazole 0.75% Topical Gel formulation demonstrate that the product is non-toxic in rats after acute oral administration 5 g/kg and produced no ocular irritation in rabbit eyes. The

formulation produced no observable effects in rabbits after dermal application of 13 mg /kg for 90 days.

No compound-related dermal or systemic effects were observed in a 13-week cutaneous route toxicity study, in which Metronidazole Gel containing metronidazole 0.75% w/w was applied daily to rabbits at doses ranging between 0.13 and 13 mg/kg. Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats but not in studies involving hamsters.

One study showed a significant enhancement of UV induced skin tumours in hairless mice treated with metronidazole intraperitoneally (15 μg per g body weight and per day for 28 weeks). Although the significance of these studies to man is not clear, patients should be advised to avoid or minimise exposure of metronidazole treated sites to sun.

Metronidazole has shown mutagenic activity in several in vitro bacterial assay systems. In addition, a dose-response increase in the frequency of micronuclei was observed in mice after intraperitoneal injection and an increase in chromosome aberrations have been reported in patients with Crohn's disease who were treated with 200 to 1200 mg/day of metronidazole for 1 to 24 months. However, no excess chromosomal aberrations in circulating human lymphocytes have been observed in patients treated for 8 months.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Bronopol
Hydroxybenzoic Acid Esters
Hydroxyethylcellulose
Propylene Glycol
Phosphoric Acid
Purified Water

6.2. Incompatibilities

Not applicable.

6.3 Shelf life

The unopened shelf-life is 2 years.
The opened shelf-life is 28 days.

6.4 Special precautions for storage

Do not store above 25°C. Keep container in outer carton.

6.5. Nature and contents of container

The gel is packaged in internally lacquered membrane sealed aluminium tubes each fitted with a low density polyethylene cap.

Anabact is licensed in 5g, 10g, 15g, 25g, 30g and 40g pack sizes.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Cambridge Healthcare Supplies Ltd
Unit 1 Chestnut Drive
Wymondham
Norfolk
NR18 9SB

8. MARKETING AUTHORISATION NUMBER

PL 16794/0006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/11/2005

10 DATE OF REVISION OF THE TEXT

19/12/2024