RENNIE ® DUAL ACTION TABLETS
PL 00010/0514

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RENNIE ® DUAL ACTION TABLETS
PL 00010/0514

LAY SUMMARY

The MHRA granted Bayer plc a Marketing Authorisation (licence) for the medicinal product Rennie ® Dual Action Tablets (PL 00010/0514). This product is available on the general sale list (GSL) for the treatment of heartburn and acid indigestion.

Rennie ® Dual Action Tablets contain the active ingredients calcium carbonate, magnesium carbonate and alginic acid. Calcium carbonate and magnesium carbonate are antacids; alginic acid acts as an anti-reflux agent.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Rennie ® Dual Action Tablets outweigh the risks, hence a Marketing Authorisation has been granted.

RENNIE ® DUAL ACTION TABLETS
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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation for the medicinal product Rennie ® Dual Action Tablets (PL 00010/0514) to Bayer plc on 30 January 2007. The product is on the general sales list.

The application was submitted as an abridged application according to Article 10a of Directive 2001/83/EC, as a line extension of Rennie Duo ® chewable tablets.

The product contains the active ingredients calcium carbonate, magnesium carbonate and alginic acid and is indicated for the treatment of heartburn and acid indigestion.

Calcium carbonate and magnesium carbonate are both antacids that have strong neutralising action. Alginic acid creates a viscous gel which floats on the stomach contents, acting as a physical barrier against reflux.

The application for Rennie ® Dual Action Tablets compares the applicant's product with Rennie Duo ® chewable tablets.

PHARMACEUTICAL ASSESSMENT

COMPOSITION

The product is formulated as a chewable tablet containing the active pharmaceutical ingredients calcium carbonate, magnesium carbonate and alginic acid at strengths of 625 mg, 73.50 mg and 150 mg per tablet respectively. The excipients present are sodium hydrogen carbonate, sucrose, glucose monohydrate, povidone, talc, magnesium stearate, dextrates, lemon cream flavour, peppermint flavour and saccharin sodium.

The tablets are presented in hard tempered aluminium strip packs with a LDPE sealing layer, in packs of 12 and 24 tablets.

DRUG SUBSTANCE

Alginic Acid

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Alginic acid is tested as per the Ph Eur specification.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Alginic acid is stored in appropriate packaging.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated that support the retest period for the drug substance when stored in the proposed packaging.

Calcium carbonate

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Calcium carbonate is tested as per the Ph Eur specification.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Calcium carbonate is stored in appropriate packaging.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated that support the retest period for the drug substance when stored in the proposed packaging.

Magnesium Carbonate
Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Magnesium carbonate is tested as per the Ph Eur specification.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Magnesium carbonate is stored in appropriate packaging. The specifications and typical analytical test reports are provided and appear to be satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated that support the retest period for the drug substance when stored in the proposed packaging.

DRUG PRODUCT

Rennie ® Dual Action Tablets are developed on the basis of Rennie Duo® chewable tablets, which were too big for patient comfort. One tablet of Rennie Duo ® chewable tablets (3486 mg) was split into two tablets of half weight (i.e., 1743 mg). The therapeutic regimen remains unchanged; therefore, patients have to take two Rennie ® Dual Action Tablets at a time.

Other ingredients
All excipients used in the manufacture of the tablets are routinely tested for compliance with current relevant international standards.

Satisfactory certificates of analysis have been provided for all excipients.

None of the excipients used contain material of animal or human origin.

Manufacture
A GMP certificate has been provided for the manufacturing site. A full description and a detailed flow-chart of the manufacturing method, including in-process control steps has been provided.

In-process controls are satisfactory based on process validation data and controls on the finished product. Satisfactory process validation has been carried out.

Satisfactory batch formulae have been provided for the manufacture of the product along with an appropriate account of the manufacturing process. The manufacturing process has been validated and appropriate in-process controls are applied.

Additionally, a commitment has been provided that the next three full-scale commercial production batches will be validation batches.

Finished product specification
The proposed finished product specification is acceptable and the analytical methods used have been suitably validated. Certificates of analysis have been provided for all reference standards used. Batch analysis data has demonstrated compliance with the proposed release specification.

Container Closure System
Satisfactory specifications and certificates of analysis have been provided for the packaging components.

Stability
Finished product stability data support the proposed shelf-life of 18 months with storage conditions of 'Do not store above 25°C. Store in the original packaging'.

SPC, PIL, Labels
The SPC, PIL and Labels are pharmaceutically acceptable.

CONCLUSION
It is recommended that a Marketing Authorisation is granted for this application.

The requirement for a line extension of the reference product has been met with respect to qualitative and quantitative content of the active substances and pharmaceutical form.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Rennie ® Dual Action Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for Rennie Duo ® chewable tablets.

RISK BENEFIT ASSESSMENT

Extensive clinical experience with calcium carbonate, magnesium carbonate and alginic acid is considered to have demonstrated the therapeutic value of the compounds. The risk benefit is, therefore, considered to be positive.

RENNIE ® DUAL ACTION TABLETS
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STEPS TAKEN FOR ASSESMENT

1 The MHRA received the marketing authorisation application on 07 March 2006

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 27 March 2006.

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 27 July 2006, 10 November 2006 and 06 December 2006.

4 The applicant responded to the MHRA's requests, providing further information on 03 October 2006, 23 November 2006 and 16 January 2007 for the quality section.

5 The application was determined on 30 January 2007.

RENNIE ® DUAL ACTION TABLETS
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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Rennie ® Dual Action Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of 1743mg contains the following active substances:
Alginic acid 150mg, calcium carbonate 625mg and heavy magnesium carbonate 73.50mg.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Chewable tablets.

Off white, speckled circular tablet, flat on both sides with a bevelled edge.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of complaints resulting from gastro-oesophageal reflux and hyperacidity, such as regurgitation and heartburn.

4.2 Posology and method of administration

The usual dose is 2 tablets to be chewed. It should preferably be taken one hour after meals and before going to bed. An additional dose of 2 tablets can also be taken in between in the case of heartburn. Do not take more than 16 tablets in any 24-hour period. Only for use by adults (over 12 years of age).

4.3 Contraindications

Severe renal i nsufficiency, hypercalcaemia and pre-existing hypophosphataemia. Nephrolithiasis due to calculi containing calcium deposits.

Hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings and precautions for use

Prolonged use should be avoided.

If the symptoms persist or only partly disappear, further medical advice should be sought

As with other antacids, Rennie® Dual Action tablets may mask a malignancy in the stomach.

In general, caution should be exercised in patients with impaired renal function.

If Rennie® Dual Action tablets are used in such patients, plasma concentrations of calcium and magnesium should be monitored regularly.

Prolonged use of high doses may result in undesirable side-effects such as hypercalcaemia, magnesaemia and the milk alkali syndrome, particularly in patients suffering from renal insufficiency. Prolonged use increases the risk of formation of renal calculi. Patients on a restricted-sodium diet should note that the product contains 14mg sodium per tablet. Diabetic patients should note that the product contains 230 mg sucrose and about 520mg glucose per tablet. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucraseisomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Changes in the level of acidity of gastric juice such as those caused by taking antacids may affect the degree and speed of absorption of medicines administered concomitantly. It has been shown that antacids containing calcium and magnesium can hinder the absorption of some antibiotics (such as the tetracyclines and quinolones). Thiazide diuretics reduce the urinary excretion of calcium. Due to increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics. Calcium salts and magnesium salts can hinder the absorption of phosphates. In view of possible changes in the rate of absorption o f medicines taken concomitantly, it is recommended that antacids are not administered at the same time as these medicines but taken 1 to 2 hours later.

4.6 Pregnancy and lactation

Up to now, no increased risk of congenital defects has been observed after the use of calcium carbonate, magnesium carbonate and alginic acid during pregnancy. Rennie® Dual Action tablets can be used during pregnancy if taken as instructed but prolonged intake of high dosages should be avoided. Rennie® Dual Action tablets can be used during lactation if taken as instructed.

4.7 Effects on ability to drive and use machines

Rennie® Dual Action tablets are not expected to affect these functions.

4.8 Undesirable effects

Prolonged use of high doses may possibly result in hypermagnesaemia or hypercalcaemia and alkalosis (GI symptoms such as nausea and vomiting, fatigue, confusion, polyuria, polydypsia, dehydration), particularly in patients with impaired renal function. Prolonged use of high doses of calcium carbonate with milk may lead to Burnett syndrome (milk-alkali syndrome). Although magnesium compounds may have a laxative effect, the low magnesium content in Rennie® Dual Action tablets is not expected to result in undesirable effects in view of the recommended dose. Hypersensitivity reactions, including anaphylactic shock and Quincke oedema have been rarely reported.

4.9 Overdose

Prolonged ingestion of high doses of calcium carbonate may result in hypercalcaemia and alkalosis, which may be expressed in the form of digestive symptoms (nausea, vomiting) and abnormal muscular weakness. In such cases, discontinue administration and take an adequate volume of liquid.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC AO2 AX

Rennie® Dual Action tablets are a combination of two antacids (calcium carbonate and magnesium carbonate) and an alginic acid.

The mode of action of Rennie® Dual Action tablets is local and is not dependent on systemic absorption.

Calcium carbonate has a rapid, long -lasting and powerful neutralising action. This effect is increased by the addition of magnesium carbonate which also has a strong neutralising action. In healthy volunteers, a significant increase in the pH of stomach contents was achieved within 2 minutes. The total neutralising capacity of two tablets of the product is 29 mEq/H^+ (titration to end-point pH 2.5). Apart from the neutralising action of the antacids, the alginic acid present in Rennie® Dual Action tablets cause a viscous gel to be formed which floats on the stomach contents and acts as a physical barrier against reflux.

5.2 Pharmacokinetic properties

Calcium and magnesium In the stomach: calcium carbonate and magnesium carbonate react with the acid in the gastric juice, forming soluble salts. Calcium and magnesium can be absorbed from these (soluble) salts. However, the degree of absorption is dependent on the patient and the dose. Approx. 10% calcium and 15-20% magnesium is absorbed. The small quantities of calcium and magnesium absorbed are usually excreted rapidly via the kidneys in healthy individuals. In the case of impaired renal function, serum concentrations of calcium and magnesium may be increased. Due to the effect of various digestive juices outside the stomach, the soluble salts are converted to insoluble salts in the intestinal canal and then excreted with the faeces.

Alginic acid After oral ingestion, alginic acid is not co nverted in the gastro-intestinal tract; 80100% of the quantity ingested is excreted. Absorption of alginic salts is negligible.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydrogen carbonate, sucrose, glucose monohydrate, povidone K30, talc, magnesium stearate, dextrate, lemon cream flavour (primarily composed of lemon oil,

orange oil, isopropyl myristate, maltodextrin, gum arabic), peppermint flavour (primarily composed of peppermint oil, maltodextrin, gum arabic), saccharin sodium.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Do not store above 25°C. Store in the original packaging

6.5 Nature and contents of container

Strip pack consisting of hard temper aluminum with a LDPE sealing layer.

Pack-sizes 12 and 24.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Bayer plc Bayer House Strawberry Hill Newbury RG14 1JA United Kingdom

Trading as Bayer plc, Consumer Care Division

8 MARKETING AUTHORISATION NUMBER(S)

PL 00010/0514

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30/01/2007

10 DATE OF REVISION OF THE TEXT

30/01/2007

Rennie ® Dual Action Tablets Patient Information Leaflet

PACKAGE LEAFLET: INFORMATION FOR THE USER

RENNIE® DUAL ACTION TABLETS

calcium carbonate, magnesium carbonate, alginic acid

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to take Rennie Dual Action Tablets carefully to get the best results from them. Keep this leaflet, you may need to read it again. Ask your pharmacist if you need more information or advice. You must contact a doctor if your symptoms worsen or do not improve. If you have any unusual effects after taking Rennie Dual Action, please tell your doctor or pharmacist.

In this leaflet

1. WHAT ARE RENNIE DUAL ACTION TABLETS AND WHAT ARE THEY USED FOR?

Rennie Dual Action tablets provide fast, soothing and long lasting relief from heartburn and acid indigestion.

The tablets contain two antacids: calcium carbonate and magnesium carbonate and also alginic acid

Rennie Dual Action tablets work in two differentways:

1. forming a protective barrier in the stomach to stop acid escaping upwards.
2. neutralising excess acid in the stomach

2. BEFORE YOU TAKE RENNIEDUAL ACTION TABLETS

Do not take Rennie Dual Action:

- If you have kidney disease or suffer from kidney stones.
- If you have high calcium or low phosphate levels in the blood.
- If you are allergic (hypersensitive) to any of the ingredients.

Take special care with Rennie Dual Action
As with other antacid products, taking these tablets can mask the symptoms of other, more serious, underlying medical conditions, and therefore tablets should not be used for a prolonged period without consulting a doctor.
If you have been told by your doctor you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
As these tablets contain sugar (sucrose) which can cause tooth decay, remember to brush your teeth regularly.

Taking other medicines:

- If taking antibiotics (tetracyclines, quinolones) or other prescribed medicines speak to your doctor before taking Rennie Dual Action Tablets because it can affect how these other

medicines work. To maximise the benefit of all medicines being used, take Rennie Dual Action Tablets 1 to 2 hours after taking any other medicines.

- If you are taking any thiazide diuretics (e.g. bendroflumethiazide), which are used to increase urine production, then you should tell your doctor before taking the product because he or she may want to monitor the calcium levels in your blood.

Important information about some of the ingredients in Rennie Dual Action:

This product contains 28mg of sodium per dose of 2 tablets, which should be taken into consideration by patients on a sodium restricted diet.
This product also contains 460mg sucrose and about 1040mg glucose per dose of 2 tablets, which should be taken into account in patients with diabetes.

3. HOW TO TAKE RENNIE DUAL ACTION TABLETS

Adults and children over 12 only: 2 tablets to be chewed, preferably 1 hour after meals and before bedtime. For heartburn an extra 2 tablets may be taken between these times. These doses may also be used during pregnancy and breastfeeding. Do not take more than 16 tablets in 24 hours.
If symptoms persist consult your doctor. Prolonged use should be avoided.

If you take more Rennie Dual Action then you should: Drink plenty of water and consult your doctor or pharmacist. Symptoms of an overdose include nausea and vomiting, tiredness, increased urine production, increased thirst and dehydration.

If you have any questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS
Side effects are unlikely at the recommended dose. Long term use of high doses can cause high blood levels of calcium and magnesium, especially in people with kidney conditions. This can cause nausea and vomiting, tiredness, confusion, increased urine production, increased thirst and dehydration.

Use of Rennie Dual Action with milk over a long period of time may cause milk alkali syndrome, which can cause high blood levels of calcium.

Very rare side effects may include swelling, itching or asthma.

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5. HOW TO STORE RENNIE DUAL ACTION TABLETS
Keep out of the reach and sight of children.
Do not use Rennie Dual Action after the expiry date which is stated on the carton and foil (EXP). The expiry date refers to the last day of that month.
Do not store above 25°C. Store in the original packaging.
Medicines should not be disposed of via waste water or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Rennie Dual Action contains
Each tablet contains the active ingredients calcium carbonate (625 mg), magnesium carbonate (73.5mg) and alginic acid (150mg).
The other ingredients are Sodium hydrogen carbonate, sucrose, glucose monohydrate, povidone, talc, magnesium stearate, dextrate, saccharin sodium, lemon cream flavour (contains lemon oil, orange oil, isopropyl myristate, maltodextrin, gum arabic), peppermint flavour (contains peppermint oil, maltodextrin, gum arabic).

What Rennie Dual Action looks like and the contents of the pack
Rennie Dual Action are offwhite, speckled circular, flat on both sides with a bevelled edge.
They are supplied in foil strips in a carton wth this leaflet.
The tablets are available in pack-sizes of 12s and 24s.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Bayer plc, Consumer Care Division, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA. Manufacturer: Bayer Santé Familiale, 74240 Gaillard, France.

This leaflet was last approved in: MM/YYYY

LABELLING


Rennie
DUAL ACTION TABLETS
12
NEW
Rennie
DUAL ACTION TABLETS
Calcium Carbonate, Magnesium Carbonate, Alginic Acid
fast & long lasting relief from heartburn & indigestion
12 chewable tablets
Rennie
DUAL ACTION TABLETS
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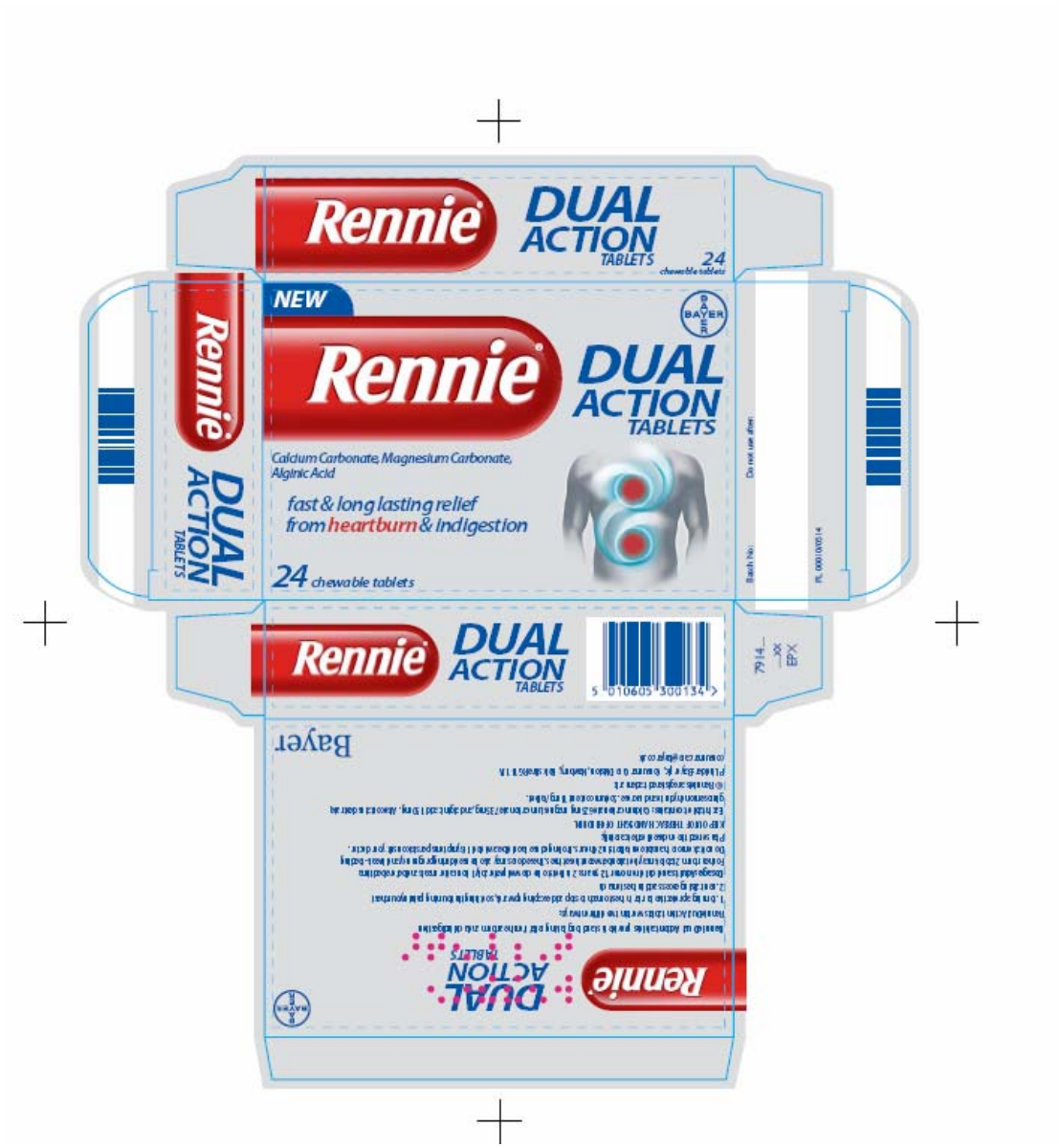
Bayer


Rennie
DUAL ACTION TABLETS
24
NEW
Rennie
DUAL ACTION TABLETS
Calcium Carbonate, Magnesium Carbonate, Alginic Acid
fast & long lasting relief from heartburn & indigestion
24 chewable tablets
Rennie
DUAL ACTION TABLETS
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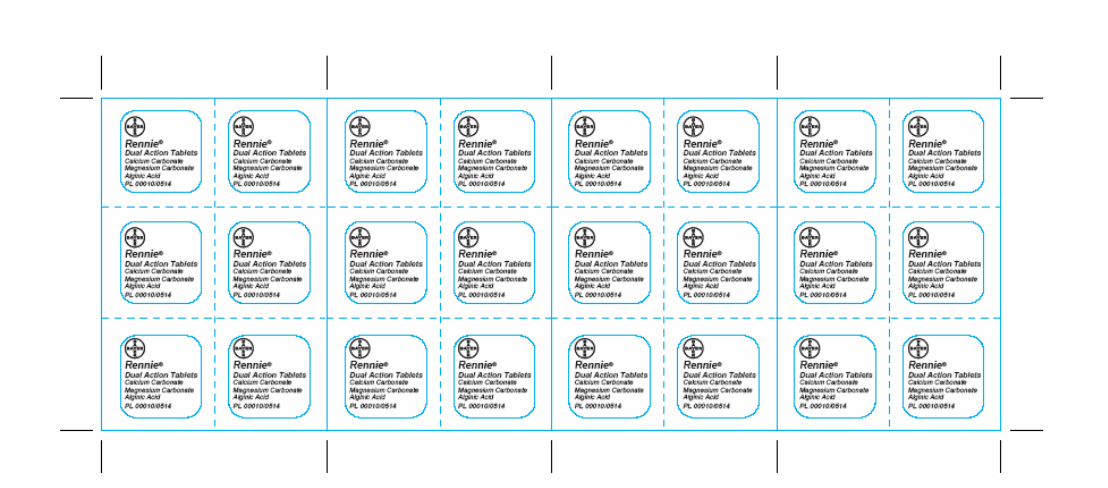
Bayer


Rennie®
Dual Action Tablets
Calcium Carbonate
Magnesium Carbonate
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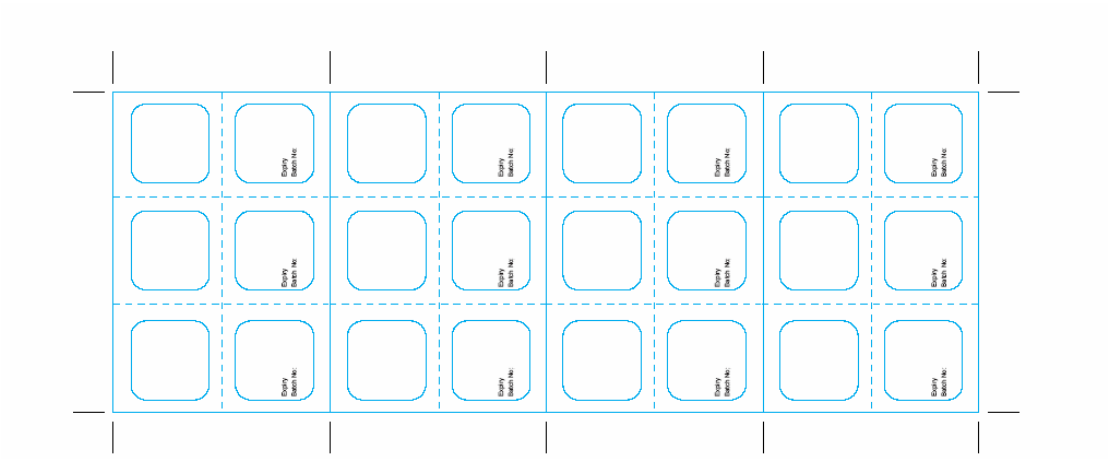
PL 00010/0514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