COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Gattart 680 mg/80 mg chewable tablet (calcium carbonate/magnesium carbonate 680 mg/80 mg)

NL/H/4696/001/DC

Date: 6 March 2023

This module reflects the scientific discussion for the approval of Gattart 680 mg/80 mg chewable tablet. The procedure was finalised in the United Kingdom (UK/H/6426/001/DC). After a transfer in 2018, the current RMS is the Netherlands. The report presented below reflects the original procedure at the time of finalisation in the UK and has not been changed or updated since.

Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

Decentralised Procedure

GATTART 680 MG/ 80 MG CHEWABLE TABLETS
(calcium carbonate, magnesium carbonate heavy)

Procedure No: UK/H/6426/001/DC

UK Licence No: PL 34088/0046

ALKALOID-INT d.o.o.

LAY SUMMARY

Gattart 680 mg/ 80 mg Chewable Tablets
(calcium carbonate, magnesium carbonate heavy)

This is a summary of the Public Assessment Report (PAR) for Gattart 680 mg/ 80 mg Chewable Tablets (PL 34088/0046; UK/H/6426/001/DC). It explains how the application for Gattart 680 mg/ 80 mg Chewable Tablets was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Gattart 680 mg/ 80 mg Chewable Tablets.

This medicinal product will be referred to as Gattart Tablets for the remainder of this summary, for ease of reading.

For practical information about using this product, patients should read the package leaflet or contact their doctor or pharmacist.

What are Gattart Tablets and what are they used for?
Gattart Tablets are mint flavoured antacid tablets which neutralise stomach acid in the body. Gattart Tablets are used for the treatment of heartburn and associated symptoms, e.g. stomach complaints and acid regurgitation.

The patient must talk to their doctor if they do not feel better or if they feel worse after 7 days.

How do Gattart Tablets work?
The active substances are calcium carbonate and magnesium carbonate, heavy, which neutralise excess acid in the stomach.

How are Gattart Tablets used?
The patient should always take this medicine exactly as his/her doctor or pharmacist has advised. The patient should check with his/her doctor or pharmacist if unsure.

Recommended dose in adults and adolescents (over 12 years):

1-2 tablets to be sucked or chewed, in case of heartburn and associated symptoms, preferably 1 hour after meals and before bedtime.

The patient should not take more than 11 tablets a day.

The patient must talk to a doctor if they do not feel better or if they feel worse after 7 days. Prolonged use of this medicine should be avoided.

This medicine is not recommended for children under 12 years of age
Please read Section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

This medicine can be obtained without a prescription.

What benefits of Gattart Tablets have been shown in studies?
It was concluded that, in accordance with EU requirements, Gattart Tablets have been shown to have the same quality and to be similar to Rennie Sugar Free 680 mg / 80 mg chewable tablets. The Marketing Authorisation Holder has provided data from an *in vitro* study which indicates Gattart Tablets are comparable to the reference product. Therefore, the MHRA decided that, as for Rennie Sugar Free 680 mg / 80 mg chewable tablets, the benefits are greater than the risks and recommended that Gattart Tablets can be approved for use.

What are the possible side effects of Gattart Tablets?
Like all medicines, Gattart Tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Gattart Tablets, see Section 4 of the package leaflet. For the full list of restrictions, see the package leaflet.

Why were Gattart Tablets approved?
It was concluded that, in accordance with EU requirements Gattart Tablets have been shown to have comparable quality and to be comparable to Rennie Sugar Free 680 mg / 80 mg chewable tablets. Therefore, the MHRA decided that, as for Rennie Sugar Free 680 mg / 80 mg chewable tablets, the benefits outweigh the identified risks and recommended that Gattart Tablets can be approved for use.

What measures are being taken to ensure the safe and effective use of Gattart Tablets?
A Risk Management Plan (RMP) has been developed to ensure that Gattart Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics (SmPC) and the package leaflet for Gattart Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Gattart Tablets
On 26 January 2018, Austria, Belgium, Germany, Estonia, Hungary, Ireland, Italy, Lithuania, Latvia, the testNetherlands, Portugal, and the UK agreed to grant a Marketing Authorisation for Gattart Tablets. Following a subsequent national phase, a Marketing Authorisation was granted on 23 February 2018 in the UK.

The full PAR for Gattart Tablets follows this summary.

For more information about treatment with Gattart Tablets, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in April 2018.

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

I	Introduction	Page 5
II	Quality aspects	Page 6
III	Non-clinical aspects	Page 8
IV	Clinical aspects	Page 8
V	User consultation	Page 10
VI	Overall conclusion, benefit/risk assessment and recommendation	Page 10
	Annex 1 Table of content of the PAR update for MRP and DCP	Page 15

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the member states considered that the application for Gattart 680 mg/ 80 mg Chewable Tablets (PL 34088/0046; UK/H/6426/001/DC) could be approved. The application was submitted via the Decentralised Procedure, with the UK as Reference Member State (RMS), and Austria, Belgium, Germany, Estonia, Hungary, Ireland, Italy, Lithuania, Latvia, the Netherlands, and Portugal as Concerned Member States (CMS).

This product is a general sales list medicine (legal classification GSL).

This is a decentralised abridged application submitted under Article 10(3) of Directive 2001/83/EC, as amended, claiming to be a hybrid medicinal product of the reference product, Rennie Sugar Free 680 mg / 80 mg chewable tablets, which was originally granted to Nicholas Laboratories Limited in 1990. The current marketing authorisation holder is Bayer plc (PL 00010/0362).

Gattart 680 mg/ 80 mg Chewable Tablets are for the treatment of heartburn and associated symptoms, e.g. stomach complaints and acid regurgitation. Calcium carbonate and magnesium carbonate react with excess acid in the gastric juice to produce soluble chlorides. Calcium carbonate has a rapid and powerful neutralising action. This effect is increased by the addition of magnesium carbonate which also has a strong neutralising action.

This medicinal product contains the active ingredients calcium carbonate and magnesium carbonate, heavy, and the formulation contains the same functional categories of excipients as the reference product.

As the medicinal product is locally applied and locally acting in the gastrointestinal tract, bioavailability studies cannot be used to demonstrate bioequivalence to the reference product. Therefore, therapeutic equivalence has been demonstrated by data from an *in vitro* study. With the exception of these data, no new clinical or non-clinical studies were conducted, which is acceptable given that the application was based on being similar to a reference product that has been licensed for over 10 years.

The RMS has been assured that acceptable standards of Good Manufacturing Practice are in place for this product type at all sites responsible for its manufacture, assembly and batch release.

The RMS and CMS considered that the application could be approved at the end of procedure on 26 January 2018. After a subsequent national phase, a Marketing Authorisation was granted in the UK on 23 February 2018.

II QUALITY ASPECTS

II.1 Introduction

Gattart 680 mg/ 80 mg Chewable Tablets contain 680 mg calcium carbonate and 80 mg magnesium carbonate, heavy. Other ingredients consist of the pharmaceutical excipients: silica, colloidal anhydrous, pregelatinised starch, copovidone, xylitol (E 967), low-substituted hydroxypropylcellulose LH-11, talc, magnesium stearate, spearmint flavour SD and menthol L flavour spraydried.

Spearmint Flavour SD consists of flavouring preparations, natural flavouring substances– (pulegone and menthofuran), maltodextrin and gum arabic (E 414).

Menthol L flavour spraydried consists of flavouring substances and gum arabic (E 414).

The finished product is packaged in push-through polyvinylchloride (PVC) / polyvinylidene chloride (PVdC) / aluminium blisters that are packed into cartons in pack sizes of 16, 24, 48 or 96 tablets.

Not all pack sizes may be marketed, however, the marketing authorisation holder has agreed to provide mock-ups of any pack size to the relevant regulatory authorities before marketing.

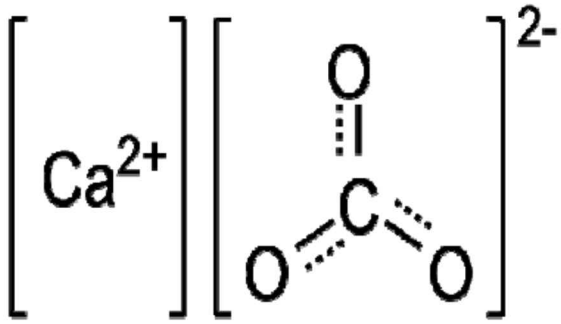
All primary product packaging complies with the current requirements. Satisfactory specifications and Certificates of Analysis have been provided for all packaging components.

II.2 Drug substance

Calcium carbonate

Chemical Name: Calcium carbonate

Structure:



Molecular Formula: $CaCO_3$

Molecular Weight: 100.1 g/mol

Appearance: White or almost white powder

Solubility: Practically insoluble in water

Magnesium carbonate, heavy

Chemical Name: Magnesium carbonate, heavy

Structure: Not applicable

Molecular Formula: $4MgCO_3 \times Mg(OH)_2 \times 4H_2O$

Molecular Weight: 467.64 g/mol

Appearance: White or almost white powder

Solubility: Practically insoluble in water, dissolves in dilute acids with effervescence

All aspects of the manufacture and control of the active substances, calcium carbonate and magnesium carbonate, heavy, are covered by European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificates of Suitability.

II.3 Medicinal Product

Pharmaceutical Development

The objective of the development programme was to formulate a robust and stable product, which could be considered a hybrid medicinal product of the currently licensed product Rennie Sugar Free 680 mg / 80 mg chewable tablets, which was originally granted to Nicholas Laboratories Limited in 1990. The current marketing authorisation holder is Bayer plc (PL 00010/0362).

A satisfactory account of the pharmaceutical development has been provided.

Satisfactory comparative *in vitro* dissolution and impurity profiles have been provided for the applicant's product versus the reference product (Rennie Sugar Free 680 mg / 80 mg chewable tablets).

With the exception of spearmint flavour SD and menthol L flavour SD, which are controlled to in-house specifications, all the excipients comply with their respective European Pharmacopoeia monographs.

This product contains no materials of animal or human origin.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacturing Process

Satisfactory batch formulae have been provided for the manufacture of the product, along with an appropriate description of the manufacturing process. Suitable in-process controls are in place to ensure the quality of the finished product. The manufacturing process has been validated at the commercial-scale batch size and has shown satisfactory results.

Finished Product Specification

The finished product specification proposed is acceptable. Test methods have been described that have been adequately validated. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for all working standards used.

Stability of the product

Stability studies were performed, in accordance with current guidelines, on batches of finished product in the packaging proposed for marketing.

The results from these studies support a shelf life of 3 years, with the special storage condition of "Store in the original package in order to protect from moisture. This medicinal product does not require any special temperature storage conditions".

II.4 Discussion on chemical, pharmaceutical and biological aspects

It is recommended that a Marketing Authorisation is granted for Gattart 680 mg/ 80 mg Chewable Tablets.

III NON-CLINICAL ASPECTS

III.1 Introduction

The pharmacodynamic, pharmacokinetic and toxicological properties of calcium carbonate and magnesium carbonate heavy are well known. No new non-clinical data have been submitted for this application and none are required.

The applicant has provided an overview based on published literature. The non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the product's pharmacology and toxicology.

III.2 Pharmacology

No new pharmacology data are required for this application and none have been submitted.

III.3 Pharmacokinetics

No new pharmacokinetic data are required for this application and none have been submitted.

III.4 Toxicology

No new toxicology data are required for this application and none have been submitted.

III.5 Ecotoxicity/Environmental risk Assessment (ERA)

Since Gattart 680 mg/80 mg Chewable Tablets are intended for generic substitution, it is anticipated that this will not lead to an increased exposure to the environment. An environmental risk assessment is, therefore, not deemed necessary.

III.6 Discussion of the non-clinical aspects

It is recommended that a Marketing Authorisation is granted for Gattart 680 mg/ 80 mg Chewable Tablets.

IV. CLINICAL ASPECTS

IV.1 Introduction

Consistent with the relevant Committee for Medicinal Products for Human Use (CHMP) guidelines regarding the demonstration of therapeutic equivalence for locally acting products in the gastrointestinal tract, the applicant has provided data from an *in vitro* study to demonstrate equivalence between the reference and test products.

Except for the data from the *in vitro* study, no other clinical data have been submitted with this application.

IV.2 Pharmacokinetics

No new pharmacokinetic data were submitted, as comparability between the test and reference products was shown through an *in vitro* study which is considered to mimic *in vivo* antacid activity.

The results from the *in vitro* study showed that the antacid activity of the test product Gattart 680 mg/ 80 mg Chewable Tablets and the reference product Rennie Sugar Free 680 mg / 80 mg chewable tablets (Bayer plc) were comparable.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted and none are required for applications of this type.

IV.4 Clinical efficacy

No new data on efficacy have been submitted and none are required for applications of this type.

IV.5 Clinical Safety

No new data on safety have been submitted and none are required for applications of this type.

IV.6 Risk Management Plan (RMP)

The MAH has submitted an RMP in accordance with the requirements of Directive 2001/83/EC, as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Gattart 680 mg/ 80 mg Chewable Tablets.

A summary of the safety concerns in the RMP is presented below:

Table 1. Summary of safety concerns

Summary of safety concerns	
Important identified risks	Hypersensitivity reactions Hypercalcaemia Milk-alkali syndrome/alkalosis Drug interactions- Decreased absorption of concurrently administered medicine due to reduced gastric acidity or calcium and magnesium complexes
Important potential risks	Hypermagnesemia
Missing information	None

IV.7 Discussion of the clinical aspects

It is recommended that a Marketing Authorisation is granted for Gattart 680 mg/ 80 mg Chewable Tablets.

V. USER CONSULTATION

A package leaflet for Gattart 680 mg/80 mg Chewable Tablets (PL 34088/0046) has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the package leaflet was English.

The results show that the package leaflet meets the criteria for readability as set out in the *guideline on the readability of the label and package leaflet of medicinal products for human use.*

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The data supplied support the claim that the applicant's product and the reference product are interchangeable. Extensive clinical experience with calcium carbonate and heavy magnesium carbonate is considered to have demonstrated the therapeutic value of the compounds. The benefit-risk assessment is, therefore, considered to be positive.

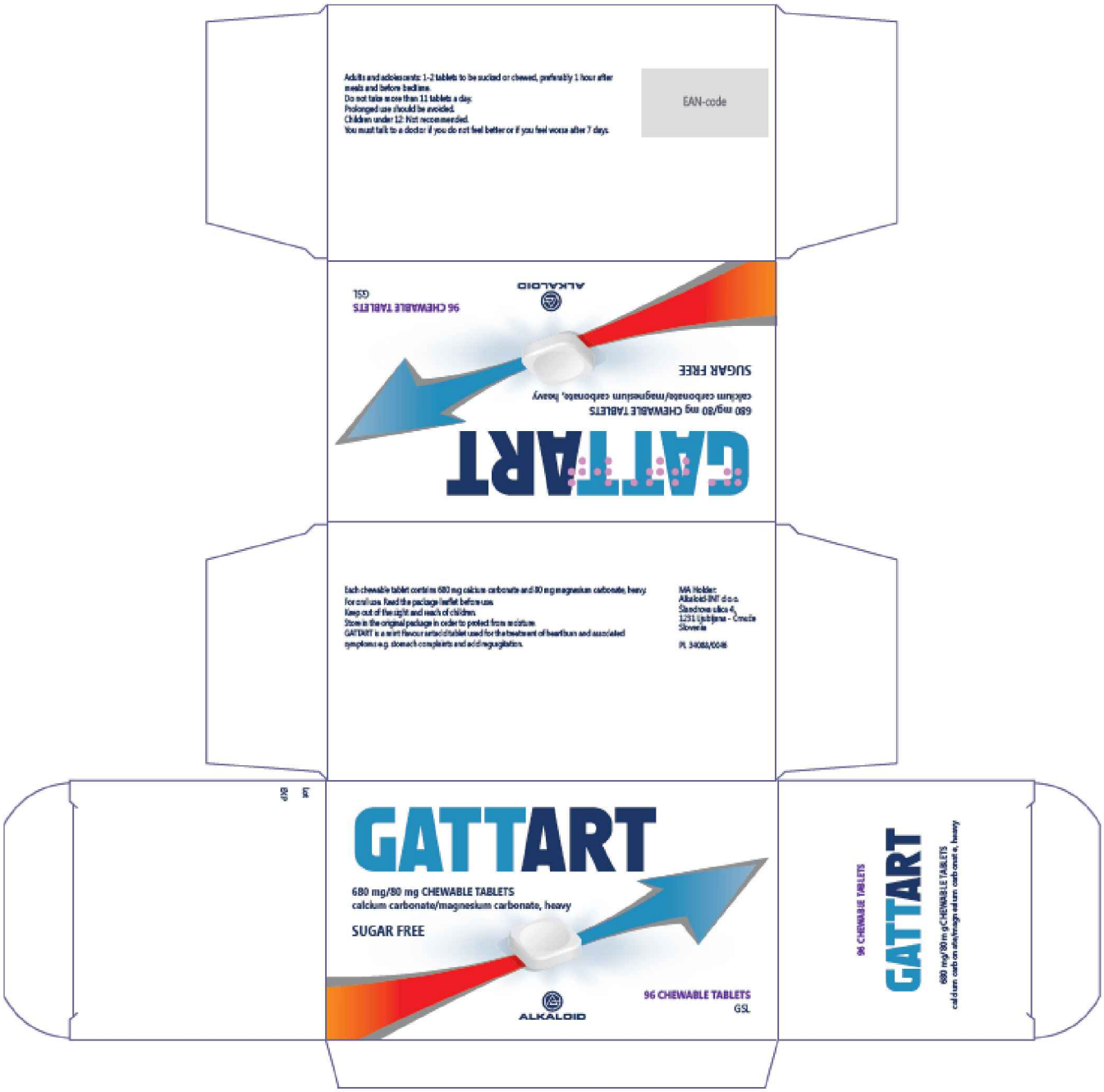
II.5 Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling

The SmPC, PIL and labelling are satisfactory and, where appropriate, in line with current guidance.

In accordance with Directive 2010/84/EU, the current versions of the SmPC and PIL are available on the MHRA website. The current labelling is shown below:


Adults and adolescents: 1-2 tablets to be sucked or chewed, preferably 1 hour after meals and before bedtime.
Do not take more than 11 tablets a day.
Prolonged use should be avoided.
Children under 12: Not recommended.
You must talk to a doctor if you do not feel better or if you feel worse after 7 days.
EAN-code
ALKALOID
24 CHEWABLE TABLETS
GSL
SUGAR FREE
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy
GATTART
Each chewable tablet contains 680 mg calcium carbonate and 80 mg magnesium carbonate, heavy.
For oral use. Read the package leaflet before use.
Keep out of the sight and reach of children.
Store in the original package in order to protect from moisture.
GATTART is a mint flavour antacid tablet used for the treatment of heartburn and associated symptoms e.g. stomach complaints and acid regurgitation.
MA Holder:
Alkaloid-INT d.o.o.
Skandrova ulica 4,
1231 Ljubljana - Črnuče
Slovenia
PL 34088/0046
EXP
LOT
GATTART
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy
SUGAR FREE
ALKALOID
24 CHEWABLE TABLETS
GSL
24 CHEWABLE TABLETS
GATTART
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy


Adults and adolescents: 1-2 tablets to be sucked or chewed, preferably 1 hour after meals and before bedtime.
Do not take more than 11 tablets a day.
Prolonged use should be avoided.
Children under 12: Not recommended.
You must talk to a doctor if you do not feel better or if you feel worse after 7 days.
EAN-code
ALKALOID
GSL
48 CHEWABLE TABLETS
SUGAR FREE
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy
GATTART
Each chewable tablet contains 680 mg calcium carbonate and 80 mg magnesium carbonate, heavy.
For oral use. Read the package leaflet before use.
Keep out of the sight and reach of children.
Store in the original package in order to protect from moisture.
GATTART is a mint flavour antacid tablet used for the treatment of heartburn and associated symptoms e.g. stomach complaints and acid regurgitation.
MA Holder:
Alkaloid INT d.o.o.
Skandrova ulica 4,
1231 Ljubljana - Črnuče
Slovenia
PL 34088/0046
GATTART
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy
SUGAR FREE
ALKALOID
48 CHEWABLE TABLETS
GSL
48 CHEWABLE TABLETS
GATTART
680 mg/80 mg CHEWABLE TABLETS


Adults and adolescents: 1-2 tablets to be sucked or chewed, preferably 1 hour after meals and before bedtime.
Do not take more than 11 tablets a day.
Prolonged use should be avoided.
Children under 12: Not recommended.
You must talk to a doctor if you do not feel better or if you feel worse after 7 days.
EAN-code
ALKALOID
96 CHEWABLE TABLETS
GSL
SUGAR FREE
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy
GATTART
Each chewable tablet contains 680 mg calcium carbonate and 80 mg magnesium carbonate, heavy.
For oral use. Read the package leaflet before use.
Keep out of the sight and reach of children.
Store in the original package in order to protect from moisture.
GATTART is a mint flavour antacid tablet used for the treatment of heartburn and associated symptoms e.g. stomach complaints and acid regurgitation.
MA Holder:
Alkaloid-INT d.o.o.
Skedenjska ulica 4,
1231 Ljubljana - Črnuče
Slovenia
M. 34088/0048
LOT
EXP
GATTART
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy
SUGAR FREE
ALKALOID
96 CHEWABLE TABLETS
GSL
96 CHEWABLE TABLETS
GATTART
680 mg/80 mg CHEWABLE TABLETS
calcium carbonate/magnesium carbonate, heavy


Lot
EXP
GATTART
680 mg/80 mg Chewable Tablets
calcium carbonate/magnesium carbonate, heavy
ALKALOID

Annex 1 Table of content of the PAR update for MRP and DCP

Steps taken after the initial procedure with an influence on the Public Assessment Report

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)