Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Ondansetron 4 mg Tablets
Ondansetron 8 mg Tablets

(Ondansetron hydrochloride dihydrate)

PL 20395/0331-0332

Relonchem Limited

LAY SUMMARY

Ondansetron 4 mg Tablets
Ondansetron 8 mg Tablets
(Ondansetron hydrochloride dihydrate)

This is a summary of the Public Assessment Report (PAR) for Ondansetron 4 mg and 8 mg Tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use this these products.

These products will be referred to as Ondansetron Tablets in this lay summary for ease of reading.

For practical information about using Ondansetron Tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Ondansetron Tablets and what are they used for?
These applications are the same as Ondansetron 4 mg and 8 mg Tablets which are already authorised.

The Company responsible for Ondansetron 4 mg and 8 mg Tablets has agreed that its scientific data can be used as the basis for the grant of an identical licences for Ondansetron Tablets.

Ondansetron Tablets are used for:

- preventing nausea and vomiting caused by chemotherapy (in adults and children) or radiotherapy for cancer (adults only)
- preventing nausea and vomiting after surgery (adults only)

How do Ondansetron Tablets work?
The active ingredient in these medicines is ondansetron. This belongs to a group of medicines known as anti-emetics which work by blocking the actions of chemicals in the body that can trigger nausea and vomiting.

How are Ondansetron Tablets used?
The pharmaceutical form of these medicines is a film-coated tablet and the route of administration is oral (via the mouth).

For further information on how Ondansetron Tablets are used, refer to the PIL and Summaries of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Ondansetron Tablets have been shown in studies?
Ondansetron Tablets are considered identical to the previously authorised products with the same benefits and risks. No new studies have been provided for Ondansetron Tablets, however, reference is made to the studies for Ondansetron 4 mg and 8 mg Tablets.

What are the possible side effects of Ondansetron Tablets?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Ondansetron Tablets are considered to be identical to the previously authorised products with the same benefits and risks.

Why were Ondansetron Tablets approved?
The MHRA decided that the benefits of Ondansetron Tablets are greater than the risks and recommended that these medicines are approved for use.

What measures are being taken to ensure the safe and effective use of Ondansetron Tablets?
A Risk Management Plan (RMP) has been developed to ensure that Ondansetron Tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, 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 Ondansetron Tablets
Marketing Authorisations were granted in the United Kingdom (UK) on 31 August 2021.

The full PAR for Ondansetron Tablets follows this summary.

This summary was last updated in October 2021.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Ondansetron 4 mg and 8 mg Tablets (PL 20395/0331-0332) could be approved.

The products are approved for the following indications:

Adults:

Ondansetron is indicated for the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy.

Ondansetron is indicated for the prevention and treatment of post-operative nausea and vomiting (PONV).

For treatment of established PONV, administration by injection is recommended.

Paediatric Population:

Ondansetron is indicated for the management of chemotherapy-induced nausea and vomiting (CINV) in children aged ≥ 6 months, and for the prevention and treatment of PONV in children aged ≥ 1 month, administration by injection is recommended.

Ondansetron is a potent, highly selective $5HT_3$ receptor-antagonist. Its precise mode of action in the control of nausea and vomiting is not known. Chemotherapeutic agents and radiotherapy may cause release of 5HT in the small intestine initiating a vomiting reflex by activating vagal afferents via $5HT_3$ receptors. Ondansetron blocks the initiation of this reflex. Activation of vagal afferents may also cause a release of 5HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism. Thus, the effect of ondansetron in the management of the nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of $5HT_3$ receptors on neurons located both in the peripheral and central nervous system.

The mechanisms of action in post-operative nausea and vomiting are not known but there may be common pathways with cytotoxic induced nausea and vomiting.

Ondansetron does not alter plasma prolactin concentrations.

The role of ondansetron in opiate-induced emesis is not yet established.

These are national abridged applications approved under Regulation 56 of The Human Medicines Regulations 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as informed consent applications. The applications cross-refer to the reference products Ondansetron 4 mg and 8 mg Tablets (PL 45841/0016 & PL 45841/0017) currently held by Cadila Pharmaceuticals (Europe) Limited, which were originally granted in the UK to the Marketing Authorisation Holder, Neolab Limited on 14/03/2007 (PL 08137/0104 & PL 08137/0105).

No new non-clinical or clinical data have been supplied and none are required for these informed consent applications.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the applications are for identical versions of already authorised products, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

National marketing authorisations were granted in the United Kingdom (UK) on 31 August 2021.

II. EXPERT REPORT

The applicant cross-refers to the data for Ondansetron 4 mg and 8 mg Tablets (PL 45841/0016 & PL 45841/0017; Cadila Pharmaceuticals (Europe) Limited), to which these applications are claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARIES OF PRODUCT CHARACTERITICS (SmPC)

The SmPCs are in line with those for Ondansetron 4 mg and 8 mg Tablets (PL 45841/0016 & PL 45841/0017), dated 09/2020.

PATIENT INFORMATION LEAFLET (PIL)

A leaflet mock-up has been provided which has been aligned with that for Ondansetron 4 mg and 8 mg Tablets (PL 45841/0016 & PL 45841/0017), dated for 08/2020. The user test report submitted for PL 45841/0016 & PL 45841/0017 has been provided.

LABEL

Label mock-ups have been provided.

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specification

The source of the active substance is in line with the cross-reference products. The proposed drug substance specification is consistent with the details registered for the cross-reference products.

IV.2. Drug Product

Name

The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Ondansetron Tablets are available in blister strips comprising PVC/PVdC/Aluminium foil enclosed in an outer carton in a pack sizes of 10, 30 or 100 tablets. Not all packs may be marketed.

The appearance of the products is identical to that of the cross-reference products.

The proposed shelf life of the products is 36 months with the storage conditions 'Store in the original package. Keep blister in the outer carton'.

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference product.

Legal status
Prescription only medicine (POM).

Manufacturers
The proposed manufacturing sites are consistent with the details registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative compositions
The composition of the proposed products is consistent with the details registered for the cross-reference products.

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference products and the maximum batch size is stated.

Finished product release/shelf life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference products.

TSE Compliance
With the exception of lactose monohydrate no excipients of animal or human origin are used in the final products.

The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

These products do not contain or consist of genetically modified organisms (GMO).

V. NON-CLINICAL ASPECTS

As these applications are submitted under Regulation 56 of The Human Medicines Regulations 2012, as amended, (as informed consent applications) no new non-clinical data have been supplied and none are required.

VI. CLINICAL ASPECTS

As these applications are submitted under Regulation 56 of The Human Medicines Regulations 2012, as amended, (as informed consent applications) no new clinical data have been supplied and none are required.

VII. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulations 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VIII. USER CONSULTATION

A full colour mock-up of the PIL has been provided with the application, in accordance with legal requirements.

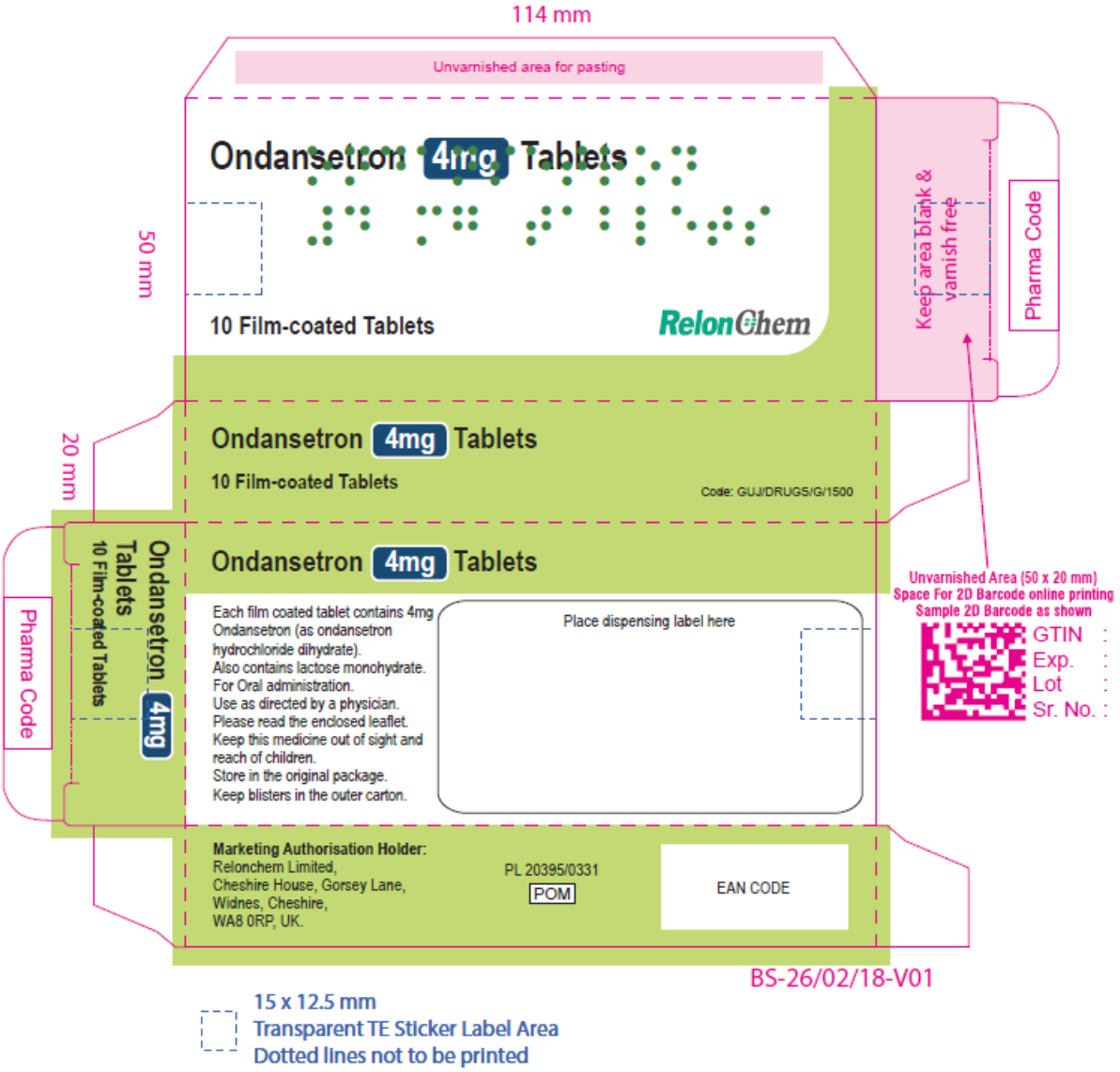
The PIL has been evaluated via a user consultation with target patient groups, in accordance with legal requirements, on the basis of a bridging report making reference to Ondansetron 4 mg and 8 mg Tablets (PL 45841/0016-0017; Cadila Pharmaceuticals (Europe) Limited). The bridging report submitted by the applicant is acceptable.

IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference products and positive.

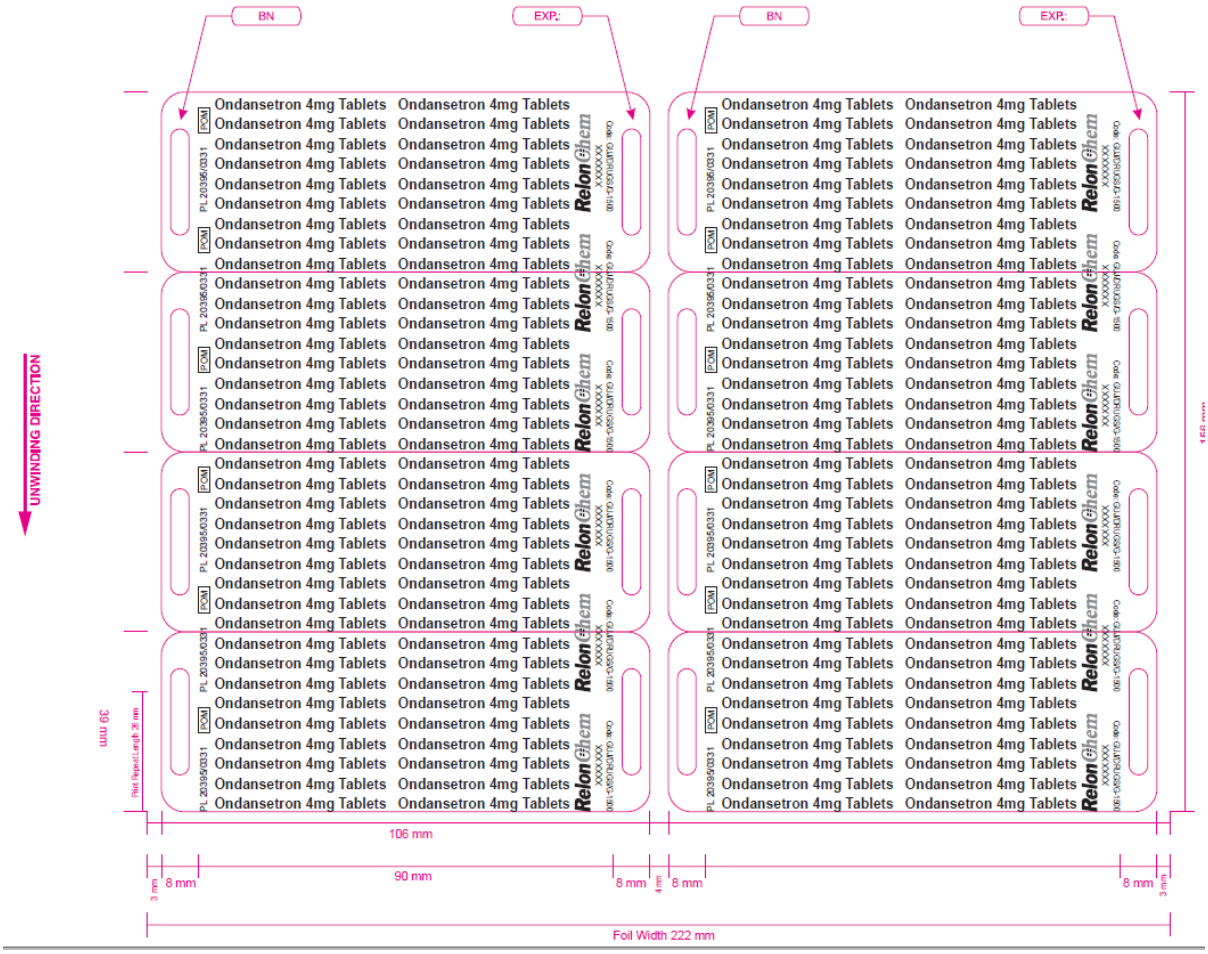
The SmPC, Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product(s).

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for these products are available on the MHRA website.



Ondansetron
4 mg Tablets


114 mm
Unvarnished area for pasting
Ondansetron 4mg Tablets
30 Film-coated Tablets
RelonChem
Keep area blank & varnish free
50 mm
22 mm
Ondansetron 4mg Tablets
30 Film-coated Tablets
Code: GUJ/DRUGS/G-1500
Ondansetron 4mg Tablets
Each film coated tablet contains 4mg Ondansetron (as ondansetron hydrochloride dihydrate).
Also contains lactose monohydrate.
For Oral administration.
Use as directed by a physician.
Please read the enclosed leaflet.
Keep this medicine out of sight and reach of children.
Store in the original package.
Keep blisters in the outer carton.
Place dispensing label here
Unvarnished Area (50 x 22 mm)
Space For 2D Barcode online printing
Sample 2D Barcode as shown
GTIN : 05055144202884
Exp. : MM/YYYY
Lot : XXXXXXXX
Sr. No. : Cadila specific serial number to be used
Marketing Authorisation Holder:
Relonchem Limited,
Cheshire House, Gorsey Lane,
Widnes, Cheshire,
WA8 0RP, UK.
PL 20395/0331
POM
15 x 12.5 mm
Transparent TE Sticker Label Area
Dotted lines not to be printed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EXP:
Ondansetron 4mg Tablets
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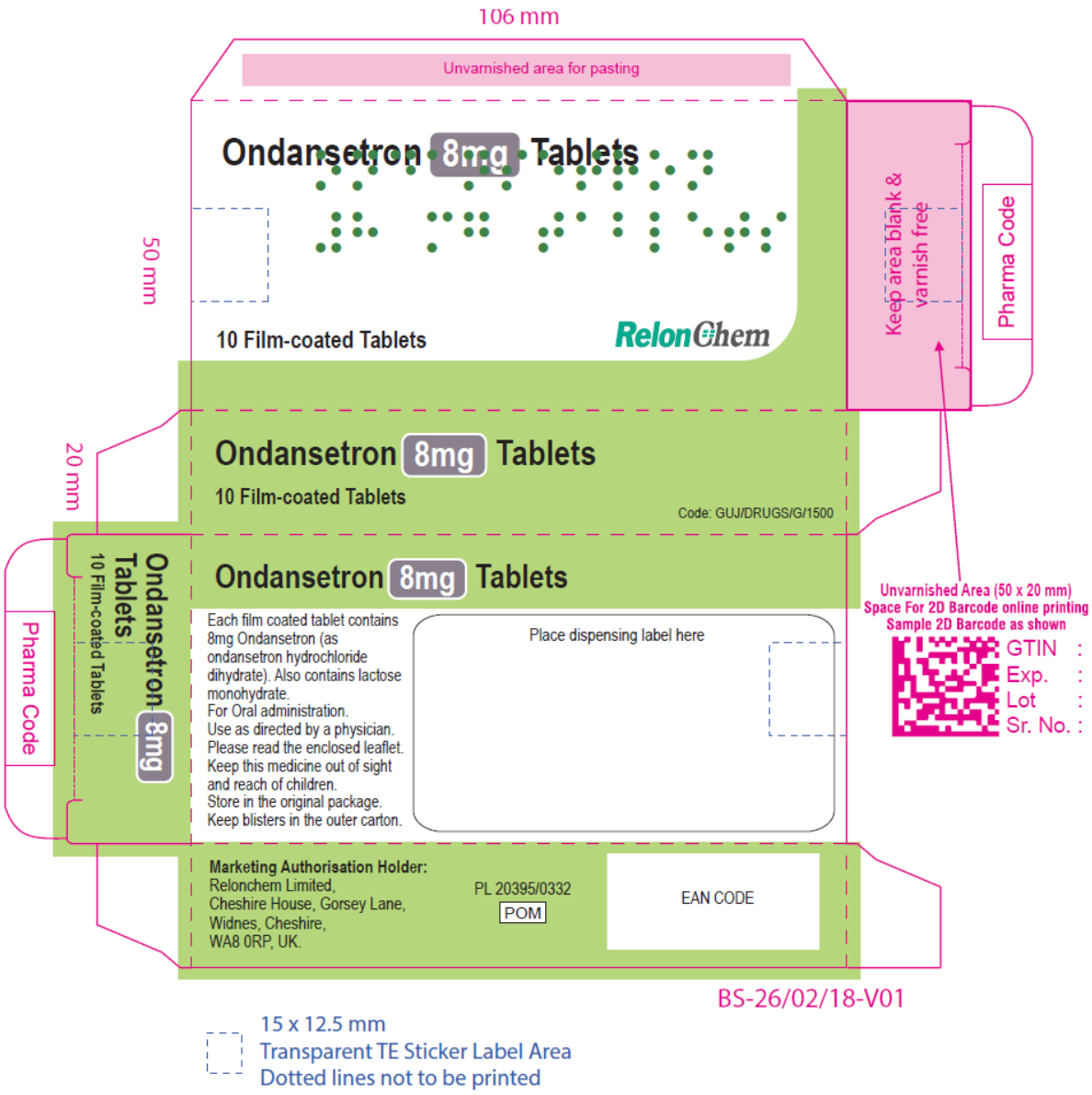
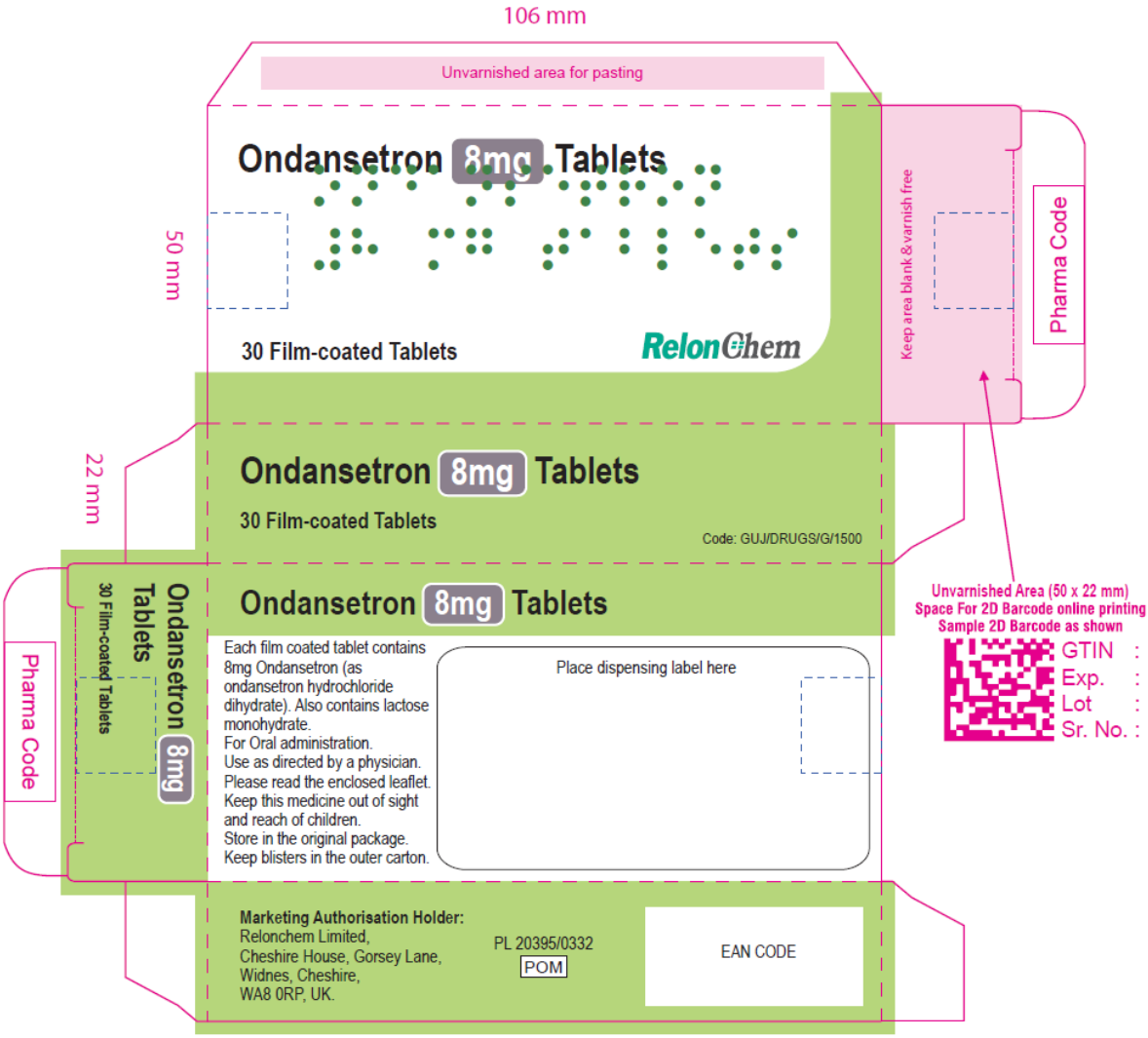
106 mm
90 mm
8 mm
Foil Width 222 mm



Ondansetron
8 mg Tablets


106 mm
Unvarnished area for pasting
Ondansetron 8mg Tablets
50 mm
30 Film-coated Tablets
RelonChem
Keep area blank & varnish free
Pharma Code
Ondansetron 8mg Tablets
22 mm
30 Film-coated Tablets
Code: GUJ/DRUGS/G/1500
Ondansetron 8mg Tablets
Ondansetron 8mg Tablets
30 Film-coated Tablets
Pharma Code
Each film coated tablet contains 8mg Ondansetron (as ondansetron hydrochloride dihydrate). Also contains lactose monohydrate.
For Oral administration.
Use as directed by a physician.
Please read the enclosed leaflet.
Keep this medicine out of sight and reach of children.
Store in the original package.
Keep blisters in the outer carton.
Place dispensing label here
Unvarnished Area (50 x 22 mm)
Space For 2D Barcode online printing
Sample 2D Barcode as shown
GTIN :
Exp. :
Lot :
Sr. No. :
Marketing Authorisation Holder:
Relonchem Limited,
Cheshire House, Gorsey Lane,
Widnes, Cheshire,
WA8 0RP, UK.
PL 20395/0332
POM
EAN CODE
15 x 12.5 mm
Transparent TE Sticker Label Area
Dotted lines not to be printed
BS-27-/04/19-V01
Ondansetron
8 mg Tablets


BN
EXP:
UNWINDING DIRECTION
Ondansetron 8mg Tablets
POM
PL 20395/0332
Relon Chem
Code: GLUDRUSIS-1500
XXXXXXX
XXXXXXXX
138 mm
40 mm
Print Repeat Length 26.6 mm
98 mm
2 mm
8 mm
82 mm
4 mm
Foil Width 204 mm

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**