Co-tenidone 100/25 mg Film-coated Tablets BP
Co-tenidone 50/12.5 mg Film-coated Tablets BP
(atenolol/chlortalidone)

PL 28444/0100-0101

UKPAR

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LAY SUMMARY

Co-tenidone 100/25 mg Film-coated Tablets BP
Co-tenidone 50/12.5 mg Film-coated Tablets BP
(atenolol/chlortalidone)

This is a summary of the Public Assessment Report (PAR) for Co-tenidone 100/25 mg and 50/12.5 mg Film-coated Tablets BP (PL 28444/0100-0101). It explains how Co-tenidone 100/25 mg and 50/12.5 mg Film-coated Tablets BP 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 Co-tenidone 100/25 mg and 50/12.5 mg Film-coated Tablets BP.

For practical information about using Co-tenidone 100/25 mg and 50/12.5 mg Film-coated Tablets BP, patients should read the package leaflet or contact their doctor or pharmacist.

The products may be referred to as using Co-tenidone Film-coated Tablets in this report.

What are Co-tenidone Film-coated Tablets and what are they used for?

Co-tenidone Film-coated Tablets contain two active ingredients atenolol and chlorthalidone. Co-tenidone Film-coated Tablets are prescribed for adults only to treat high blood pressure.

These medicines are identical to Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102), which were granted Marketing Authorisations to Medreich plc on 18 May 2010 following several change of ownership procedures of Co-Tenidone 100/25 mg and 50/12.5 mg Tablets BP (PL 18909/0022 and 0021). Co-Tenidone 100/25 mg and 50/12.5 mg Tablets BP (PL 18909/0022 and 0021) were authorised to Arrow Generics on 24 April 2002 and cross-refer to Co-tenidone 100 and 50 Tablets BP (PL 04543/0338-0339), which were granted to CP Pharmaceuticals Limited on 10 October 1994.

How are Co-tenidone Film-coated Tablets used?

Co-tenidone Film-coated Tablets are taken by mouth. The tablets must be swallowed with water.

The recommended dosage is as follows:

- Adults - one 50/12.5 mg tablet or one 100/25 mg tablet a day.
- Elderly or patients with kidney disease - the doctor may prescribe a reduced dose.
- Children - not recommended

The tablets should be taken exactly as prescribed by the doctor.

For further information on how Co-tenidone Film-coated Tablets are used, refer to the package leaflet and Summaries of Product Characteristics.

Co-tenidone Film-coated Tablets can only be obtained on prescription.

How do Co-tenidone Film-coated Tablets work?

The active ingredient atenolol belongs to a group of medicines called beta-blockers, which help the heart beat more slowly and with less force. The active ingredient chlortalidone belongs to a group of medicines called thiazide diuretics which remove excess water and salt.

How have Co-tenidone Film-coated Tablets been studied?

These applications are identical to the previously granted applications for Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102).

The company (Activase Pharmaceutical Limited) referred to data provided by Medreich plc for the grant of licences for Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102) as a basis for the grant of identical licences for Co-tenidone 100/25 mg and 50/12.5 mg Film-coated Tablets BP (PL 28444/0100-0101).

What are the benefits and risks of Co-tenidone Film-coated Tablets?

As Co-tenidone Film-coated Tablets are considered to be identical to Co-tenidone 100/25 mg and 50/12.5 mg Tablets BP (PL 21880/0103 and 0102), their benefits and risks are taken as being the same as that for Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102).

Why are Co-tenidone Film-coated Tablets approved?

No new or unexpected safety concerns arose from these applications. It was, therefore, considered that the benefits of Co-tenidone Film-coated Tablets outweigh their risks; and the grant of Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Co-tenidone Film-coated Tablets?

A Risk Management Plan has been developed to ensure that Co-tenidone Film-coated Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the package leaflet for Co-tenidone Film-coated Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Co-tenidone Film-coated Tablets

Marketing Authorisations were granted in the UK on 14 April 2014.

The full PAR for Co-tenidone Film-coated Tablets follows this summary.

For more information about treatment with Co-tenidone Film-coated Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in June 2014.

Co-tenidone 100/25 mg Film-coated Tablets BP
Co-tenidone 100/25 mg Film-coated Tablets BP
(atenolol and chlorthalidone)

PL 28444/0100-0101

SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Activase Pharmaceuticals Limited Marketing Authorisations for the medicinal products Co-tenidone 100/25 mg and 50mg/12.5 mg film-coated tablets BP (PL 28444/0100-0101) on 14 April 2014. The products are prescription-only medicines (POM) used in the management of hypertension.

The applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Co-tenidone 100/25mg and 50/12.5mg film-coated tablets BP (PL 21880/0103 and 0102), which were granted Marketing Authorisations to Medreich plc on 18 May 2010 following several change of ownership procedures of Co-Tenidone 100/25 mg and 50/12.5 mg Tablets BP (PL 18909/0022 and 0021). Co-Tenidone 100/25 mg and 50/12.5 mg Tablets BP (PL 18909/0022 and 0021) were authorised to Arrow Generics on 24 April 2002 and cross-refer to Co-tenidone 100 and 50 Tablets BP (PL 04543/0338-0339), which were granted to CP Pharmaceuticals Limited on 10 October 1994.

Co-tenidone 100/25 mg and 50/12.5 mg film-coated tablets BP contain the active ingredients atenolol and chlortalidone. Atenolol is $beta_1$-selective (that is, acts preferentially on $beta_1$-adrenergic receptors in the heart). Selectivity decreases with increasing dose. As with other beta-blockers, the mode of action in the treatment of hypertension is unclear. Chlortalidone, a monosulfonamyl diuretic, increases excretion of sodium and chloride. Natriuresis is accompanied by some loss of potassium. The mechanism by which chlortalidone reduces blood pressure is not fully known but may be related to the excretion and redistribution of body sodium. The combination of atenolol with thiazide-like diuretics has been shown to be compatible and generally more effective than either drug used alone.

No new data were submitted nor were necessary to be submitted for these applications, as the data are identical to those of the previously granted cross-reference products.

PHARMACEUTICAL ASSESSMENT

LICENCE NO:	PL 28444/0100-0101
PROPRIETARY NAME(S):	Co-tenidone 100/25 mg film-coated tablets BP Co-tenidone 50mg/12.5 mg film-coated tablets BP
ACTIVE(S):	Atenolol and chlortalidone
COMPANY NAME:	Medreich plc
E.C. ARTICLE:	Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS:	POM

1. INTRODUCTION

These are abridged applications for Co-tenidone 100/25 mg and 50mg/12.5 mg Film-coated tablets BP (PL 28444/0100-0101) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102), which were granted Marketing Authorisations to Medreich plc on 18 March 2010. The applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name

The proposed names of the products are Co-tenidone 100/25 mg and 50/12.5 mg Film-coated tablets BP (PL 21880/0103 and 0102). The products have been named in line with current requirements.

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

Each film-coated tablet for oral use contains 100 mg or 50 mg of atenolol and 25 mg or 12.5 mg of chlorthalidone. The products are packaged in white opaque polvinylchloride film and hard tempered aluminium foil blisters). The blisters are packed with the Patient Information Leaflet into cardboard outer cartons, in pack sizes of 28, 30, 56, and 60 film-coated tablets. Not all pack sizes may be marketed.

The proposed shelf life for the product is 36 months, with the special storage conditions 'Do not store above 25°C. Store in the original package to protect from light and moisture.'

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

2.3 Legal status

On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company

Activase Pharmaceuticals Limited, 11 Boumpoulinas, 3rd Floor, P.C. 1060, Nicosia, Cyprus

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

2.5 Manufacturers

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

2.6 Qualitative and quantitative composition

The proposed compositions are consistent with the details registered for the cross-reference products.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the respective cross-reference products and the maximum batch sizes are stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the respective cross-reference products.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference product.

2.11 Bioequivalence
No bioequivalence data are required to support these simple abridged application because the proposed products are manufactured to the same formula and utilise the same processes as the reference products Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102).

3. EXPERT REPORT
The applicant cross-refers to the data for Co-tenidone 100/25mg and 50/12.5mg film-coated tablets BP (PL 21880/0103 and 0102) to which these applications are claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See Section 2.1 for details of the proposed product names. The appearance of each product is identical to the respective cross-reference product.

5. SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs)
The proposed Summaries of Product Characteristics are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The Patient Information Leaflet has been prepared in line with the details registered for the cross-reference product.

User-testing of the PIL for Co-tenidone 100/25 mg and 50mg/12.5 mg film-coated tablets BP (PL 28444/0100-0101) has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102) as the 'parent PIL'.

Carton and label
The proposed artwork is consistent with the artwork registered for the cross-reference products and complies with statutory requirements. In line with current legislation, the applicant has also included the names of the products in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSION
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.

NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment As the applications are identical versions of already authorised products, it is not expected that environmental exposure will increase following approval of the Marketing Authorisations for the proposed products.

The grant of Marketing Authorisations is recommended.

CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

An acceptable Risk Management Plan (RMP) has been submitted.

The grant of Marketing Authorisations is recommended.

OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the cross-reference products and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
These applications are identical to the previously granted applications for Co-tenidone 100/25mg and 50/12.5mg Tablets BP (PL 21880/0103 and 0102).

SAFETY
No new safety data were supplied or required for these applications. Atenolol and chlorthalidone have well-established safety profiles. No new or unexpected safety concerns arose from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory, and consistent with those for the cross-reference products.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference products. Extensive clinical experience with atenolol and chlorthalidone in combination is considered to have demonstrated the therapeutic value of the compounds. The benefit/risk balance is, therefore, considered to be positive.

Co-tenidone 100/25 mg Film-coated Tablets BP
Co-tenidone 50/12.5 mg Film-coated Tablets BP
(atenolol and chlorthalidone)

PL 28444/0100-0101

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation applications on 23 January 2012.

2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 20 April 2012.

3 Following assessment of the applications the MHRA requested further information relating to the dossiers on 20 April 2012 and 10 April 2013.

4 The applicant responded to the MHRA's request, providing further information on the 31 December 2012 and 09 July 2013.

5 The applications were granted on 14 April 2014.

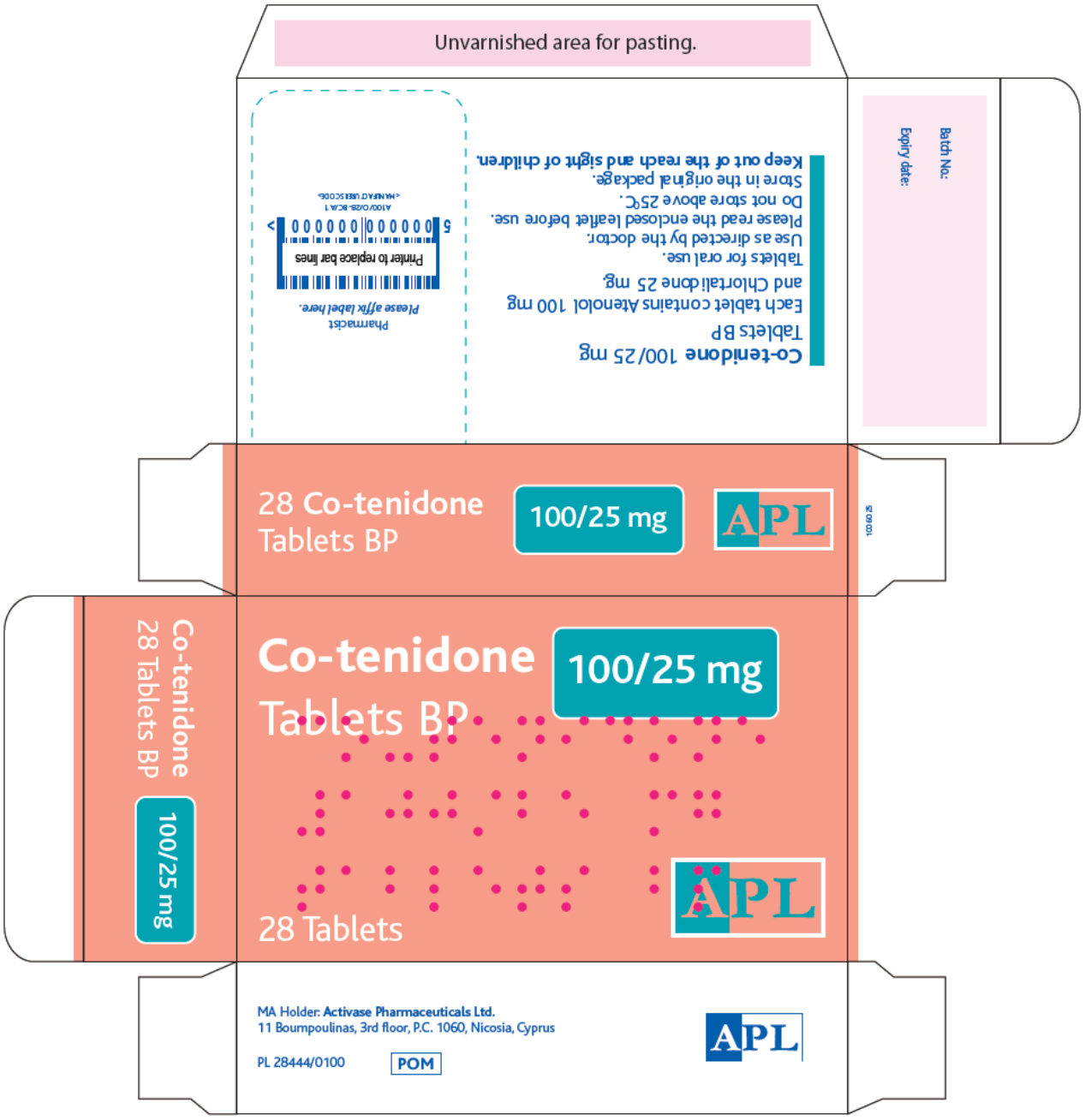
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

LABELLING


Unvarnished area for pasting.
Batch No:
Expiry date:
Co-tenidone 100/25 mg
Tablets BP
Each tablet contains Atenolol 100 mg
and Chlortalidone 25 mg.
Tablets for oral use.
Use as directed by the doctor.
Please read the enclosed leaflet before use.
Do not store above 25°C.
Store in the original package.
Keep out of the reach and sight of children.
Pharmacist
Please affix label here.
Printer to replace bar lines
28 Co-tenidone
Tablets BP
100/25 mg
APL
Co-tenidone
28 Tablets BP
100/25 mg
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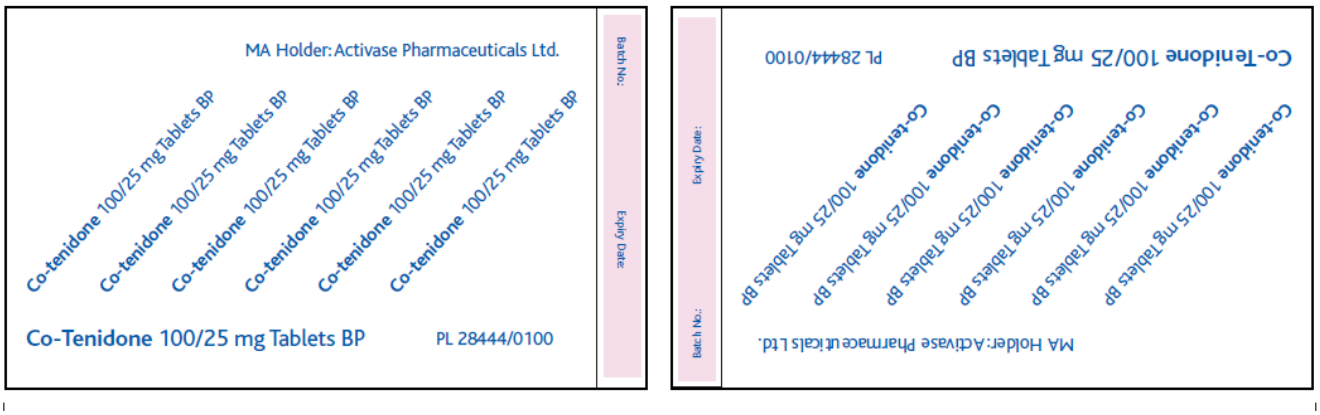
28 Tablets
APL
MA Holder: Activase Pharmaceuticals Ltd.
11 Boumpoulinas, 3rd floor, P.C. 1060, Nicosia, Cyprus
PL 28444/0100
POM
APL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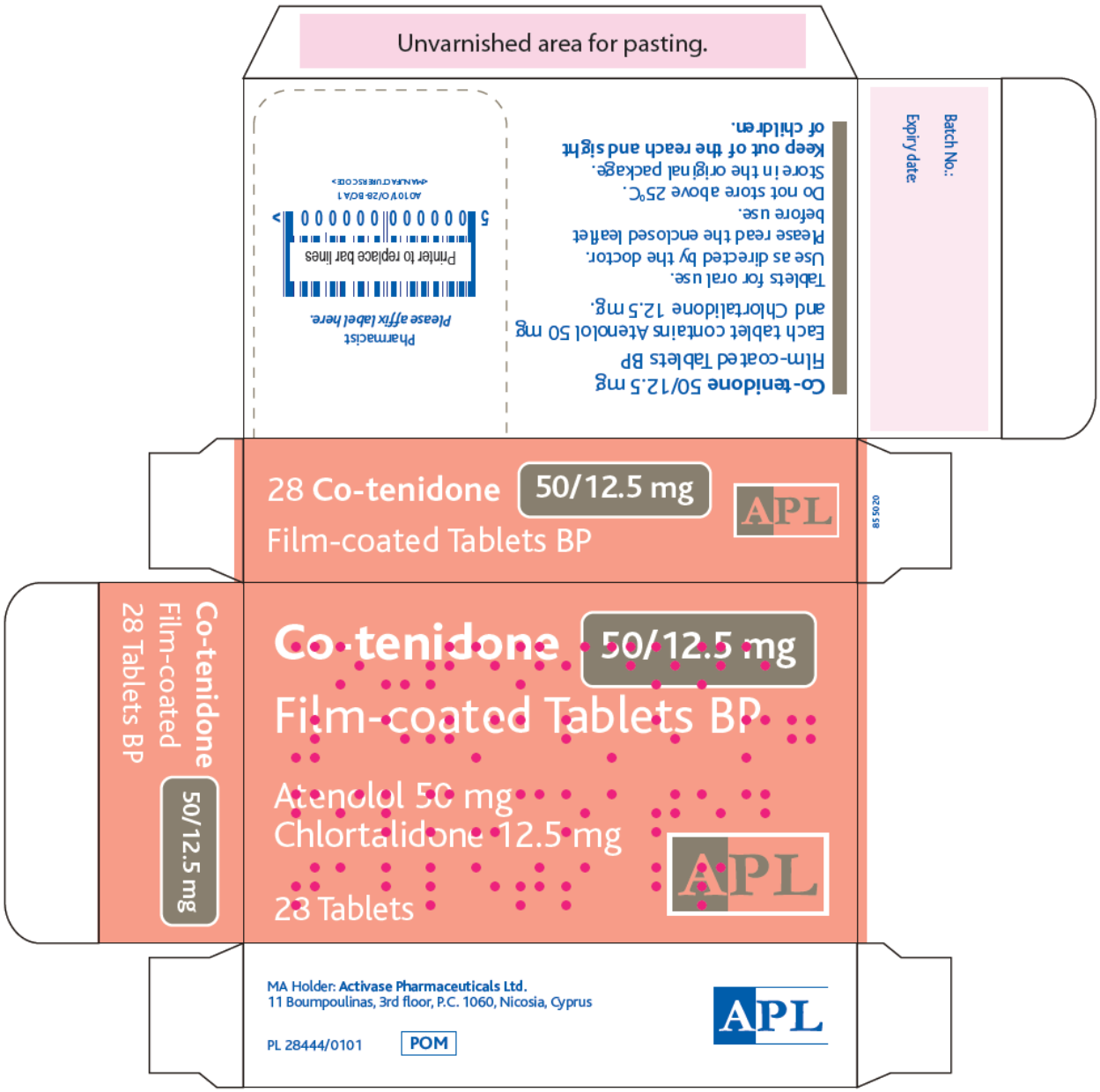
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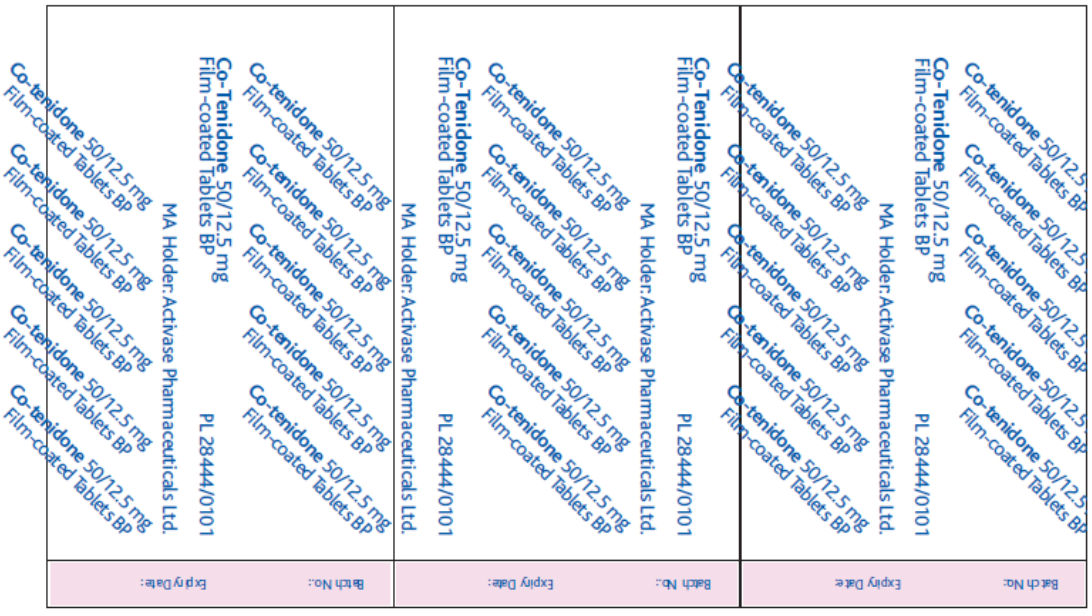
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