IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Perrigo Cold & Flu Tablets Paracetamol 250 mg Guaifenesin 100 mg Phenylephrine 5 mg
Phenylephrine hydrochloride
Guaifenesin
Paracetamol
PA1186/021/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

This product was initially authorised under procedure number UK/H/1127/001/DC with the UK as RMS. The responsibility of RMS was transferred to Ireland on 10th April 2019 under procedure number IE/H/0901/001/DC.

Please note the following detail for the product in IE:
Marketing Authorisation Number: PA1186/021/001
Marketing Authorisation Holder: Chefaro Ireland DAC

The current Summary of Product Characteristics (SmPC) for this medicinal product is available on the HPRA website at www.hpra.ie.

The UK public assessment report published at the time of the initial marketing authorisation is provided herein.

On 12th April 2010, Ireland and the UK agreed to grant a Marketing Authorisation to Wrafton Laboratories Limited for the medicinal product Tesco Flu-Max All-In-One Chesty Cough and Cold Tablets (PL 12063/0079; UK/H/1127/001/DC). The licence was granted via the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS). After the national phase, a licence was granted in the UK on 4th May 2010.

This application was made under Article l0a of Directive 2001/83 EC for Tesco Flu-Max All-In-One Chesty Cough and Cold Tablets, containing the known active substances guaifenesin, phenylephrine and paracetamol.

This product is a general sales licence (GSL) product for the relief of symptoms associated with colds and flu, including aches and pains, headache, blocked nose and sore throat, chills and chesty cough.

Paracetamol has both analgesic and antipyretic activities, which are believed to be mediated principally through its inhibition of prostaglandin synthesis within the central nervous system. Guaifenesin is an expectorant, which reduces the viscosity of tenacious sputum. Phenylephrine is a post-synaptic alpha-receptor agonist with low cardioselective beta receptor affinity and minimal central stimulant activity. It is a recognised decongestant and acts by vasoconstriction to reduce oedema and nasal swelling.

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

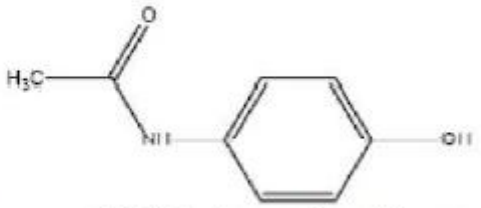
ABOUT THE PRODUCT

Name of the product in the Reference Member State	Tesco Flu-Max Ali-In-One Chesty Cough and Cold Tablets
Name(s) of the active substance(s) (USAN)	Guaifenesin, phenylephrine hydrochloride and paracetamol
Pharmacotherapeutic classification (ATC code)	Paracetamol, combinations excl. psycholeptics (N02BE51)
Pharmaceutical form and strength(s)	Tablets containing guaifenesin 100mg, phenylephrine 5mg and paracetamol 250mg
Reference numbers for the Mutual Recognition Procedure	UK/H/1127/001/DC
Reference Member State	United Kingdom
Member States concerned	Ireland
Marketing Authorisation Number(s)	PL12063/0079
Name and address of the authorisation holder	Wrafton Laboratories Limited (T/A Perrigo), Braunton, Devon, EX332DL

II. QUALITY ASPECTS

DRUG SUBSTANCE
Paracetamol

rINN: Paracetamol CAS: 103-90-2
Formula: $C_8H_9NO_2$ MW: 151.2
Structure:



Chemical name: N-(4-hydroxyphenyl)acetamide
Description: White odourless crystalline powder

Paracetamol is the subject of a European Pharmacopoeial monograph.

Synthesis of the drug substance from the designated starting materials 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.

An appropriate specification is provided for the active substance lamotrigine. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Certificates of analysis have been provided for any working standards used.

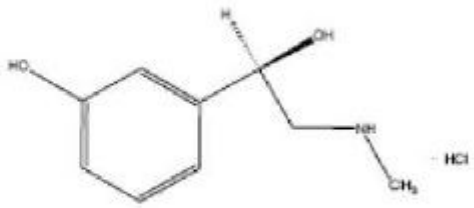
Batch analysis data are provided and comply with the proposed specification.

The active substance paracetamol is packaged into fibre drums, lined with double-layer polyethylene bags. Suitable specifications for all packaging have been provided. It has been confirmed that the primary packaging complies with current European regulations concerning materials in contact with food.

A suitable retest period has been set based on appropriate stability data.

Phenylephrine hydrochloride

rINN: Phenylephrine hydrochloride CAS: 59-42-7
Formula: $C_9H_{14}ClNO_2$ MW: 203.7
Structure:



Chemical name: (S)-1-(3-Hydroxyphenyl)-2-methylaminoethanol hydrochloride
Description: White or almost white crystalline powder

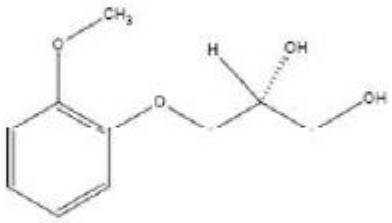
Phenylephrine hydrochloride is the subject of a European Pharmacopoeial monograph.

All aspects of the manufacture and control of guaifenesin are covered by European Directorate for the Quality of Medicines (EDQM) certificates of suitability.

Guaifenesin

Guaifenesin

rINN: Guaifenesin CAS: 93-14-1
Formula: $C_{10}H_{14}O_4$ MW: 198.22
Structure:



Chemical name: 3-(2-methoxyphenoxy)-1,2-propanediol
Description: White or almost white crystalline powder, sparingly soluble in water and soluble in alcohol.

Guaifenesin is the subject of a European Pharmacopoeial monograph.

All aspects of the manufacture and control of guaifenesin are covered by a European Directorate for the Quality of Medicines (EDQM) certificate of suitability.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients microcrystalline cellulose, stearic acid, povidone, hypromellose and polyethylene glycol. All excipients are controlled to their respective European Pharmacopoeia monograph. Satisfactory Certificates of Analysis have been provided for all excipients. None of the excipients used are sourced from materials of animal or human origin. None of the excipients are sourced from genetically modified organisms.

Pharmaceutical Development

Suitable pharmaceutical development data have been provided for this application.

Manufacture

A description and flow-cha11of the manufacturing method have been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of the product. The results appear satisfactory.

Finished product specification

The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Cet1ificates of Analysis have been provided for any working standards used.

Container Closure System

The finished product is packaged in child-resistant polyvinylchloride/aluminium blisters in pack sizes of 8 and 16 tablets.

Specifications and Certificates of Analysis for the primary packaging material have been provided. These are satisfactory. All primary packaging is controlled to European Pharmacopoeia standards and complies with guidelines concerning materials in contact with food.

Stability

Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 3 years has been set with the storage conditions "Do not store above 25°C".

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and Labelling

The SPC, PIL and labelling are pharmaceutically satisfactory.

The applicant has submitted results of PIL user testing. The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
The MAA form is pharmaceutically satisfactory.

Expert Report
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

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

III. NON-CLINICAL ASPECTS

PHARMACODYNAMICS, PHARMACOKINETICS, TOXICOLOGY
The pharmacodynamic, pharmacokinetic and toxicological properties of guaifenesin, phenylephrine hydrochloride and paracetamol are well-known. Therefore, no further studies are required and the applicant provides none. An overview based on a literature review is, thus, appropriate.

ENVIRONMENTAL RISK ASSESSMENT (ERA)
A suitable justification has been provided for non-submission of an environmental risk assessment.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC is satisfactory from a preclinical viewpoint.

NON-CLINICAL EXPERT REPORT
The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

OVERALL CONCLUSION ON THE NON-CLINICAL PART
The applicant has provided an adequate review of the available non-clinical data. There are no objections to the grant of a licence from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetic, Pharmacodynamic, Efficacy and Safety
The pharmacokinetics, pharmacodynamics, efficacy and safety properties of guaifenesin, phenylephrine hydrochloride and paracetamol are well-known. Therefore, no further studies are required and the applicant provides none. An overview based on a literature review is, thus, appropriate.

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and labelling
The SPC, PIL and labelling are medically satisfactory.

Clinical Expert Report
The clinical expert report is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

MAA Form
The MAA Form is medically satisfactory.

Clinical Conclusion
The grant of a marketing authorisation is recommended.

V. OVERALL CONCLUSIONS

The important quality characteristics of Tesco Flu-Max All-In-One Chesty Cough and Cold 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.

PRECLINICAL
The pharmacodynamic, pharmacokinetic and toxicological properties of guaifenesin, phenylephrine hydrochloride and paracetamol are well-known. No new studies have been submitted with these applications and none are required.

EFFICACY
The efficacious properties of guaifenesin, phenylephrine hydrochloride and paracetamol are well-known. No new studies have been submitted with these applications and none are required.

The SPC, PIL and labelling are satisfactory.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable, and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with guaifenesin, phenylephrine hydrochloride and paracetamol is considered to have demonstrated the therapeutic value of the compounds. The benefit-risk is, therefore, considered to be positive.

VI. REVISION DATE

December 2021

VII. UPDATES

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval
RMS Transfer	From UK/H/1127/001/DC to IE/H/0901/001/DC	N/A	N/A	N/A	Approved 10/04/2019