1.4.3 PACKAGE INSERT

1. NAME OF THE MEDICINAL PRODUCT

HYDROXYZINE MEVON FILM-COATED TABLETS 25 MG
HYDROXYZINE MEVON FILM-COATED TABLETS 10 MG

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

HYDROXYZINE MEVON FILM-COATED TABLETS 25 MG
Each film-coated tablet contains 25 mg hydroxyzine hydrochloride.

HYDROXYZINE MEVON FILM-COATED TABLETS 10 MG
Each film-coated tablet contains 10 mg hydroxyzine hydrochloride.

Excipient with known effect:

HYDROXYZINE MEVON FILM-COATED TABLETS 25 MG
Each 25 mg film-coated tablet contains 55 mg lactose monohydrate.

HYDROXYZINE MEVON FILM-COATED TABLETS 10 MG
Each 10 mg film-coated tablet contains 22 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

HYDROXYZINE MEVON FILM-COATED TABLETS 25 MG
White to off-white, 10.0 mm x 4.0 mm caplet shaped, biconvex, film coated tablets with score line on both sides.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

HYDROXYZINE MEVON FILM-COATED TABLETS 10 MG
White to off-white, 5.0 mm round shaped, biconvex, film coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- To assist in the management of anxiety in adults.
- As a sedative used as premedication
- As symptomatic relief in atopic pruritus

The effectiveness of hydroxyzine as an antianxiety agent for long term use, that is more than 4 months, has not been assessed by systematic clinical studies. The physician should reassess periodically the usefulness of the drug for the individual patient.

Hydroxyzine may potentiate meperidine and barbiturates, so their use in pre-anaesthetic adjunctive therapy should be modified on an individual basis. Atropine and other belladonna alkaloids are not affected by the drug. Hydroxyzine is not known to interfere with the action of digitalis in any way and it may be used concurrently with this agent

4.2 Posology and method of administration

Hydroxyzine MEVON film-coated tablets should be used at the lowest effective dose and for the shortest possible duration (see section 4.4).

- In adults, the maximum daily dose should not exceed 100 mg per day.

For symptomatic relief in atopic pruritus: Starting dose of 25 mg at night, increasing as necessary to 25 mg three to four times daily.
For symptomatic treatment of anxiety: 50-100 mg daily in divided doses.
For premedication before surgery: 100 mg given in divided doses.

- In children (from 30 months of age) (see section 4.4):

The maximum daily dose should not exceed 100 mg per day.

For symptomatic treatment of pruritus:
In children up to 40 kg in weight, the maximum daily dose is 2 mg/kg/day in divided doses.
In children over 40 kg in weight, the maximum daily dose is 100 mg/day.

For premedication before surgery:
1 mg/kg/day in divided doses.

The dosage of Hydroxyzine MEVON film-coated tablets must be adapted to the patient's response.
For a shorter effect, half the usual dose can be given.

- In elderly:

Use of hydroxyzine in the elderly is not recommended. However, if needed, it is advised to start with half the recommended dose due to a prolonged action.
In the elderly, the maximum daily dose is 50 mg per day (see section 4.4).

- Renal impairment:

Dosage should be reduced in patients with moderate or severe renal function impairment due to decreased excretion of its metabolite cetirizine.

- Hepatic impairment:

In patients with hepatic dysfunction, it is recommended to reduce the daily dose by 33%.

4.3 Contraindications

Hydroxyzine MEVON film-coated tablets is contraindicated in:
• History of hypersensitivity to hydroxyzine or to any of the excipients, to cetirizine, to other piperazine derivatives, to aminophylline, or to ethylenediamine.
• Pregnancy and lactation (see section 4.6).
• Severe hepatic or renal failure
• Prostate adenoma with urinary retention
• Narrow angle glaucoma
• Patients with porphyria
• Children below 12 months
• Concomitant therapy with monoamine oxidase inhibitors (see section 4.5)

• Patients with known acquired or congenital QT interval prolongation
• Patients with a known risk factor to QT interval prolongation including a known cardiovascular disease, significant electrolytes imbalance (hypokalaemia, hypomagnesaemia), family history of sudden cardiac death, significant bradycardia, concomitant use with drugs known to prolong the QT interval and/or induce Torsade de Pointes (see section 4.5).
• Hydroxyzine MEVON film-coated tablets include lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use

Cardiovascular effects
Hydroxyzine has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been cases of QT interval prolongation and Torsade de Pointes in patients taking hydroxyzine. Most of these patients had other risk factors, electrolyte abnormalities or concomitant treatment that may have been contributory (see section 4.8). Caution is needed in patients who have a known predisposing factor to cardiac arrhythmia, including electrolyte imbalance (hypokalaemia, hypomagnesaemia), who have pre-existing heart disease, or who are concomitantly treated with a potentially arrhythmogenic drug. In those patients, use of alternative treatments is to be considered.
Hydroxyzine MEVON film-coated tablets should be used at the lowest effective dose and for the shortest possible duration. Treatment with Hydroxyzine MEVON film-coated tab should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patients seek immediate medical attention.
Patients should be advised to promptly report any cardiac symptoms.

Convulsions
Hydroxyzine MEVON film-coated tablets should be administered cautiously in patients with increased potential for convulsions.

Children
Young children are more susceptible to develop adverse events related to the central nervous system (see Section 4.8). In children, convulsions have been more frequently reported than in adults.
The recommended doses should be strictly followed in children (possibility of central nervous system stimulation).

Elderly
Hydroxyzine is not recommended in elderly patients because of a decrease of hydroxyzine elimination in this population as compared to adults and greater risk of adverse reactions (e.g. anticholinergic effects) (see section 4.8). In elderly patients, it is recommended to reduce the dose of hydroxyzine due to a possible increase in the volume of distribution, prolonged action, and the possible effect of age-related changes on pharmacologic functions, including hepatic metabolism and renal excretion.

Hydroxyzine anticholinergic effects
Because of its potential anticholinergic effects, Hydroxyzine MEVON film-coated tablets should be used cautiously in patients suffering from obstructive respiratory disorders (e.g. asthma), hyperthyroidism, hypotension, hepatic insufficiency, glaucoma, bladder outflow obstruction, decreased gastro-intestinal motility, myasthenia gravis, dementia and in patients with a history of seizures.

Pheochromocytoma
Caution should be exercised in patients with pheochromocytoma because the administration of antihistamines may lead to catecholamine release.

Co-administration with CNS depressants
Dosage adjustments may be required if Hydroxyzine MEVON film-coated tablet is used simultaneously with other central nervous system depressant drugs or with drugs having anticholinergic properties (see Section 4.5).

Alcohol
The concomitant use of alcohol or other sedating drugs and Hydroxyzine MEVON film-coated tablets should be avoided (see Section 4.5).

Hepatic and renal impairment
Hydroxyzine dosage should be reduced in patients with hepatic dysfunction and in patients with moderate or severe renal impairment.

Test results
The treatment should be stopped at least 5 days before allergy testing or metacholine bronchial challenge, to avoid effects on the test results.

Hydroxyzine MEVON film-coated tablets contain lactose (see section 6.1).

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Hydroxyzine MEVON film-coated tablets contain sodium.

HYDROXYZINE MEVON FILM-COATED TABLETS 25 MG
This medicine contains less than 1 mmol sodium (23 mg) per 25 mg tablet, that is to say essentially 'sodium-free'.

HYDROXYZINE MEVON FILM-COATED TABLETS 10 MG
This medicine contains less than 1 mmol sodium (23 mg) per 10 mg tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Associations contraindicated
Co-administration of hydroxyzine with drugs known to prolong the QT interval and/or induce Torsade de Pointes e.g. class IA (e.g. quinidine, disopyramide) and III antiarrthymics (e.g. amiodarone, sotalol), some antihistamines, some antipsychotics (e.g. haloperidol), some antidepressants (e.g. citalopram, escitalopram), some antimalarial drugs (e.g. mefloquine, hydroxychloroquine), some antibiotics (e.g. erythromycin, levofloxacin, moxifloxacin), some antifungal agents (e.g. pentamidine), some gastrointestinal medicines (e.g. prucalopride), some medicines used in cancer (e.g. toremifene, vandetanib), methadone, increase the risk of cardiac arrhythmia. Therefore, the combination is contraindicated (see section 4.3).

Associations requiring precaution of use
Caution is needed with bradycardia-inducing and hypokalaemia-inducing drugs.
Hydroxyzine is metabolized by alcohol dehydrogenase and CYP3A4/5 and an increase in hydroxyzine blood concentrations may be expected when hydroxyzine is co-administered with drugs known to be potent inhibitors of these enzymes. However, when only one metabolic pathway is inhibited, the other pathway may partially compensate for it.

Antihypertensive drugs
The concomitant use of hydroxyzine with antihypertensive drugs may lead to increased sedation.

CNS depressants
Patients should be informed that hydroxyzine may potentiate the effects of barbiturates, other CNS (central nervous system) depressants or drugs having anticholinergic properties. Dosage should be adjusted on an individual basis.

Alcohol
Alcohol also potentiates the effects of Hydroxyzine.

Betahistine and cholinomimetic drugs
Hydroxyzine antagonises the effects of betahistine and cholinomimetic drugs.

Test results
The treatment should be stopped at least 5 days before allergy testing or metacholine bronchial challenge, to avoid effects on the test results.

Monoamine oxidase inhibitors
Concomitant use of monoamine oxidase inhibitors can also potentiate the antiholinergic effect of hydroxyzine. Manifestations may include: paralytic ileus, urinary retention or attack of glaucoma. Combined administration of hydroxyzine with monoamine oxidase inhibitors may also lead to hypotension and increased CNS (central nervous system) and respiratory depression. Consequently, concomitant use of these substances should be avoided.

Adrenaline
Hydroxyzine antagonises the vasopressor effect of adrenaline.

Phenytoin
In rats, hydroxyzine antagonised the anticonvulsant action of phenytoin.

Cimetidine
Cimetidine 600 mg twice daily has been shown to increase the serum concentrations of hydroxyzine by 36% and to decrease peak concentrations of the metabolite cetirizine by 20%.

CYP2D6 substrates
Hydroxyzine is an inhibitor of cytochrome P450 2D6 (Ki: 3.9 μM; 1.7 μg/ml) and may cause at high doses drug-drug interactions with CYP2D6 substrates (e.g. fluoxetine).

Effect on other drug metabolism
Hydroxyzine has no inhibitory effect at 100 μM on UDP-glucuronyl transferase isoforms 1A1 and 1A6 in human liver microsomes. It inhibits cytochrome P4502C9/C10, 2C19 and 3A4 isoforms at concentrations (IC_{50}: 19 to 140 μM; 7 to 52 μg/ml) well above peak plasma concentrations. The metabolite cetirizine at 100 μM has no inhibitory effect on human liver cytochrome P450 (1A2, 2A6, 2C9/C10, 2C19, 2D6, 2E1, and 3A4) and UDP-glucuronyl transferase isoforms. Therefore, hydroxyzine is unlikely to impair the metabolism of drugs which are substrates for these enzymes.

4.6 Fertility, pregnancy and lactation

Fertility
There are no relevant data available.

Pregnancy
Hydroxyzine is contraindicated during pregnancy (see Section 4.3).
Animal studies have shown reproductive toxicity.
Hydroxyzine crosses the placental barrier leading to higher foetal than maternal concentrations.

To date, no relevant epidemiological data are available relating to exposure to hydroxyzine during pregnancy.
In neonates whose mothers received hydroxyzine during late pregnancy and/or labour, the following events were observed immediately or only a few hours after birth: hypotonia, movement disorders including extrapyramidal disorders, clonic movements, CNS depression, neonatal hypoxic conditions, or urinary retention.

Lactation
Hydroxyzine is contraindicated during lactation (see Section 4.3).
Breast-feeding should be stopped if hydroxyzine therapy is needed.
Cetirizine, the principal metabolite of hydroxyzine, is excreted in human milk.
Although no formal studies have been performed on the excretion of hydroxyzine in human milk, severe adverse effects have been shown in breastfed newborns/infants of hydroxyzine treated mothers.

4.7 Effects on ability to drive and use machines

Hydroxyzine may cause fatigue, dizziness, sedation, and visual disturbances; consequently, it may have a moderate to major influence on the ability to react and to concentrate, particularly at high doses. Patients should be warned of this possibility and cautioned against driving a car or operating machinery.
Concomitant use of hydroxyzine with alcohol or other sedative drugs should be avoided as it aggravates these effects.

4.8 Undesirable effects

Undesirable effects are mainly related to CNS (central nervous system) depressant or paradoxical CNS stimulation effects, to anticholinergic activity, or to hypersensitivity reactions.

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency.
Frequencies are defined as :
Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100
Rare ≥1/10000 to <1/1000
Very rare <1/10000
Not known (cannot be estimated from the available data).

Clinical Trial Data

The following undesirable effects were reported in placebo-controlled clinical trials for hydroxyzine and including 735 subjects exposed to hydroxyzine up to 50 mg daily.

Nervous system disorders
Very common: somnolence
Common: headache
Uncommon: dizziness, insomnia, disturbance in attention

Gastrointestinal disorders
Common: dry mouth
Uncommon: constipation, nausea

General disorders and administration site conditions
Common: fatigue
Uncommon: asthenia

Post Marketing Data

Immune system disorders
Not known: hypersensitivity, anaphylactic shock

Psychiatric disorders
Not known: agitation, confusion, disorientation, hallucination

Nervous system disorders
Very common : somnolence
Rare : convulsions, dyskinesia, syncope
Not known: sedation, tremor, headache, vertigo, insomnia, ataxia

Eye disorders
Not known: accommodation disorder, vision blurred, elevated intraocular pressure

Cardiac disorders
Not known: tachycardia, QT interval prolongation, ventricular arrhythmias (e.g. Torsade de Pointes) (see section 4.4)

Vascular disorders
Not known: hypotension

Respiratory, thoracic and mediastinal disorders
Not known: bronchospasm
Not known: dry mouth, nausea, constipation, vomiting

Hepatobiliary disorders
Not known: jaundice hepatic, jaundice cholestatic, liver function tests abnormal, hepatitis

Skin and subcutaneous tissue disorders
Not known: pruritus, erythematous rash, maculo-papular rash, urticaria, dermatitis, angioneurotic oedema, hyperhidrosis, fixed drug eruption, acute generalized exanthematous pustulosis (AGEP), erythema multiforme, bullous conditions e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), pemphigoid

Renal and urinary disorders
Not known: urinary retention

General disorders and administration site conditions
Not known: fatigue, malaise, pyrexia

The following adverse reactions have been observed with cetirizine, the principal metabolite of hydroxyzine: thrombocytopenia, aggression, depression, tic, dystonia, paraesthesia, oculogyric crisis, diarrhoea, dysuria, enuresis, asthenia, oedema, weight increased and could potentially occur with hydroxyzine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via SUSPECTED ADVERSE DRUG REACTION (ADR) ONLINE REPORTING FORM on HSA’s website.

4.9 Overdose

Symptoms and Signs

Symptoms observed after an important overdose are mainly associated with excessive anticholinergic load, CNS depression or CNS paradoxical stimulation. They include nausea, vomiting, tachycardia, pyrexia, somnolence, impaired pupillary reflex, tremor, confusion, or hallucination. This may be followed by depressed level of consciousness, respiratory depression, convulsions, hypotension, or cardiac arrhythmia including bradycardia. Deepening coma and cardiorespiratory collapse may ensue.

Treatment

Airway, breathing and circulatory status must be closely monitored with continuous ECG (electrocardiography) recording and adequate oxygen supply should be available. Cardiac and blood pressure monitoring should be maintained until the patient is free of symptoms for 24 hours. Patients with altered mental status should be checked for simultaneous intake of other drugs or alcohol and should be given oxygen, naloxone, glucose and thiamine if deemed necessary.

Norepinephrine or metaraminol should be used if vasopressor is needed. Epinephrine should not be used due to a possible paradoxical blood pressure decrease (‘reverse epinephrine response’). Severe shock may, however, be treated with norepinephrine.

Syrup of ipecac should not be administered in symptomatic patients or those who could rapidly become obtunded, comatose or convulsing, as this could lead to aspiration pneumonitis. Activated charcoal may be left in the stomach but there are scant data to support its efficacy.
It is doubtful that haemodialysis or haemoperfusion would be of any value.
There is no specific antidote.

Literature data indicate that, in the presence of severe, life-threatening, intractable anticholinergic effects unresponsive to other agents, a therapeutic trial dose of physostigmine may be useful in patients with supraventricular tachyarrhythmia or seizures unresponsive to other agents. Physostigmine should not be used just to keep the patient awake. If cyclic antidepressants have been co-ingested, use of physostigmine may precipitate seizures and intractable cardiac arrest. Also avoid physostigmine in patients with cardiac conduction defects.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group
Anxiolytics; Diphenylmethane derivatives

ATC Code
N05BB01

Mechanism of Action
Hydroxyzine is a first generation antihistamine that crosses the blood/brain barrier extensively and has a high affinity for histaminic receptors into the brain, thereby producing sedative-anxiolytic effects.

Pharmacodynamic effects

Antihistaminic and bronchodilator activities have been demonstrated experimentally and confirmed clinically. Pharmacological and clinical studies indicate that hydroxyzine at therapeutic dosage does not increase gastric secretion or acidity and in most cases has mild antisecretory activity. Wheal and flare reduction have been demonstrated in adult healthy volunteers and in children after intradermal injections of histamine or antigens. Hydroxyzine has also revealed its efficacy in relieving pruritus in various forms of urticaria, eczema and dermatitis.

Onset of action
The antihistaminic effect begins approximately after 1 hour with oral pharmaceutical forms. The sedative effect starts after 5-10 minutes with oral liquid and after 30-45 minutes with tablets. Hydroxyzine has a weak affinity for muscarinic receptors.

5.2 Pharmacokinetic properties

Absorption
Hydroxyzine is rapidly absorbed from the gastrointestinal tract. The peak plasma level (C_{max}) is reached approximately two hours after oral intake. After single oral doses of 25 mg and 50 mg in adults, C_{max} concentrations are typically 30 and 70 ng/ml, respectively.
The rate and extent of exposure to hydroxyzine is very similar when given as tablet or as a syrup. Following repeat administration once a day, concentrations are increased by 30%.
The oral bioavailability of hydroxyzine with respect to intramuscular (IM) administration is about 80%. After a single 50 mg IM dose, C_{max} concentrations are typically 65 ng/ml.

Distribution
Hydroxyzine is widely distributed in the body and generally more concentrated in the tissues than in plasma. The apparent volume of distribution is 7 to 16 l/kg in adults.
Hydroxyzine enters the skin following oral administration. Skin concentrations of hydroxyzine are higher than serum concentrations, following both single and multiple administration. Hydroxyzine crosses the blood-brain and placental barriers leading to higher foetal than maternal concentrations.

Metabolism
Hydroxyzine is extensively metabolised. The formation of the major metabolite cetirizine, a carboxylic acid metabolite (approximately 45% of the oral dose), is mediated by alcohol dehydrogenase. This metabolite has significant peripheral H1-antagonist properties. The other metabolites identified include a N-dealkylated metabolite, and an O-dealkylated metabolite with a plasma half-life of 59 hours. These pathways are mediated principally by CYP3A4/5.

Elimination
Hydroxyzine half-life in adults is approximately 12 ± 5 hours (range: 7 - 20 hrs). The apparent total body clearance calculated across studies is 13 ml/min/kg. Only 0.8% of the dose is excreted unchanged in urine. The major metabolite cetirizine is excreted mainly unchanged in urine (25% and 16 % of the hydroxyzine oral and IM dose, respectively).

Special patient populations
Children
The pharmacokinetics of hydroxyzine was evaluated in 12 paediatric patients aged 1 to 14 years (mean 6.1 ± 4.6 yrs) with severe atopic dermatitis. A 0.7 mg/kg single dose of hydroxyzine was administered orally. The mean peak serum concentration was 47 ± 17 ng/ml and occurred at a mean time of 2.0 ± 0.9h after the dose. The mean plasma clearance was higher than in adults (32 ± 11 ml/min/kg). The half-life was shorter than in adults and increased with age from 4 hours at 1 year of age to 11 hours at 14 years of age. No data was available regarding the metabolite cetirizine.
Like in adults, the antipruritic effect lasted longer than anticipated for the half-life as pruritus was significantly suppressed from 1 to 24 hours post-dose with >85% suppression from 2 to 12 hours.

Dosage should be adjusted in paediatric population (see Section 4.2).

Elderly
The pharmacokinetics of hydroxyzine was investigated in 9 healthy elderly subjects (69.5 ± 3.7 years) following a single 0.7 mg/kg oral dose. The elimination half-life of hydroxyzine was prolonged to 29 ± 10 hours (range 20-53 hours) and the apparent volume of distribution was increased to 22 ± 6 l/kg (range 13-31 l/kg). In view of the longer t½ and of the prolonged pharmacodynamic effect (suppression of the wheal and flare response to histamine), it is advised to start with half the recommended dose (see Section 4.2).

Renal impairment
The pharmacokinetics of hydroxyzine was studied in 8 severe renally impaired subjects (Creatinine clearance: 24 ± 7 ml/min). The extent of exposure (AUC) to hydroxyzine was not altered in a relevant manner while that to the carboxylic metabolite, cetirizine, was increased. This metabolite is not removed efficiently by haemodialysis. In order to avoid any important accumulation of the cetirizine metabolite following multiple doses of hydroxyzine, the daily dose of hydroxyzine should be reduced in subjects with impaired renal function (see Section 4.2).

Hepatic impairment
In subjects with hepatic dysfunction secondary to primary biliary cirrhosis, total body clearance was approximately 66% that of normal subjects. The half-life was increased to 37 hours and the serum concentrations of the carboxylic metabolite, cetirizine, were higher than in young patients with a normal liver function. Daily dose or dose frequency should be reduced in patients with impaired liver function (see Section 4.2).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Cellulose microcrystalline
Lactose monohydrate
Croscarmellose sodium
Silica, colloidal anhydrous
Talc
Magnesium stearate

Coating:
Hypromellose 5cPs
Macrogol 400
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 Years

6.4 Special precautions for storage

PVC/PVdC- Alu blister:

Store at or below 30ºC.

6.5 Nature and contents of container

The 25 mg film-coated tablets are supplied in PVC/PVdC - Alu blisters
PVC/PVdC- Alu blister:
20, 25, 28, 30, 50, 60, 100 and 250 tablets.

The 10 mg film-coated tablets are supplied in PVC/PVdC - Alu blisters.
PVC/PVdC- Alu blister:
25, 30, 84, 100 and 250 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novem Pharma Pte Ltd
23 New Industrial Road #03-08
Solstice Business Center
Singapore 536209

8. MARKETING AUTHORISATION NUMBER(S)

HYDROXYZINE MEVON FILM-COATED TABLETS 25 MG	SIN16328P
HYDROXYZINE MEVON FILM-COATED TABLETS 10 MG	SIN16329P

9. DATE OF REVISION OF THE TEXT

9 Mar 2021