SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Tenoxicam Symgens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:

Each vial contains;

Tenoxicam 20 mg

Excipients:

Each vial contains;

Disodium edetate	0.200 mg
Sodium hydroxide (10% solution)	0.028 ml
Sodium hydroxide	q.s.
Hydrochloric acid	q.s.
Mannitol	80.00 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilized powder for injection

Yellow colored lyophilized powder

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Tenoxicam Symgens is indicated for the symptomatic treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis and the treatment of acute gouty arthritis, acute musculoskeletal pain, postoperative pain and dysmenorrhea.

4.2 Posology and method of administration

Posology/frequency and duration of administration:

Intramuscular (I.M.) or intravenous (I.V.) route

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

A single daily dose of 20 mg should be administered at the same time each day for all the indications except acute gouty and postoperative pain.

The recommended dose for postoperative pain is daily 40 mg for 5 days and the recommended dose for acute gout attacks is 40 mg once daily for 2 days and 20 mg daily for following 5 days.

In the treatment of chronic disorders, therapeutic efficacy of Tenoxicam Symgens is significant at the beginning of the treatment and the obtained response increases with time. It should not be exceeded 20 mg dose per day in chronic disorders. Otherwise, the frequency and severity of the adverse reactions will increase without a significant increment in therapeutic efficacy.

In cases requiring long-term treatment, reducing of daily dose to 10 mg can be tried for maintenance treatment in patients.

If necessary, the treatment is started with a single daily dose intramuscular (I.M.) or intravenous (I.V.) administration for 1 or 2 days and it is continued to orally or rectally Tenoxicam Symgens administration.

Lyophilized powder for injection has been developed for i.m. and i.v. bolus administration; infusion use is not recommended due to precipitation possibility.

Additional information relating to specific populations:

Renal impairment:

Recommended doses indicated above can be administrated in patients with renal impairment. However, it is recommended to monitor renal functions carefully when Tenoxicam Symgens is

used in patients with renal impairment. It should not be used in patients with severe renal impairment.

Hepatic impairment:

Recommended doses indicated above can be administrated in patients with hepatic impairment. However, it is recommended to monitor liver functions carefully when Tenoxicam Symgens is used in patients with hepatic impairment. It should not be used in patients with severe hepatic impairment.

Pediatric population:

Dose recommendation cannot be made due to absence of clinical experiment for adolescents and children. It is not used in this group of age.

Geriatric population:

Elderly patients are at higher risk of gastrointestinal bleeding, ulceration or perforation and fatal consequences may arise. Treatment should begin with the lowest dose in these patients and combined treatment with protective medicines (eg, misoprostol or proton pump inhibitors) should be considered for patients who are using low-dose aspirin or other drugs that increase the risk of gastrointestinal (see Section 4.4).

4.3 Contraindications

- Tenoxicam Symgens is contraindicated:

• in patients known hypersensitivity to tenoxicam or to any excipient placed in the compound of Tenoxicam Symgens,

• in patients who have previously shown symptoms of asthma, rhinitis, angioedema or urticaria due to salicylates or other non-steroidal anti-inflammatory drugs (NSAIDs),

• in patients with active or a history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy (see Section 4.4),

• in patients with active, or history of recurrent peptic ulcer (two or more distinct episodes of proven ulceration or bleeding) (see Section 4.4),

• in patients with severe heart failure, renal and hepatic impairment as with other NSAIDs,

• in patients in third trimester of pregnancy.

4.4 Special warnings and precautions for use

NSAIDs inhibit renal prostaglandin synthesis and consequently may have an undesirable effect on renal haemodynamics and on salt and water balance. It is necessary to adequately monitor the patient with a special emphasis on cardiac and renal function (blood urea nitrogen (BUN), creatinine, development of oedema, weight gain, etc.) when giving Tenoxicam Symgens to patients with conditions that could increase their risk of developing renal failure, such as pre-existing renal disease, impaired renal function in diabetics, hepatic cirrhosis, congestive heart failure, hypovolemia or concomitant treatment with potentially nephrotoxic drugs, diuretics and corticosteroids. This group of patients is at special risk in peri- and post-operative phases of major surgery due to possibility of serious blood loss. They therefore require close monitoring in the post-operative and recovery periods.

Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced.

The use of Tenoxicam Symgens with concomitant NSAIDs including cyclooxygenase-2 (COX-2) selective inhibitors should be avoided.

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and gastrointestinal bleeding, ulceration and perforation given below).

Gastrointestinal bleeding, ulceration and perforation:

Gastrointestinal (GI) bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs including Tenoxicam Symgens treatment at any time during treatment, with or without warning symptoms or a previous history of serious GI events. In the studies performed so far, a patient subgroup without a risk peptic ulcer and bleeding development has not been detected.

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal. The tolerance of debilitated patients to ulceration or bleeding is lower than the other patients. Most of the fatal gastrointestinal events associated with non-steroidal anti-inflammatory drugs occurred in the elderly and/or debilitated

patients. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available or combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see section 4.5).

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated. Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.
If peptic ulceration or gastro-intestinal bleeding occurs, Tenoxicam Symgens should be withdrawn immediately.

Caution should be advised in patients receiving Tenoxicam Symgens concomitant use with medication which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

Skin reactions
Some of severe skin reactions which can be fatal, related with NSAIDs including very rarely exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome) were reported (see Section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. When severe skin reactions occur, Tenoxicam Symgens treatment should be discontinued immediately.

Haematological effects:
Tenoxicam inhibits platelet aggregation and may affect hemostasis. Tenoxicam Symgens has no significant influence on blood coagulation factors, coagulation time, prothrombin time or activated

thromboplastin time. Patients using a drug with an effect on hemostasis or with a coagulation disorder should be carefully monitored during Tenoxicam Symgens treatment.

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) and selective COX-2 inhibitors may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with Tenoxicam Symgens after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease. (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Opthalmic effects:

Adverse eye findings have been reported during the treatment with Tenoxicam Symgens and the other NSAIDs. Thus, ophthalmic examination is recommended in patients with suspected visual impairment.

Antipyretic effects

As known for other anti-inflammatory drugs, Tenoxicam Symgens may mask the usual signs of infection.

Laboratory Tests

NSAIDs inhibit renal prostaglandin synthesis and consequently may have an undesirable effect on renal haemodynamics and on salt and water balance. It is necessary to adequately monitor the patient with a special emphasis on cardiac and renal function (BUN, creatinine, development of edema, weight gain, etc.) when giving Tenoxicam Symgens to patients with conditions that could increase their risk of developing renal failure, such as pre-existing renal disease, impaired renal

function in diabetics, hepatic cirrhosis, congestive heart failure, volume depletion or concomitant treatment with potentially nephrotoxic drugs, diuretics and corticosteroids. This group of patients is at special risk in peri- and post-operative phases of major surgery due to possibility of serious blood loss. Therefore, they require close monitoring in the post-operative and recovery periods.

Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium- free'.

Tenoxicam Symgens contains 80 mg mannitol. Caution is not needed because of its dose.

4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicylate and salicylates

Salicylates increase the clearance and volume of distribution of NSAIDs including tenoxicam by displacing them from protein binding sites. Concurrent treatment with salicylate or other NSAIDs is not recommended because of increased risk of Tenoxicam Symgens in the undesirable reactions.

Gastrointestinal interactions:

There is an increased risk of gastrointestinal bleeding (see section 4.4) when antithrombotic drugs and selective serotonin reuptake inhibitors are combined with NSAIDs.

Methotrexate:

The co-administration of some NSAIDs and methotrexate has been associated with reduced renal tubular secretion of methotrexate, higher plasma concentrations, and severe methotrexate toxicity. Therefore, caution should be exercised when Tenoxicam Symgens is administered concurrently with methotrexate.

Zidovudine:

Increased erythrocyte toxicity over reticulocytes accompanied with severe anaemia is observed one week after treatment initiated when NSAIDs are concomitantly given with zidovudine in AIDS treatment. After two weeks beginning to treatment with NSAIDs drugs, blood levels should be followed.

Mifepristone:

NSAIDs should not be used for 8 – 12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.

Lithium:

As Tenoxicam Symgens may decrease the renal clearance of lithium, concomitant use of Tenoxicam Symgens and lithium may lead to increased plasma levels and toxicity of lithium. Therefore, the plasma levels of lithium should be closely monitored.

Ciclosporin and Tacrolimus:

Caution should be exercised when NSAIDs are co-administrated with ciclosporin or tacrolimus as it increases risk of nephrotoxicity.

Quinolones:

Patients taking quinolones may have an increased risk of developing convulsions.

Diuretics and antihypertensive:

As with NSAIDs in general, Tenoxicam Symgens should not be administered concurrently with potassium sparing diuretics. There is a known interaction between these two classes of compounds, which may cause hyperkalaemia and renal failure.

No clinically significant interaction between Tenoxicam Symgens and furosemide was detected. However, Tenoxicam Symgens attenuates the blood pressure lowering effect of hydrochlorothiazide. As known from other NSAIDs, Tenoxicam Symgens might attenuate the antihypertensive effects of alpha-adrenergic blockers and ACE-inhibitors and ARB.

No interactions have been reported between Tenoxicam Symgens and centrally acting alpha agonists or calcium channel blockers.

There was no clinically relevant interaction when Tenoxicam Symgens was administered together with atenolol. During clinical trials no interaction was reported for patients treated concomitantly with digitalis products. Thus concurrent dosing of Tenoxicam Symgens and digoxin appears to be without major risk.

Antacids and H_2-receptor blockers

No clinically significant interaction has been found with concomitantly administration of antacid and cimetidine at the recommended dosages.

Probenecid

Co-administration of probenecid and tenoxicam treatment may increase plasma concentration of tenoxicam. However, the clinical significance of this observation has not been established.

Anticoagulants:

No clinically relevant interaction has been found with concomitantly administered warfarin and phenprocoumon, and low molecular weight heparin at the recommended dosages. Nevertheless, as for other NSAIDs, careful monitoring is recommended when patients concomitantly receive anticoagulants.

Oral Antidiabetics

The clinical effect of the oral antidiabetic medicines glibornuride, glibenclamide and tolbutamide was likewise not modified by Tilcotil. Nevertheless, as for other NSAIDs, careful monitoring is recommended when patients concomitantly receive oral antidiabetic drugs.

Alcohol

When alcohol is taken with tenoxicam, gastric mucosal damage increases.

No clinically relevant interaction was found in small numbers of patients using Tenoxicam Symgens with *gold* or *penicillamine*.

4.6 Pregnancy and lactation

General Recommendation

Pregnancy Category: C/D (3rd trimester)

Women of childbearing potential / Contraception

There is no data about the effects of Tenoxicam Symgens on contraception. Use of tenoxicam may damage the fertility as the other drugs that are known to inhibit cyclooxygenase/prostaglandin synthesis, and therefore, use of tenoxicam is not recommended in women trying to be pregnant. Use of Tenoxicam Symgens in women trying to be pregnant, the dosage should kept as low as possible and the treatment period should be as short as possible. Tenoxicam Symgens is contraindicated in third trimester of pregnancy.

Pregnancy Period:

No clinical data is available related to tenoxicam exposure in pregnancy (see Section 5.3).

Studies performed on animals show that there are no directly or indirectly harmful effects related with pregnancy/embryonal/foetal/natal or postnatal development (see Section 5.3).

Caution is advised while Tenoxicam Symgens is given to pregnant women.

NSAIDs have an inhibitory effect on prostaglandin synthesis and when given during late pregnancy may cause closure of the foetal ductus arteriosus, prolong labor and delay parturition. Treatment with Tenoxicam Symgens during the third trimester of pregnancy should be avoided.

Lactation period:

Based on findings from single dose administration, a very small amount (mean value less than 0.3% of the dose) of tenoxicam passes into breast milk (see section 5.2).

So far, there is no evidence of adverse reactions in breast-fed infants of mothers taking Tenoxicam Symgens; nevertheless, a potential side effect should not be ignored and infants should be weaned or the medicine discontinued in suspect situation.

Reproductive ability / Fertility:

The use of tenoxicam, as with any drug known to inhibit cyclooxygenase/ prostaglandin synthesis, may impair fertility and thus, is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of tenoxicam should be considered. (See section 5.3).

4.7 Effects on ability to drive and use machines

Patients experiencing adverse events that might affect driving or using machines, such as vertigo, dizziness or visual disturbances should refrain from driving a car or using machines.

4.8 Undesirable effects

According to clinical studies including large number of patients, Tenoxicam Symgens has been well-tolerated in recommended doses. Undesirable effects reported have been mild and temporary in general. Interruption of the treatment has been required in a small number of patients due to undesirable effects. Local tolerance of parenteral administration of tenoxicam have been found well.

For adverse reactions related to use of Tenoxicam Symgens, following terms and frequencies have been used:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Blood and lymphatic disorders

Not known: Anaemia, agranulocytosis, leukopenia, thrombocytopenia

Immune system disorders

Not known: Hypersensitivity reactions such as dyspnoea, asthma, anaphylaxis, angioedema

Metabolism and nutrition disorders

Uncommon: Appetite loss

Psychiatric disorders

Uncommon: Sleep disturbances

Nervous system disorders

Common: Dizziness, headache

Eye disorders

Not known: Visual disturbances

Ear and labyrinth disorders

Uncommon: Vertigo

Cardiac disorders

Uncommon: Palpitations

Not known: Cardiac failure

Vascular disorders

Not known: Vasculitis. Clinical trial and epidemiological data suggest that use of selective Cyclooxygenase 2 inhibitors (COX2 inhibitors) and some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Also tenoxicam has not shown to increase thrombotic events such as myocardial infarction, there are insufficient data to exclude such a risk with tenoxicam.

Gastrointestinal disorders

Common: Gastric, epigastric and abdominal discomfort, dyspepsia, nausea, heartburn, gastrointestinal perforation

Uncommon: Gastrointestinal bleeding including haematemesis and melena, ulcers, constipation, diarrhoea, stomatitis, gastritis, vomiting, dry mouth.

Not known: Exacerbation of colitis and Crohn disease have been reported after administration.

Hepatobiliary disorders

Not known: Hepatitis

Skin and subcutaneous tissue disorders

Uncommon: Itching (in anal region after rectal administration), erythema, exanthema, rash, urticarial

Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), photosensitivity reactions

Pregnancy, pueperium cases and perinatal disorders

Not known: Isolated cases of female infertility have been reported with drugs known to suppress cyclooxygenase/prostaglandin synthesis including tenoxicam.

General disorders and administration site conditions

Uncommon: fatigue, oedema

Investigations

Uncommon: increase in liver enzyme activity, increase in blood urea nitrogen (BUN) or in creatinine

Unknown: Increase in blood pressure, mainly in patients treated with cardiovascular medicines

Post-marketing data

The safety profile from post-marketing experience is consistent with the experience from clinical trials.

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 Food and drug administration thailand (Website: https://www.fda.moph.go.th/).

4.9 Overdose and Treatment

Symptoms

There is no reported experience of acute overdosage with Tenoxicam Symgens, more significantly appearance of adverse reactions given in Section 4.8 may be expected.

Gastrointestinal bleeding may occur. After taking NSAIDs, hypertension, acute renal failure, respiration depression and coma occasionally appear.

Anaphylactic reactions have been reported with NSAIDs at therapeutic doses, and these reactions may occur following an overdose.

Treatment

There are no specific antidotes for Tenoxicam Symgens. However, supportive treatments such as symptomatic treatment and absorption-reducing (e.g., gastric lavage or active coal) and excretion accelerator (e.g., cholestyramine) should be administrated to patients in overdose of NSAIDs. Dialysis does not significantly clear NSAIDs from the blood stream.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic products (Oxicams)

ATC Code: M01AC02

Tenoxicam, active substance of Tenoxicam Symgens, is a non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic, antirheumatic properties and it also inhibits platelet aggregation. Tenoxicam inhibits prostaglandin biosynthesis, both in vitro and in vivo. In vitro

investigation on cyclo-oxygenase isoenzymes prepared from human COS-7 cells have shown that tenoxicam inhibits COX-1 and COX-2 isoenzymes approximately to the same extent i.e. COX-2/COX-1 ratio equals to 1.34.

In vitro tests of leukocyte peroxidase suggest that tenoxicam may act as a scavenger for active oxygen at the site of inflammation.

Tenoxicam Symgens is a potent inhibitor of human metalloproteinase (stromelysin and collagenase) which induce cartilage breakdown. These pharmacological effects explain the therapeutic benefit of Tenoxicam Symgens in the treatment of painful inflammatory and degenerative disorders of the musculoskeletal system.

5.2 Pharmacokinetic properties

General Properties

Absorption:

The bioavailability after an I.M. dose is complete. Following intramuscular injection levels at or above 90% of the maximally achieved concentrations are reached as early as 15 minutes after a dose.

With the recommended dosage regimen of 20 mg once daily, steady-state plasma concentrations are reached within 10 – 15 days, with no unexpected accumulation. The average concentration at steady state is 11 mg/L with recommended dose of 20 mg once daily and this does not change even on treatment for up to four years. As can be predicted from a single dose kinetics, steady state plasma concentration is 6 times higher compared to a single dose.

Distribution:

During the first two hours following intravenous administration of tenoxicam, plasma levels of the medicine decline rapidly. After this short term, no difference is observed between intavenous and oral administrations in terms of plasma concentrations. The mean volume of distribution at steady state is 10 to 12 L.

In blood at least 99 % of the medicine binds to albumin. Tenoxicam penetrates well into the synovial fluid. However, peak concentrations are reached later than in plasma.

Based on findings from single dose administration a very small amount (mean value less than 0.3% of the dose) of tenoxicam passes into breast milk (see Section 4.6).

Biotransformation:

Tenoxicam is excreted by pharmacologically being converted to completely inactive metabolites in liver.

Elimination:

Up to two thirds of an oral dose is excreted in the urine (mainly as the inactive 5-hydroxy tenoxicam) and the rest via the bile (a significant portion in the form of glucuronidated compounds). Less than 1% of the administered dose is excreted without changing in the urine. The elimination half-life of tenoxicam is 72 hours (range 59 to 74 hours). The total plasma clearance is 2 mL/min.

Linearity / Non-linear case:

The pharmacokinetics of Tenoxicam is linear in the investigated dose range of 10 - 100 mg.

Characteristic properties in patients

Renal Impairment:

In studies performed in patients with renal impairment, it has been reported that dosage adjustment is not required to reach plasma concentrations achieved in healthy subjects.

Liver Impairment:

In studies performed in patients with liver impairment, it has been reported that dosage adjustment is not required to reach plasma concentrations achieved in healthy subjects.

Geriatric population:

In studies performed in elderly, it has been reported that dosage adjustment is not required to reach plasma concentrations achieved in healthy person. In elderly, kinetic profile similar to healthy subjects has been observed.

Other:

Patients with rheumatic disease show similar kinetics profile as healthy subjects.

Since tenoxicam highly binds to plasma proteins, caution is required when plasma albumin levels are markedly reduced (see Section 4.4).

5.3 Preclinical safety data

Carcinogenicity:

Tenoxicam did not show carcinogenic effect on animals.

Mutagenicity:

Tenoxicam did not show mutagenic effect on animals.

Fertility disorders:

The use of tenoxicam, as with any drug known to inhibit cyclooxygenase/ prostaglandin synthesis, may impair fertility and thus, is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Tenoxicam should be considered.

Teratogenicity:

Tenoxicam did not show mutagenic effect on animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Disodium edetate

Ascorbic acid

Trometamol

Sodium hydroxide (10% solution)

Sodium hydroxide

Hydrochloric acid

Water for injection

6.2 Incompatibilities

Do not use water for injection lyophilisate of Tenoxicam Symgens with infusions due to possibility of precipitation.

6.3 Shelf life

24 months

Use immediately after reconstitution.

6.4 Special precautions for storage

Store at room temperature below 30 °C.

6.5 Nature and contents of container

4 ml transparent type I glass vial containing 20 mg lyophilized powder for injection and 1 transparent type I ampoule containing sterile water for injection carton box with a patient information leaflet.

6.6 Disposal of materials remaining from the product and other special precautions

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

7. MARKETING AUTHORISATION HOLDER

Symgens Co., Ltd.,

110 Vibhavadi 4, Ratchadapisek Dindaeng, Bangkok 10400, Thailand.

8. MARKETING AUTHORISATION NUMBER(S)

1C___/___ (NG)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of authorization: XX/XX/XXXX

10. DATE OF REVISION OF THE TEXT

XX/XX/XXXX