ITEM / PACK DESIGN STYLE CODE DIMENSIONS (MM) ART WORK SIZE DATE Note: Pharma code/ Bar code and adjacent text must be visible on folded leaflet

PRODUCT NAME

antidepressant-treated patients age 24 years and younger was greater than in placebo-treated patients. There was considerable escitalop Generalize Adults Among tł due to an nausea (2 ncidence Maior De <u>Adults</u> The most approxim sweating Table 2 en patients w are thos escitalopr

> Adverse Dry Mo Sweating Central

Constina Indigesti

Influenz Fatigue Psychiat Psychiat Insomnia Appetite Decr Libido Decreas abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon Respiratory S Rhinitis

Urogenital

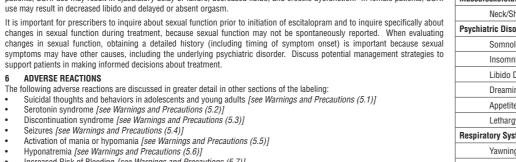
General

Ejaculation Dis Impotence² Anorgasmia ¹Primarily eiaculatory delay Pediatric Patients to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and was reversible when escitalopram was discontinued. Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted may Adult

> than the incidence in placebo-treated patients Adverse Reactio

Autonomic Ner Dry Mo Sweati Central & Periph Headach Paresth Gastrointestina Nausea

Diarrhea Constip Indigest Vomiti Abdom Flatuler Toothac adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with escitalopram tablets, however, it should be used with caution in such patients [see Dosage and Administration (2.5) and Use in Specific General Fatigue Influenz



roaenital

¹Primarily ejaculatory delay ²Denominator used was for males only (N=182 escitalopram; N=195 placebo).

Sweating adverse reactions in patients receiving 10 mg/day escitalopram was not significantly different from the rate of discontinuation for adverse reactions in patients receiving placebo. The rate of discontinuation for adverse reactions in patients assigned to a

patients, SSRI use may result in ejaculatory delay or failure, decreased libido, and erectile dysfunction. In female patients, SSRI Musculoskeletal Neck/Sh Somno Insom Libido I Dreamir Appetite Lethargy Yawnin Ejaculati

Anorgasi Menstru

Inso

Diarr Dry Mo Somno Dizzir Consti Fatio

Indige

fixed dose of 20 mg/day escitalopram was 10%, which was significantly different from the rate of discontinuation for adverse Although change reactions in patients receiving 10 mg/day escitalopram (4%) and placebo (3%). Adverse reactions that were associated with disorder, they r the discontinuation of at least 1% of patients treated with escitalopram tablets, and for which the rate was at least twice that of cause such untov

HIGHLIGHTS OF PRESCRIBING INFORMATION use ESCITALOPRAM TABLETS safely and effectively. See full prescribing information for ESCITALOPRAM TABLETS. ESCITALOPRAM tablets, for oral use Initial U.S. Approval: 2002

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS See full prescribing information for complete boxed warning. Increased risk of suicidal thoughts and behavior in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors (5.1). Escitalopram tablets are not approved for use in pediatric patients less than 7 years of age (8.4).

-- RECENT MAJOR CHANGES -Indications (1) 5/2023 Dosage and Administration (2.2, 2.3, 2.5) 5/2023 Dosage and Administration, Use of Escitalopram with Other MAOIs such as Linezolid or Methylene Blue (2.7) - Remove

Warnings and Precautions (5.2, 5.7) 8/2023 ---- INDICATIONS AND USAGE Escitalopram is a selective serotonin reuptake inhibitor (SSRI)

indicated for the: treatment of major depressive disorder (MDD) in adults and pediatric patients 12 years of age and older (1) treatment of generalized anxiety disorder (GAD) in adults

--- DOSAGE AND ADMINISTRATION Indication and Population Recommended Dosage MDD in Adults (2.1) Initial: 10 mg once daily Recommended: 10 mg once daily Maximum: 20 mg once daily MDD in Pediatric Initial: 10 mg once daily Patients 12 years and Recommended: 10 mg once daily Maximum: 20 mg once daily

- GAD in Adults (2.2) Initial: 10 mg once daily Recommended: 10 mg once daily Maximum: 20 mg once daily No additional benefits were seen at 20 mg once daily (2.1)
- Administer once daily, morning or evening, with or without food (2.3)
- Elderly patients: recommended dosage is 10 mg once daily (2.4)
- daily (2.4, 8.6) · When discontinuing Escitalopram tablets, reduce dose gradually whenever possible (2.5)
- --- DOSAGE FORMS AND STRENGTHS ----• Tablets: 5 mg, 10 mg (scored), and 20 mg (scored) ---- CONTRAINDICATIONS ----
- Do not use MAOIs intended to treat psychiatric disorders with escitalopram or within 14 days of stopping treatmen with escitalopram. Do not use escitalopram within 14 days of stopping an MAOI intended to treat psychiatric disorders. In
- addition, do not start escitalopram in a patient who is being treated with linezolid or intravenous methylene blue (4)
- Concomitant use of pimozide (4) Known hypersensitivity to escitalopram or citalopram or
- any of the inactive ingredients (4)
- FULL PRESCRIBING INFORMATION: CONTENTS* WARNING: SUICIDAL THOUGHTS AND BEHAVIORS INDICATIONS AND USAGE DOSAGE AND ADMINISTRATION
- Major Depressive Disorde Generalized Anxiety Disorde 2.3 Administration Information 2.4 Screen for Bipolar Disorder Prior to Starting
- Escitalopram Tablets 2.5 Recommended Dosage for Specific Populations Discontinuation of Treatment with Escitalopram
- 2.7 Switching Patients to or from a Monoamine Oxidase Inhibitor (MAOI) Antidepressant

Escitalopram Tablets

USP, for oral use

08098545

DOSAGE FORMS AND STRENGTHS CONTRAINDICATIONS 5 WARNINGS AND PRECAUTIONS

- 5.1 Suicidal Thoughts and Behaviors in Adolescents and Young Adults
- 5.2 Serotonin Syndrome **Discontinuation Syndrome** 5.4 Seizures
- 5.5 Activation of Mania or Hypomania Hyponatremi
- Increased Risk of Bleeding Interference with Cognitive and Motor Performance
- 5.9 Angle Closure Glaucoma 5.10 Use in Patients with Concomitant Illness
- 5.11 Sexual Dysfunction ADVERSE REACTIONS Clinical Trials Experience
- FULL PRESCRIBING INFORMATION

6.2 Post-Marketing Experience

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors [see Warnings and Precautions (5.1)]. Escitalopram tablets is not approved for use in pediatric patients less than 7 years of age [see Use in Specific Populations (8.4)].

1 INDICATIONS AND USAGE Escitalopram tablets are indicated for the treatment of:

- major depressive disorder (MDD) in adults and pediatric patients 12 years of age and older
- e generalized anxiety disorder (GAD) in adults. Additional pediatric use information is approved for AbbVie Inc.'s LEXAPRO® (escitalopram) tablets. However, due to AbbVie Inc.'s Because escitalopram is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. Until marketing exclusivity rights, this drug product is not labeled with that information.
- 2 DOSAGE AND ADMINISTRATION 2.1 Major Depressive Disorder

The recommended dosage of escitalopram tablets in adults is 10 mg once daily. A fixed-dose trial of escitalopram tablets demonstrated the effectiveness of both 10 mg and 20 mg of escitalopram tablets, but failed to demonstrate a greater benefit of 20 mg over 10 mg [see Clinical Studies (14.1)]. Depending on clinical response and tolerability, dosage may be increased to the maximum recommended dosage of 20 mg once daily at an interval of no less than 1 week.

Pediatric Patients 12 years of age and older The recommended dosage of escitalopram tablets in pediatric patients 12 years of age and older is 10 mg once daily. Depending on clinical response and tolerability, dosage may be increased to the maximum recommended dosage of 20 mg once daily at an interval of no less than 3 weeks.

2.2 Generalized Anxiety Disorder

The recommended starting dosage of escitalopram tablets in adults is 10 mg once daily. Depending on clinical response and tolerability, dosage may be increased to the maximum recommended dosage of 20 mg once daily at an interval of no less than Additional pediatric use information is approved for AbbVie Inc.'s LEXAPRO® (escitalopram) tablets. However, due to AbbVie Inc.'s

- marketing exclusivity rights, this drug product is not labeled with that information. 2.3 Administration Information
- Administer escitalopram tablets orally once daily, in the morning or evening, with or without food.
- 2.4 Screen for Bipolar Disorder Prior to Starting Escitalopram Tablets Prior to initiating treatment with escitalopram tablets or another antidepressant, screen patients for a personal family history of Sexual Dysfunction [see Warnings and Precautions (5.11)]

bipolar disorder, mania, or hypomania [see Warnings and Precautions (5.5)]. 2.5 Recommended Dosage for Specific Populations The recommended dosage for most elderly patients and patients with hepatic impairment is 10 mg once daily [see Use in Specific

Populations (8.5, 8.6)]. The recommended dosage for escitalopram tablets in adults with a creatinine clearance less than 20 mL/minute has not been determined. No dosage adjustment is necessary for patients with mild or moderate renal impairment [see Use in Specific Populations (8.7)].

2.6 Discontinuation of Treatment with Escitalopram Tablets

Symptoms associated with discontinuation of escitalopram tablets and other SSRIs and SNRIs have been reported [see Warnings and Precautions (5.3)]. Patients should be monitored for these symptoms when discontinuing treatment. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate. 2.7 Switching Patients to or from a Monoamine Oxidase Inhibitor (MAOI) Antidepressant

At least 14 days should elapse between discontinuation of an MAOI intended to treat psychiatric disorders and initiation of therapy to classify reported adverse reactions. with escitalooram tablets. Conversely, at least 14 days should be allowed after stopping escitalopram tablets before starting an MAOI intended to treat psychiatric disorders [see Contraindications (4)].

3 DOSAGE FORMS AND STRENGTHS Escitalopram tablets, USP are film-coated, round tablets containing escitalopram oxalate in strengths equivalent to 5 mg, 10 mg Pediatric Patients and 20 mg escitalopram base. The 10 and 20 mg tablets are scored.

5 mg tablets are debossed with '135' on one side and '5' on other side. 10 mg tablets are debossed with break line on one side, separating '11' and '36' on one side, and '10' on other side.

20 mg tablets are debossed with break line on one side, separating '11' and '37' on one side, and '20' on other side. 4 CONTRAINDICATIONS

Escitalopram tablets are contraindicated in patients

• taking MAOIs with escitalopram tablets or within 14 days of stopping treatment with escitalopram tablets because of an <u>Adults</u> • taking inActis with eschaloprant tablets of within 14 days of stopping in database within 14 days of stopping in database within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated [see Dosage and Administration (2.7) and Warnings and Precautions (5.2)]. Starting escitalopram tablets in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome [see Dosage and Administration (2.6) and Warnings and Precautions (5.2)]. • taking pimozide [see Drug Interactions (7)].

with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in escitalopram tablets.

5 WARNINGS AND PRECAUTIONS 5.1 Suicidal Thoughts and Behaviors in Adolescents and Young Adults

In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included Adverse reactions in pediatric patients 6 to 17 years of age were associated with discontinuation of 3.5% of 286 patients of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual approximately 77,000 adult patients and 4,500 pediatric patients, the incidence of suicidal thoughts and behaviors in the receiving escitalopram and 1% of 290 patients receiving placebo. The most common adverse reaction (incidence at least 1% for incidence.

WARNINGS AND PRECAUTIONS and initiate supportive treatment (4, 5,2) Escitalopram, reduce dosage gradually whenever possible, Trials of Antidepressants in Pediatric and Adult Patients and monitor for discontinuation symptoms (5.3) Seizures: Use with caution in patients with a history of seizure (5.4)

Activation of Mania/Hypomania: Screen patients for bipolar disorder (5.5) Hyponatremia: Can occur in association with syndrome of inappropriate antidiuretic hormone secretion (5.6) Increased Risk of Bleeding: Concomitant use of nonsteroidal anti-inflammatory drugs, aspirin, other antiplatelet drugs, warfarin and other drugs that affect coagulation may

increase risk (5.7) Interference with Cognitive and Motor Performance: Use caution when operating machinery (5.8)

angles treated with antidepressants (5.9) metabolism or hemodynamic responses (5.10)

sexual dysfunction (5.11) ---- ADVERSE REACTIONS ---

are: insomnia, ejaculation disorder (primarily ejaculatory decreased libido, and anorgasmia (6.1)

FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*. -- DRUG INTERACTIONS

recommended (7) Use caution when concomitant use with drugs that affect Hemostasis (NSAIDs, Aspirin, Warfarin) (7) - USE IN SPECIFIC POPULATIONS

temperature instability, feeding difficulties, hypotonia, 5.3 Discontinuation Syndrome tremor, irritability) in the neonate (8.1)

• Hepatic impairment: recommended dosage is 10 mg once See 17 for PATIENT COUNSELING INFORMATION and upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, Medication Guide Additional pediatric use information is approved for AbbVie emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious

Inc.'s LEXAPRO[®] (escitalopram) tablets. However, due to discontinuation symptoms. AbbVie Inc.'s marketing exclusivity rights, this drug product is Monitor for these symptoms when discontinuing treatment with escitalopram. A gradual reduction in the dose rather than not labeled with that information Revised: 10/2024 discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may

DRUG INTERACTIONS

Pregnancy

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Hepatic Impairment

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

13 NONCLINICAL TOXICOLOGY

14.1 Major Depressive Disorder

14.2 Generalized Anxiety Disorde

17 PATIENT COUNSELING INFORMATION

information are not listed.

16 HOW SUPPLIED/STORAGE AND HANDLING

Fertility

14 CLINICAL STUDIES

13.1 Carcinogenesis, Mutagenesis, Impairment of

13.2 Animal Toxicology and/or Pharmacology

Renal Impairmer

9 DRUG ABUSE AND DEPENDENCE

9.2 Abuse and Dependence

8.2 Lactation

10 OVERDOSAGE

11 DESCRIPTION

3 USE IN SPECIFIC POPULATIONS

5.4 Seizure

5.6 Hyponatremia

5.7 Increased Risk of Bleeding

5.9 Angle Closure Glaucoma

5.10 Use in Patients with Concomitant Illness

(2.5) and Use in Specific Populations (8.6)].

Populations (8.7)].

5.11 Sexual Dysfunction

ADVERSE REACTIONS

6.1 Clinical Trials Experience

placebo in double-blind, placebo-controlled trials.

while receiving therapy following baseline evaluation.

Adverse Reactions Associated with Discontinuation of Treatment

placebo, were nausea (2%) and ejaculation disorder (2% of male patients).

or less than 7 years of age with GAD.

Major Depressive Disorder

Pediatric Patients

Clinical Trial Data Sources

care in patients with a history of seizure disorder

ponatremia and appropriate medical intervention should be instituted.

hallucination, syncope, seizure, coma, respiratory arrest, and death,

*Sections or subsections omitted from the full prescribing | Inform patients about the increased risk of bleeding associated with the concomitant use of escitalopram and antiplatelet agents

5.8 Interference with Cognitive and Motor Performance

therapy does not affect their ability to engage in such activities

use may result in decreased libido and delayed or absent orgasm.

support patients in making informed decisions about treatment.

Seizures [see Warnings and Precautions (5.4)]

yponatremia [see Warnings and Precautions (5.6)]

Angle-closure glaucoma [see Warnings and Precautions (5.9)]

continuation syndrome [see Warnings and Precautions (5.3)]

Activation of mania or hypomania [see Warnings and Precautions (5.5)]

attack in a patient with anatomically narrow angles who does not have a patent iridectomy

5.5 Activation of Mania or Hypomania

These highlights do not include all the information needed to • Serotonin Syndrome: Increased risk when co-administered variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for The safety with other serotonergic agents but also when taken alone. If it occurs, discontinue Escitalopram and serotonergic agents and behaviors areas of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors areas of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors areas of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors areas of suicidal thoughts and behaviors across the different indications, the behaviors areas of suicidal thoughts and behaviors across the different indications, the behaviors areas of suicidal thoughts and behaviors across the different indications, the behaviors areas of suicidal thoughts and behaviors across the different indications, the behaviors areas of suicidal thoughts and behaviors across the different indications, the behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts and behaviors across the differences in the number of cases of suicidal thoughts across the differences in the number of cases of suicidal thoughts across the differences in the number of cases of suicidal thoughts across the differences in the number of cases of suicidal thought behaviors per 1,000 patients treated are provided in Table 1. Discontinuation syndrome: When discontinuing Table 1: Risk Differences of the Number of Patients of Suicidal Thoughts and Behaviors in the Pooled Placebo-Controlled Age Range Drug-Placebo Difference in Number of Patients of Suicidal Thoughts and Behaviors per 1,000 Patients Treated

	Increases Compared to Placebo
<18 years old	14 additional patients
18 to 24 years old	5 additional patients
	Decreases Compared to Placebo
25 to 64 years old	1 fewer patient
≥65 years old	6 fewer patients
nown whether the risk of suicidal	thoughts and behaviors in children, adolescents, and young adults exten

xtends to longer It is unknown v Angle Closure Glaucoma: Angle closure glaucoma has term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance trials in adults occurred in patients with untreated anatomically narrow with MDD that antidepressants delay the recurrence of depression and that depression itself is a risk factor for suicidal thoughts and behaviors.

Use in Patients with Concomitant Illness: Use caution in Monitor all antidepressant-treated patients for any indication for clinical worsening and emergence of suicidal thoughts and patients with diseases or conditions that produce altered behaviors, especially during the initial few months of drug therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic Sexual Dysfunction: Escitalopram may cause symptoms of regimen, including possibly discontinuing escitalopram, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors --- 5.2 Serotonin Syndrome

Most commonly observed adverse reactions (incidence | SSRIs, including escitalopram tablets, can precipitate serotonin syndrome, a potentially life-threatening condition. The risk is \geq 5% and at least twice the incidence of placebo patients) | increased with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, meperidine, methadone, lithium, tramadol, tryptophan, buspirone, amphetamines, and St. John's Wort) and with drugs that impair metabolism delay), nausea, sweating increased, fatigue and somnolence, of serotonin, i.e., MAOIs [see Contraindications (4) and Drug Interactions (7)].

Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), To report SUSPECTED ADVERSE REACTIONS, contact autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular Quallent Pharmaceuticals Health LLC at 1-877-605-7243, or symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination) seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The concomitant use of escitalopram with MAOIs is contraindicated. In addition, do not initiate Escitalopram in a patient who is

Concomitant use with SSRIs, SNRIs or Tryptophan is not being treated with MAOIs such as linezolid or intravenous methylene blue. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection). If it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking Escitalopram, discontinue Escitalopram before initiating treatment with the MAOI [see Contraindications (4) and Dosage and Administration (2.7)]. Monitor all patients taking escitalopram tablets for the emergence of serotonin syndrome. Discontinue treatment with escitalopram Pregnancy: SSRI use, particularly later in pregnancy, may tablets and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic

increase the risk for persistent pulmonary hypertension treatment. If concomitant use of escitalopram with other serotonergic drugs is clinically warranted, inform patients of the and symptoms of poor adaptation (respiratory distress, increased risk for serotonin syndrome and monitor for symptoms. During marketing of escitalopram tablets and other SSRIs, there have been spontaneous reports of adverse reactions occurring

dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy,

Although anticonvulsant effects of racemic citalopram have been observed in animal studies, escitalopram has not been

systematically evaluated in patients with a seizure disorder. These patients were excluded from clinical studies during the product's

premarketing testing. In clinical trials of escitalopram, cases of convulsion have been reported in association with escitalopram

treatment. Like other drugs effective in the treatment of major depressive disorder, escitalopram tablets should be introduced with

In patients with bipolar disorder, treating a depressive episode with escitalopram or another antidepressant may precipitate a

mixed/manic episode. In placebo-controlled trials of escitalopram in major depressive disorder, activation of mania/hypomania

was reported in one (0.1%) of 715 patients treated with escitalopram and in none of the 592 patients treated with placebo. One

ional case of hypomania has been reported in association with escitalopram treatment. Activation of mania/hypo

patients for any personal or family history of bipolar disorder, mania, or hypomania [see Dosage and Administration (2.4)].

Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness

Drugs that interfere with serotonin reuptake inhibition, including escitalopram, increase the risk of bleeding events. Concomitant

use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may

between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Based on data from the published observational studies, exposure to SSRIs, particularly in the month before delivery, has been associated with a less

than 2-fold increase in the risk of postpartum hemorrhage [see Use in Specific Populations (8.1)]. Bleeding events related to drugs

that interfere with serotonin reuptake have ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatenin

or anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio [see Drug Interactions (7)].

In a study in normal volunteers, escitalopram 10 mg daily did not produce impairment of intellectual function or psychomoto

performance. Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be

cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that escitalopram tablets

The pupillary dilation that occurs following use of many antidepressant drugs, including escitalopram may trigger an angle closure

Clinical experience with escitalopram in patients with certain concomitant systemic illnesses is limited. Caution is advisable in

Escitalopram has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart

In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased.

The recommended dose of escitalopram tablets in hepatically impaired patients is 10 mg daily [see Dosage and Administration

Use of SSRIs, including escitalopram, may cause symptoms of sexual dysfunction [see Adverse Reactions (6.1)]. In male

changes in sexual function, obtaining a detailed history (including timing of symptom onset) is important because sexual

ecause clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a

drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Adverse reactions information for escitalopram was collected from 715 patients with major depressive disorder who were exposed

to escitalopram and from 592 patients who were exposed to placebo in double-blind, placebo-controlled trials. An additional 284

patients with major depressive disorder were newly exposed to escitalopram in open-label trials. The adverse reaction information

for escitalopram in patients with GAD was collected from 429 patients exposed to escitalopram and from 427 patients exposed to

Adverse reactions during exposure were obtained primarily by general inquiry and recorded by clinical investigators using

individuals experiencing adverse reactions without first grouping similar types of reactions into a smaller number of standardized

terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of

event categories. In the tables and tabulations that follow, standard World Health Organization (WHO) terminology has been used

The stated frequencies of adverse reactions represent the proportion of individuals who experienced, at least once, a treatment

emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened

Adverse reaction information for pediatric patients was collected in double-blind placebo-controlled studies in 576 pediatric

The safety and effectiveness of escitalopram have not been established in pediatric patients less than 12 years of age with MDD

he following adverse reactions are discussed in greater detail in other sections of the labeling:

Increased Risk of Bleeding [see Warnings and Precautions (5.7)] Interference with Cognitive and Motor Performance [see Warnings and Precautions (5.8)]

Use in Patients with Concomitant Illness [see Warnings and Precautions (5.10)]

patients 6 to 17 years of age, (286 escitalopram, 290 placebo) with major depressive disorder.

Suicidal thoughts and behaviors in adolescents and young adults [see Warnings and Precautions (5.1)] Serotonin syndrome [see Warnings and Precautions (5.2)]

using escitalopram tablets in patients with diseases or conditions that produce altered metabolism or hemodynamic responses.

disease. Patients with these diagnoses were generally excluded from clinical studies during the product's premarketing testing.

add to the risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association

continue decreasing the dose but at a more gradual rate [see Dosage and Administration (2.6)].

Escitalopram Tablets, USP	COUNTRY : US_Quallent	LOCATION : Dahej S			Supersedes A/W No.:		
Outsert	NO. OF COLORS: 1	REMARK :	REMARK :			V. No. : 01	
Front Side	PANTONE SHADE NOS.:	SUBSTRATE : 28	3 g/m ² Bible Pap	er			
8098545	Black	Activities	Department	Name	Signature	Date	
640 x 510		Prepared By	Pkg. Dev.				
S/S		Reviewed By	Pkg. Dev.				
09-10-2024	Font Size 6.5 pt_Med. 10 pt	Approved By	Quality				

These details can be moved by printed to arrange pharma code/ Bar code and adjacent text visible on folded leaflet.

opram and greater than placebo) associated with discontinuation was in	nomnia (1% accitatopram 0%					8 USE IN SPECIFIC POPULATIONS
fety and effectiveness of escitalopram have not been established in pedi	(. ,		TABLE 5		8.1 Pregnancy
alized Anxiety Disorder	iallic pallellis less tildil 12 yea	IS OF AGE WILL WIDD.	Incidence o	f Sexual Side Effects in Placebo-Controlled	Clinical Trials	
Inzeu Anxiety Disorder			Adverse Event	Escitalopram	Placebo	Pregnancy Exposure Registry There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to
the 429 GAD patients who received escitalopram 10 to 20 mg/day in pl	acebo-controlled trials, 8% dis	scontinued treatment		In Mal	es Only	Healthcare providers are encouraged to advise patients to register by calling the National Pregr
an adverse event, as compared to 4% of 427 patients receiving placeb tinuation of at least 1% of patients treated with escitalopram, and for whi				(N=407)	(N=383)	at 1-844-405-6185 or visiting online at https://womensmentalhealth.org/research/pregnancyre
i (2%), insomnia (1%), and fatigue (1%).	ICII IIIE I AIE WAS AI IEASI IWICE II	ne placebo fale, were	Ejaculation Disorder (primarily ejaculatory delay)	12%	1%	Risk Summary Based on data from published observational studies, exposure to SSRIs, particularly in the
nce of Adverse Reactions in Placebo-Controlled Clinical Trials			Libido Decreased	6%	2%	associated with a less than 2-fold increase in the risk of postpartum hemorrhage <i>[see Warnings</i>]
Depressive Disorder			Impotence	2%	<1%	Considerations].
			Impotence	In Fema		Available data from published epidemiologic studies and postmarketing reports have not esta birth defects or miscarriage. There are risks of persistent pulmonary hypertension of the new
ost commonly observed adverse reactions in escitalopram patients imately twice the incidence in placebo patients) were insomnia, ejacula				(N=737)	(N=636)	neonatal adaptation (see Clinical Considerations) with exposure to selective serotonin reup
ng increased, fatigue, and somnolence.		atory dolay), nadoba,	Libido Decreased	3%	1%	escitalopram, during pregnancy. There are risks associated with untreated depression in pregn
enumerates the incidence, rounded to the nearest percent, of adver			Anorgasmia	3%	<1%	In animal reproduction studies, both escitalopram and racemic citalopram have been shown to
s who received escitalopram at doses ranging from 10 to 20 mg/da ose occurring in 2% or more of patients treated with escitalopram an				s examining sexual dysfunction with escitalor		fetal and postnatal development, including fetal structural abnormalities, when administer therapeutic doses (see Data).
opram was greater than the incidence in placebo-treated patients.			Priapism has been reported with all SSR	с ,		The estimated background risk of major birth defects and miscarriage for the indicated popul
TABLE 2			While it is difficult to know the precise r	isk of sexual dysfunction associated with the	use of SSRIs, physicians should routinely	have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general pop risk of major birth defects and miscarriage in the clinically recognized pregnancies is 2 to 4% a
Adverse Reactions observed with a freque			inquire about such possible side effects.			Clinical Considerations
greater than placebo for Major Depressive rse Reaction	Disorder (Aduits) Escitalopram (N=715)	Placebo (N=592)	blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant channes from baseline in these variables. These analyses did not reveal any clinically important channes in vital signs sociated			Disease-associated maternal risk and/or embryo/fetal risk Women who discontinue antidepressants are more likely to experience a relapse of major dep antidepressants. This finding is from a prospective longitudinal study of 201 pregnant women who user outburnic and taking actidepresents at the heripaine of engagency Consider the
iomic Nervous System Disorders	/0	70		on, a comparison of supine and standing treatment is not associated with orthostatic (who were euthymic and taking antidepressants at the beginning of pregnancy. Consider the discontinuing or changing treatment with antidepressant medication during pregnancy and pos
louth	6%	5%	Weight Changes			Maternal Adverse Reactions Use of escitalopram tablets in the month before delivery may be associated with an increased ri
ting Increased	5%	2%		trolled trials did not differ from placebo-treate	d patients with regard to clinically important	Warnings and Precautions (5.7)].
al & Peripheral Nervous System Disorders			change in body weight. Laboratory Changes			Fetal/Neonatal adverse reactions
less	5%	3%		compared with respect to (1) mean change	from baseline in various serum chemistry,	Neonates exposed to SSRIs or SNRIs, including escitalopram, late in third trimester have or prolonged hospitalization, respiratory support, and tube feeding. Such complications can
ointestinal Disorders				I (2) the incidence of patients meeting criteria		Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, tempe
28	15%	7%	with escitalopram treatment.	nalyses revealed no clinically important chang	les in laboratory test parameters associated	vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, ar are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug disco
lea	8%	5%	ECG Changes			noted that, in some cases, the clinical picture is consistent with serotonin syndrome [see Warl
lipation	3%	1%		N=625) and placebo (N=527) groups were co		Data
estion	3%	1%		ec from baseline or absolute values over 500 ases to less than 50 bpm with a 25% change		Human Data Exposure to SSRIs, particularly later in pregnancy, may increase the risk for PPHN. PPHN occu
minal Pain	2%	1%		nts in the escitalopram group had a QTcF inter		the general populations and is associated with substantial neonatal morbidity and mortality.
ral				cebo group. The incidence of tachycardic out rdic outliers was 0.5% in the escitalopram gr		Animal Data
nza-like Symptoms	5%	4%	1 0 1	zed, placebo and active (moxifloxacin 400 mo		In a rat embryo/fetal development study, oral administration of escitalopram (56, 112, or 15 during the period of organogenesis resulted in decreased fetal body weight and associated dela
le	5%	2%	dose study in 113 healthy subjects. Th	e maximum mean (95% upper confidence	bound) difference from placebo arm were	doses [approximately ≥ 55 times the maximum recommended human dose (MRHD) of 20 mg
niatric Disorders				g and supratherapeutic 30 mg escitalopram hip, the predicted QTcF change from placeb		toxicity (clinical signs and decreased body weight gain and food consumption), mild at 56 n levels. The developmental no-effect dose of 56 mg/kg/day is approximately 27 times the MRH
nnia	9%	4%	C _{max} for the dose of 20 mg is 6.6 (7.9) ms	ec. Escitalopram 30 mg given once daily resu	Ited in mean C _{max} of 1.7-fold higher than the	malformations were observed at any of the doses tested (as high as 73 times the MRHD on a r
lolence	6%	2%		ed therapeutic dose at steady state (20 mg). T ntrations expected in CYP2C19 poor metaboli		When female rats were treated with escitalopram (6, 12, 24, or 48 mg/kg/day) during pregna increased offenting mortality and growth retardation were noted at 48 mg/kg/day which is an
			account to the orougy state composition		Loss sources and a morapound about of 20 mg.	Increased ouscound informative and drowth retargation were noted at 48 mg/kg/day which is an

	6%	2%
reased	3%	1%
ased	3%	1%
System Disorders		
	5%	4%
	3%	2%
isorder ^{1,2}	9%	<1%
	3%	<1%

Denominator used was for males only (N=225 escitalopram; N=188 placebo) ³Denominator used was for females only (N=490 escitalopram; N=404 placebo)

also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other The overall profile of adverse reactions in pediatric patients 6 to 17 years in major depressive disorder was generally similar to that **Reproductive Disorders/Female**: menstrual cramps, menstrual disorder. marketed drugs effective in the treatment of major depressive disorder. Prior to initiating treatment with escitalopram, screen seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and seen in adult studies, as shown in Table 2 and seen in adult studies, as shown in Table 2 and seen in adult studies, as shown in Table 2 and seen in adult studies, as shown in Table 2 and seen in adult studies, as shown in Table those for which the coded terms were uninformative or misleading) were reported at an incidence of at least 2% for escitalopram and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion remia may occur as a result of treatment with SSRIs, including escitalopram. In many cases, this hyponatremia appears The safety and effectiveness of escitalopram have not been established in pediatric patients less than 12 years of age with MDD.

be at greater risk [see Use in Specific Populations (8.5)]. Consider discontinuation of escitalopram in patients with symptomatic The most commonly observed adverse reactions in escitalopram patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia. 6.2 Post-Marketing Experience fatique, decreased libido, and anorgasmia. and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included infants unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included infants unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included infants unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included infants unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included infants unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included are those occurred among hallucination, syncope, seizure, coma, respiratory arrest, and death. Table 3 enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse reactions that occurred among hallucination of uncertain size, it is not always possible to reliably estimate their frequency or establish receive approximately 3.9% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of escitalopram and 1.7% of

TABLE 3 Adverse Reactions Observed with a Frequency of > 2% and

Adverse Reactions Observed with a Frequency of ≥ 2% and >placebo for Generalized Anxiety Disorder (Adults)						
ions	Escitalopram (N=429) %	Placebo (N=427) %				
vous System Disorders						
outh	9%	5%				
ing Increased	4%	1%				
pheral Nervous System Disorders						
che	24%	17%				
hesia	2%	1%				
al Disorders						
a	18%	8%				
ea	8%	6%				
pation	5%	4%				
stion	3%	2%				
ng	3%	1%				
ninal Pain	2%	1%				
nce	2%	1%				
che	2%	0%				
e	8%	2%				
iza-like Symptoms	5%	4%				
al System Disorder						
Shoulder Pain	3%	1%				
orders						
plence	13%	7%				
nia	12%	6%				
Decreased	7%	2%				
ing Abnormal	3%	2%				
te Decreased	3%	1%				
ду	3%	1%				
stem Disorders						
ng	2%	1%				
			_			
tion Disorder ^{1,2}	14%	2%				
ismia ³	6%	<1%				
rual Disorder	2%	1%				
			-			

enominator used was for females only (N=247 escitalopram; N=232 placebo) Dose Dependency of Adverse Reactions

The potential dose dependency of common adverse reactions (defined as an incidence rate of \geq 5% in either the 10 mg or 20 mg escitalopram groups) was examined on the basis of the combined incidence of adverse reactions in two fixed-dose trials. The overall incidence rates of adverse reactions in 10 mg escitalopram-treated patients (66%) was similar to that of the placebotreated patients (61%), while the incidence rate in 20 mg/day escitalopram-treated patients was greater (86%). Table 4 shows common adverse reactions that occurred in the 20 mg/day escitalopram group with an incidence that was approximately twice that of the 10 mg/day escitalopram group and approximately twice that of the placebo group.

TABLE 4 Incidence of Common Adverse Reactions in Patients with Major Depressive Disorder						
nnia	4%	7%	14%			
hea	5%	6%	14%			
louth	3%	4%	9%			
lence	1%	4%	9%			
ness	2%	4%	7%			
Increased	<1%	3%	8%			
pation	1%	3%	6%			
gue	2%	2%	6%			
stion	1%	2%	6%			
s in sexual desi	nsequence of pharmacologic tr	xual satisfaction often occur as i eatment. In particular, some evid				

Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates

se is similar to the steady state concentrations expected in CYP2C19 poor metabolizers for

reported by the 1,428 patients treated with escitalopram tablets for periods of up to one year in double-blind or open-label clinical approximately 6 times the MRHD of 20 mg on a mg/m² basis. trials during its premarketing evaluation. The listing does not include those reactions already listed in Tables 2 & 3, those reactions In two rat embryo/fetal development studies, oral administration of racemic citalopram (32, 56, or 112 mg/kg/day) to pregnant for which a drug cause was remote and at a rate less than 1% or lower than placebo, those reactions which were so general as animals during the period of organogenesis resulted in decreased embryo/fetal growth and survival and an increased inc to be uninformative, and those reactions reported only once which did not have a substantial probability of being acutely life of fetal abnormalities (including cardiovascular and skeletal defects) at the high dose, which is approximately 18 times the MRHD threatening. Reactions are categorized by body system. Reactions of major clinical importance are described in the Warnings and of 60 mg/day on a mg/m² basis. This dose was also associated with maternal toxicity (clinical signs, decreased body weight Precautions section (5). Cardiovascular: hypertension, palpitation.

Central and Peripheral Nervous System Disorders: light-headed feeling, migraine.

Gastrointestinal Disorders: abdominal cramp, heartburn, gastroenterities General: allergy, chest pain, fever, hot flushes, pain in limb.

Metabolic and Nutritional Disorders: increased weight

Musculoskeletal System Disorders: arthralgia invalgia jaw stiffness

Psychiatric Disorders: appetite increased, concentration impaired, irritability.

Skin and Annendanes Disorders: rash Special Senses: vision blurred, tinnitus

<1%

Urinary System Disorders: urinary frequency, urinary tract infection.

Additional pediatric use information is approved for AbbVie Inc.'s LEXAPRO® (escitalopram) tablets. However, due to AbbVie Inc.'s marketing exclusivity rights, this drug product is not labeled with that information

Adverse Reactions Reported Subsequent to the Marketing of Escitalopram

Blood and Lymphatic System Disorders: anemia, agranulocytis, aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia 8.4 Pediatric Use Cardiac Disorders: atrial fibrillation, bradycardia, cardiac failure, myocardial infarction, tachycardia, torsade de pointes, ventricular

arrhythmia, ventricular tachycardi

Ear and labyrinth disorders: vertico Endocrine Disorders: diabetes mellitus, hyperprolactinemia, SIADH

Eve Disorders: angle closure glaucoma, diplopia, mydriasis, visual disturbance.

Gastrointestinal Disorder: dysphagia, gastrointestinal hemorrhage, gastroesophageal reflux, pancreatitis, rectal hemorrhage, General Disorders and Administration Site Conditions: abnormal oait, asthenia, edema, fall, feeling abnormal, malaise, Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis.

Immune System Disorders: allergic reaction, anaphylaxis.

Investigations: bilirubin increased, decreased weight, electrocardiogram QT prolongation, hepatic enzymes increased, ypercholesterolemia, INR increased, prothrombin decreased. Metabolism and Nutrition Disorders: hyperglycemia, hypoglycemia, hypokalemia, hyponatremia.

Musculoskeletal and Connective Tissue Disorders: muscle cramp, muscle stiffness, muscle weakness, rhabdomyolysis. Nervous System Disorders: akathisia, amnesia, ataxia, choreoathetosis, cerebrovascular accident, dysarthria, dyskinesia, in a juvenile animal study, male and female rats were administered escitalopram at 5, 40, or 80 mg/kg/day by oral gavage from dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, Parkinsonism, restless legs, seizures, syncope, tardive dyskinesia, tremor

Pregnancy, Puerperium and Perinatal Conditions: spontaneous abortion. Psychiatric Disorders: acute psychosis, aggression, agitation, anger, anxiety, apathy, completed suicide, confusion,

depersonalization, depression agravated, delirium, delusion, disorientation, feeling unreal, halluciations (visual and auditory), mood swings, nervousness, nightmare, panic reaction, paranoia, restlessness, self-harm, suicide MRHD in pediatrics. There was no effect on learning and memory function in treated female rats. attempt, suicidal ideation, suicidal tendenc Renal and Urinary Disorders: acute renal failure, dysuria, urinary retention.

Reproductive System and Breast Disorders: menorrhagia, priapism.

Respiratory, Thoracic and Mediastinal Disorders: anosmia, dyspnea, epistaxis, pulmonary embolism, hyposmia, pulmonary hypertension of the newborn. Skin and Subcutaneous Tissue Disorders: alopecia, angioedema, dermatitis, drug reaction with eosinophilia and systemic

symptoms (DRESS), ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, Pascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, hypertensive crisis, hypertensive crisi

7 DRUG INTERACTIONS Table 6 presents clinically important drug interactions with escitalopram

TABLE 6 Clinically Important Drug Interactions with Escitalopram

Intervention

Monoamine Oxidase Inhibitors ((MAUIS)
Clinical Impact:	Concomitant use of SSRIs, including Escitalopram, and MAOIs increases the risk of serotonin syndrome.
Intervention:	Escitalopram is contraindicated in patients taking MAOIs, including MAOIs such as linezolic or intravenous methylene blue [see Dosage and Administration (2.7), Contraindications (4), and Warnings and Precautions (5.2)].
Pimozide	
Clinical Impact:	Concomitant use of racemic citalopram with pimozide increases plasma concentrations of pimozide, a drug with a narrow therapeutic index, and may increase the risk of QI prolongation and/or ventricular arrhythmias compared to use of racemic citalopram alone [see Clinical Pharmacology (12.3)].

Escitalopram is contraindicated in patients taking pimozide [see Contraindications (4)]. Other Serotonergic Drugs Concomitant use of Escitalopram and other serotonergic drugs (including other SSRIs, SNRIs, triptans, tricyclic antidepressants, opioids, lithium, buspirone, amphetamines,

tryptophan, and St. John's Wort) increases the risk of serotonin syndrome. Monitor patients for signs and symptoms of serotonin syndrome, particularly during 10 OVERDOSAGE Intervention: Escitalopram initiation and dosage increases. If serotonin syndrome occurs, consider discontinuation of Escitalopram and/or concomitant serotonergic drugs [see Warning and] • Seizures, which may be delayed, and altered mental status including coma. Precautions (5.2)].

Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.) Concomitant use of Escitalopram and an antiplatelet or anticoagulant may potentiate the Impact. risk of bleeding. Intervention Inform patients of the increased risk of bleeding associated with the concomitant use of Escitalopram and antiplatelet agents and anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio [see Warning and Precautions (5.7)].

Sumatriptan There have been postmarketing reports describing patients with weakness, hyperreflexia, 11 DESCRIPTION Clinical Impact: and incoordination following the use of an SSRI and sumatriptan If concomitant treatment with sumatriptan and an SSRI is clinically warranted, appropriate Intervention: observation of the patient is advised [see Warning and Precautions (5.2)].

Carbamazepine Clinical Combined administration of racemic citalopram (40 mg/day for 14 days) and carbamazepine (titrated to 400 mg/day for 35 days) did not significantly affect the pharmacokinetics of Impact: carbamazepine, a CYP3A4 substrate Although trough citalopram plasma levels were unaffected, given the enzyme-inducing Intervention properties of carbamazepine, the possibility that carbamazepine might increase the clearance

Drugs Metabolized by CYP2D6 Coadministration of escitalopram (20 mg/day for 21 days) with the tricyclic antidepressa desipramine (single dose of 50 mg), a substrate for CYP2D6, resulted in a 40% increase in The molecular formula is C₂₀H₂₁FN₂O • C₂H₂O₄ and the molecular weight is 414.40. nax and a 100% increase in AUC of desigramine The clinical significance of this finding is unknown. Exercise caution during coadministration

of escitalopram should be considered if the two drugs are coadministered.

of escitalopram and drugs metabolized by CYP2D6.

yregistry/antidepressants

ewborn (PPHN) (see Data) and poo

pulation is unknown. All pregnancie

postpartum.

n a mg/m² basis). gnancy and through weaning, slightly increased offspring mortality and growth retardation were noted at 48 mg/kg/day which is approximately 23 times the MRHD of Other Reactions Observed During the Premarketing Evaluation of Escitalopram Tablets Following is a list of treatment-emergent adverse reactions, as defined in the introduction to the ADVERSE REACTIONS section,

> gain). The developmental no-effect dose was 56 mg/kg/day is approximately 9 times the MRHD on a mg/m² basis. In a rabbit study, no adverse effects on embryo/fetal development were observed at doses of racemic citalopram of up to 16 mg/kg/day, or approximately 5 times the MRHD on a mo/m² basis. Thus, developmental effects of racemic citalopram were observed at a maternally toxic dose in the rat and were not observed in the rabbit.

When female rats were treated with racemic citalopram (4.8, 12.8, or 32 mg/kg/day) from late gestation through weaning ncreased offspring mortality during the first 4 days after birth and persistent offspring growth retardation were observed at the highest dose, which is approximately 5 times the MRHD of 60 mg on a mg/m² basis. The no-effect dose was 12.8 mg/kg/day is approximately 2 times the MRHD on a mg/m² basis. Similar effects on offspring mortality and growth were seen when dams were rreated throughout gestation and early lactation at doses \geq 24 mg/kg/day, approximately 4 times the MRHD on a mg/m² basis. A no-effect dose was not determined in that study. 8.2 Lactation

Risk Summary Data from the published literature report the presence of escitalopram and desmethylescitalopram in human milk (see Data). There are reports of excessive sedation, restlessness, agitation, poor feeding and poor weight gain in infants exposed to escitalopram, through breast milk (see Clinical Considerations). There are no data on the effects of escitalopram or its metabolites on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for scitalopram and any potential adverse effects on the breastfed child from escitalopram or from the underlying maternal condition.

Clinical Considerations Infants exposed to escitalopram should be monitored for excess sedation, restlessness, agitation, poor feeding and poor weigh gain

Major Depressive Disorder

The safety and effectiveness of escitalopram for the treatment of major depressive disorder have been established in pediatric nations 12 years of age and older. Use of escitalogram for this indication is supported by evidence from adequate and wellcontrolled studies in adults with additional evidence from an 8-week, flexible-dose, placebo-controlled study that compared escitalopram tablets 10 mg to 20 mg once daily to placebo in pediatric patients 12 to 17 years of age with major depressive disorder [see Clinical Studies (14.1)]. The safety of escitalopram was similar to adult patients with MDD [see Adverse Reactions The safety and effectiveness of escitalopram for the treatment of major depressive disorder have not been established in pediatric

patients younger than 12 years of age. In a 24-week, open-label safety study in 118 pediatric patients aged 7 to 11 years who had major depressive disorder, the safety findings were consistent with the known safety and tolerability profile for escitalopram. Generalized Anxiety Disorder The safety and effectiveness of escitalopram for the treatment of generalized anxiety disorder have not been established in

pediatric patients younger than 7 years of age. Antidepressants increase the risk of suicidal thoughts and behaviors in pediatric patients [see Warnings and Precautions (5.1)]. Decreased appetite and weight loss have been observed in association with the use of SSRIs. Consequently, regular monitoring of weight and growth should be performed in children and adolescents treated with an SSRI such as escitalopram. Juvenile Animal Toxicity Data

postnatal day (PND) 21 to PND 69. A delay in sexual maturation was observed in both males and females at \geq 40 mg/kg/day with a No Observed Adverse Effect Level (NOAEL) of 5 mg/kg/day. This NOAEL was associated with plasma AUC levels less than those measured at the maximum recommended dose (MRHD) in pediatrics (20 mg). However, there was no effect on reproductive function. Increased motor activity (both ambulatory and fine movements) was observed in females prior to daily dosing at \geq 40 mg/kg/day (3.5 times the MRHD based on AUC levels). A reversible disruption of learning and memory function was observed in

Additional pediatric use information is approved for AbbVie Inc.'s LEXAPRO® (escitalopram) tablets. However, due to AbbVie Inc.'s marketing exclusivity rights, this drug product is not labeled with that informatic 8.5 Geriatric Use Approximately 69 patients (6%) of the 1,144 patients receiving escitalopram in controlled trials of escitalopram in major depressive disorder and GAD were 60 years of age or older *Isee Clinical Studies (14.1, 14.2)*. The number of elderly patients in these trials

was insufficient to adequately assess for possible differential efficacy and safety measures on the basis of age. Nevertheless, greater sensitivity of some elderly individuals to effects of escitalopram cannot be ruled out. In two pharmacokinetic studies, escitalopram half-life was increased by approximately 50% in subjects 65 years and older SSRIs, including escitalopram, have been associated with cases of clinically significant hyponatremia in elderly patients, who may

be at greater risk for this adverse reaction [see Warnings and Precautions (5.6)] Of 4 422 patients in clinical studies of racemic citalopram. 1.357 were 60 and over, 1.034 were 65 and over, and 457 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the geriatric and younger patients, but again, greater sensitivity of some elderly individuals cannot be ruled out.

8.6 Hepatic Impairment Increased citalopram exposure occurs in patients with hepatic impairment [see Clinical Pharmacology (12.3)]. The recommended dosage of escitalopram tablets in patients with hepatic impairment is 10 mg daily [see Dosage and Administration (2.5)]. 8.7 Renal Impairment

Pharmacokinetics of escitalopram in patients with a creatinine clearance less than 20 mL/minute has not been evaluated. No dosage adjustment is necessary for patients with mild or moderate renal impairment [see Dosage and Administration (2.5), Clinical Pharmacology (12.3)].

9 DRUG ABUSE AND DEPENDENCE 9.2 Abuse and Dependence

Physical and Psychological Dependence Animal studies suggest that the abuse liability of racemic citalopram is low. Escitalopram has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. The premarketing clinical experience with escitalopram did ot reveal any drug-seeking behavior. However, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, physicians should carefully evaluate escitalopram patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behavior).

The following have been reported with escitalopram tablet overdosage:

Cardiovascular toxicity, which may be delayed, including QRS and QTc interval prolongation, wide complex tachyarrhythmias, and torsade de pointes. Hypertension most commonly seen, but rarely can see hypotension alone or with co-ingestants including alcohol.

Serotonin syndrome (patients with a multiple drug overdosage with other proserotonergic drugs may have a higher risk). Prolonged cardiac monitoring is recommended in escitalopram overdosage ingestions due to the arrhythmia risk. Gastrointestinal decontamination with activated charcoal should be considered in patients who present early after a escitalopram

Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendation

Escitalopram tablets contain escitalopram, a selective serotonin reuptake inhibitor (SSRI), present as escitalopram oxalate salt. scitalopram is the pure S- enantiomer (single isomer) of the racemic bicyclic phthalane derivative citalopram. Escitalopram oxalate is designated S-(+)-1- [3-(dimethyl-amino)propyl]-1-(p-fluorophenyl)-5-phthalancarbonitrile oxalate with the following structural formula

• C₂H₂O₄ Escitalopram oxalate, USP occurs as a fine, white to slightly-yellow powder and is freely soluble in methanol and dimethyl

insoluble in heptane. Escitalopram tablets, USP are white to off-white, round, biconvex, film-coated tablets containing 6.38 mg, 12.75 mg and 25.55

to antidenressants during pregnancy regnancy Registry for Antidepressants

the month before delivery, has been ings and Precautions (5.7) and Clinical established an increased risk of maior

euptake inhibitors (SSRIs), including egnancy (see Clinical Considerations) vn to have adverse effects on embrvo/ stered at doses greater than human

population, the estimated background % and 15 to 20%, respectively.

depression than women who continue en with a history of major depression, the risk of untreated depression when

ed risk of postpartum hemorrhage [see

ve developed complications requiring can arise immediately upon delivery nperature instability, feeding difficulty y, and constant crying. These features uation syndrome. It should be Narnings and Precautions (5.2)1.

occurs in 1 to 2 per 1,000 live births in

150 mg/kg/day) to pregnant animals delays in ossification at the two higher mg/day on a mg/m² basis]. Maternal 56 mg/kg/day, was present at all dose /IRHD of 20 mg on a mg/m² basis. No

sulfoxide (DMSO), soluble in isotonic saline solution, sparingly soluble in water and ethanol, slightly soluble in ethyl acetate, and



PRODUCT NAME

base. The 10 and 20 mg tablets are scored. The tablets also contain the following inactive ingredients: cellulose microcrystalline, colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, povidone and talc. The film coating contains hypromellose, polyethylene glycol 400 and titanium dioxide.

Meets USP Dissolution Test 2. 12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of antidepressant action of escitalopram, the S-enantiomer of racemic citalopram, is presumed to be linked to potentiation of serotonergic activity in the central nervous system (CNS) resulting from its in the Montgomery Asberg Depression Rating Scale (MADRS). inhibition of CNS neuronal reuptake of serotonin (5-HT). 12.2 Pharmacodynamics

In vitro and in vivo studies in animals suggest that escitalopram is a highly selective serotonin reuptake inhibitor (SSRI) with minimal effects on norepinephrine and dopamine neuronal reuptake. Escitalopram is at least 100fold more potent than the R-enantiomer with respect to inhibition of 5-HT reuptake and inhibition of 5-HT neuronal firing rate. Tolerance to a model of antidepressant effect in rats was not induced by long-term (up to 5 weeks) treatment with escitalopram. Escitalopram has no or very low affinity for serotonergic (5-HT1 to 7) or other receptors including alpha- and beta-adrenergic, dopamine ($D_{110,5}$), histamine ($H_{110,3}$), muscarinic ($M_{110,5}$), and benzodiazepine receptors. Escitalopram also does not bind to, or has low affinity for, various ion channels including Na^{*}, K^{*}, Cl^{*}, and Ca^{*+} channels. Antagonism of muscarinic, histaminergic, and adrenergic receptors has been hypothesized to be associated with various anticholinergic, sedative, and cardiovascular side effects of other psychotropic drugs.

12.3 Pharmacokinetics

The single- and multiple-dose pharmacokinetics of escitalopram are linear and dose-proportional in a dose range of 10 to 30 mg/day. With once-daily dosing, steady state plasma concentrations are achieved within approximately one week. At steady state, the extent of accumulation of escitalopram in plasma in young healthy subjects was 2.2 to 2.5 times the plasma concentrations observed after a single dose.

The absolute bioavailability of citalopram is about 80% relative to an intravenous dose. The tablet and the oral solution dosage forms of escitalopram oxalate are bioequivalen Following a single oral dose (20 mg tablet or solution) of escitalopram, peak blood levels occur at about 5

hours. Absorption of escitalopram is not affected by food.

The binding of escitalopram to human plasma proteins is approximately 56%. The volume of distribution of citalopram is about 12 L/kg. Data specific on escitalopram are unavailable.

Biotransformation of escitalopram is mainly hepatic, with a mean terminal half-life of about 27 to 32 hours. The oral clearance of escitalopram is 600 mL/min, with approximately 7% of that due to renal clearance. Metabolism

Escitalopram is metabolized to S-DCT and S-didemethylcitalopram (S-DDCT). In humans, unchanged escitalopram is the predominant compound in plasma. At steady state, the concentration of the escitalopram metabolite S-DCT in plasma is approximately one-third that of escitalopram. The level of S-DDCT was not detectable in most subjects. In vitro studies show that escitalopram is at least 7 and 27 times more potent than S-DCT and S-DDCT, respectively, in the inhibition of serotonin reuptake, suggesting that the metabolites of escitalopram do not contribute significantly to the antidepressant actions of escitalopram. S-DCT and S-DDCT also have no or very low affinity for serotonergic (5-HT1 to 7) or other receptors including alpha- and betaadrenergic, dopamine (D_{1 to 5}), histamine (H_{1 to 3}), muscarinic (M_{1 to 5}), and benzodiazepine receptors. S-DCT and S-DDCT also do not bind to various ion channels including Na⁺, K⁺, Cl⁻, and Ca⁺⁺ channels. In vitro studies using human liver microsomes indicated that CYP3A4 and CYP2C19 are the primary isozymes involved in the N-demethylation of escitalopram

Excretion Following oral administrations of escitalopram, the fraction of drug recovered in the urine as escitalopram and S-demethylcitalopram (S-DCT) is about 8% and 10%, respectively.

Specific Populations Pediatric Patients

Pediatric patients 12 to 17 years of age: In a single dose study of 10 mg escitalopram, AUC of escitalopram decreased by 19%, and C_{max} increased by 26% in healthy pediatric subjects 12 to 17 years of age compared **16 HOW SUPPLIED/STORAGE AND HANDLING** to adults. Following multiple dosing of 40 mg/day citalopram, escitalopram elimination half-life, steady-state Cmax and AUC were similar in pediatric patients 12 to 17 years of age with MDD compared to adults [see Use in Specific Populations (8.4)]. Geriatric Patients

Escitalopram pharmacokinetics in subjects \ge 65 years of age were compared to adults in a single-dose and a multiple-dose study. Escitalopram AUC and half-life were increased by approximately 50% in elderly subjects, and Cmax was unchanged [see Dosage and Administration (2.5), Use in Specific Populations (8.5)]. Male and Female Patients Based on data from single- and multiple-dose studies measuring escitalopram in elderly, young adults, and

adolescents, no dosage adjustment on the basis of gender is needed Patients with Hepatic Impairmen Citalopram oral clearance was reduced by 37% and half-life was doubled in patients with reduced hepatic

function compared to normal subjects [see Dosage and Administration (2.5), Use in Specific Populations (8.6)]. Patients with Renal Impairment In patients with mild to moderate renal function impairment, oral clearance of citalopram was reduced by 17 PATIENT COUNSELING INFORMATION 17% compared to normal subjects. No information is available about the pharmacokinetics of escitalopram in patients with severely reduced renal function (creatinine clearance < 20 mL/min) [see Use in Specific Suicidal Thoughts and Behaviors

Populations (8.7)1 Drug Interaction Studies

n vitro enzyme inhibition data did not reveal an inhibitory effect of escitalopram on CYP3A4, -1A2, -2C9, -2C19, and -2E1. Based on *in vitro* data, escitalopram would be expected to have little inhibitory effect on *in* metabolism mediated by these cytochromes. While in vivo data to address this question are limited, results from drug interaction studies suggest that escitalopram, at a dose of 20 mg, has no 3A4 inhibitory effect and a modest 2D6 inhibitory effect [see Drug Interactions (7)]. CYP3A4 and CYP2C19 Inhibitor

In vitro studies indicated that CYP3A4 and -2C19 are the primary enzymes involved in the metabolism of their health care provider or report to the emergency room if they experience signs or symptoms of serotonin escitalopram. However, coadministration of escitalopram (20 mg) and ritonavir (600 mg), a potent inhibitor of syndrome [see Warnings and Precautions (5.2), Drug Interactions (7)]. CYP3A4, did not significantly affect the pharmacokinetics of escitalopram. Because escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease escitalopram clearance. Cimetidine

In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of 400 mg twice a day cimetidine for 8 days resulted in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown.

In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of citalopram and digoxin (single dose of 1 mg) did not significantly affect the pharmacokinetics of either citalopram or

Lithium Coadministration of racemic citalopram (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) had no significant effect on the pharmacokinetics of citalopram or lithium. Plasma lithium levels should be monitored with appropriate adjustment to the lithium dose in accordance with standard clinical practice. Because lithium may enhance the serotonergic effects of escitalopram, caution should be exercised when escitalopram tablets and lithium are coadministere

Theophvlline Combined administration of racemic citalopram (40 mg/day for 21 days) and the CYP1A2 substrate theophylline (single dose of 300 mg) did not affect the pharmacokinetics of theophylline. The effect of theophylline on the if they are susceptible [see Warnings and Precautions (5.9)]. pharmacokinetics of citalopram was not evaluated.

Ketoconazole Combined administration of racemic citalopram (40 mg) and ketoconazole (200 mg), a potent CYP3A4 inhibitor, decreased the Cmax and AUC of ketoconazole by 21% and 10%, respectively, and did not significantly affect the strategies with their healthcare provider [see Warnings and Precautions (5.11)]. pharmacokinetics of citalopram

Ritonavir Combined administration of a single dose of ritonavir (600 mg), both a CYP3A4 substrate and a potent inhibitor of CYP3A4, and escitalopram (20 mg) did not affect the pharmacokinetics of either ritonavir or escitalopram.

Combined administration of racemic citalopram (titrated to 40 mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25 mg) did not significantly affect the pharmacokinetics of either citalopram or triazolam

Metoproloi Administration of 20 mg/day escitalopram tablets for 21 days in healthy volunteers resulted in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of escitalopram tablets and metoprolol had no clinically significant effects on blood pressure or heart rate.

Alcohol Escitalopram did not potentiate the cognitive and motor effects of alcohol in a clinical trial. As with other psychotropic medications, the use of alcohol by patients taking escitalopram tablets are not recommended.

Warfarin Administration of 40 mg/day racemic citalopram for 21 days did not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time was increased by 5%. The clinical significance of these findings is

Additional pediatric use information is approved for AbbVie Inc.'s LEXAPRO® (escitalopram) tablets. However, due to AbbVie Inc.'s marketing exclusivity rights, this drug product is not labeled with that information. 13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

<u>Carcinogenesis</u> Racemic citalopram was administered in the diet to NMRI/BOM strain mice and COBS WI strain rats for 18 and 24 months, respectively. There was no evidence for carcinogenicity of racemic citalopram in mice receiving up to 240 mg/kg/day. There was an increased incidence of small intestine carcinoma in rats receiving 8 or 24 mg/kg/day racemic citalopram. A no-effect dose for this finding was not established. The relevance of these findings to humans is unknown

Racemic citalopram was mutagenic in the in vitro bacterial reverse mutation assay (Ames test) in 2 of 5 bacterial strains (Salmonella TA98 and TA1537) in the absence of metabolic activation. It was clastogenic in the in vitro Chinese hamster lung cell assay for chromosomal aberrations in the presence and absence of metabolic activation. Racemic citalopram was not mutagenic in the *in vitro* mammalian forward gene mutation assay (HPRT) in mouse lymphoma cells or in a coupled in vitro/in vivo unscheduled DNA synthesis (UDS) assay in rat liver. It was not clastogenic in the *in vitro* chromosomal aberration assay in human lymphocytes or in two in vivo mouse micronucleus assays.

Impairment of Fertility When racemic citalopram was administered orally to 16 male and 24 female rats prior to and throughout mating and gestation at doses of 32, 48, and 72 mg/kg/day, mating was decreased at all doses, and fertility was decreased at doses \geq 32 mg/kg/day. Gestation duration was increased at 48 mg/kg/day. 13.2 Animal Toxicology and/or Pharmacology

Retinal Changes in Rats

Pathologic changes (degeneration/atrophy) were observed in the retinas of albino rats in the 2-year carcinogenicity study with racemic citalopram. There was an increase in both incidence and severity of retinal pathology in both male and female rats receiving 80 mg/kg/day. Similar findings were not present in rats receiving 24 mg/kg/day of racemic citalopram for two years, in mice receiving up to 240 mg/kg/day of racemic citalopram for 18 months, or in dogs receiving up to 20 mg/kg/day of racemic citalopram for one year. Additional studies to investigate the mechanism for this pathology have not been performed, and the potential

significance of this effect in humans has not been established. Cardiovascular Changes in Dogs In a one-year toxicology study, 5 of 10 beagle dogs receiving oral racemic citalopram doses of 8 mg/kg/day

died suddenly between weeks 17 and 31 following initiation of treatment. Sudden deaths were not observed in rats at doses of racemic citalopram up to 120 mg/kg/day, which produced plasma levels of citalopram and its netabolites demethylcitalopram and didemethylcitalopram (DDCT) similar to those observed in dogs at 8 mg/

mg escitalopram oxalate in strengths equivalent to 5 mg, 10 mg, and 20 mg, respectively, of escitalopram kg/day. A subsequent intravenous dosing study demonstrated that in beagle dogs, racemic DDCT caused QT prolongation, a known risk factor for the observed outcome in dogs.

14.1 Major Depressive Disorder

The efficacy of escitalopram as a treatment for major depressive disorder was established in three, 8-week, placebo-controlled studies conducted in outpatients between 18 and 65 years of age who met DSM-IV criteria for major depressive disorder. The primary outcome in all three studies was change from baseline to endpoint A fixed-dose study compared 10 mg daily escitalopram and 20 mg daily escitalopram to placebo and 40 mg daily citalopram. The 10 mg daily and 20 mg daily escitalopram treatment groups showed statistically significant greater mean improvement compared to placebo on the MADRS. The 10 mg and 20 mg escitalopram

groups were similar on this outcome measure. In a second fixed-dose study of 10 mg daily escitalopram and placebo, the 10 mg daily escitalopram treatment group showed statistically significant greater mean improvement compared to placebo on the MADRS. In a flexible-dose study, comparing escitalopram, titrated between 10 mg and 20 mg daily, to placebo and citalopram, titrated between 20 mg and 40 mg daily, the escitalopram treatment group showed statistically significant greater mean improvement compared to placebo on the MADRS.

Analyses of the relationship between treatment outcome and age, gender, and race did not suggest any differential responsiveness on the basis of these patient characteristics In a longer-term trial, 274 patients meeting (DSM-IV) criteria for major depressive disorder, who had responded during an initial 8 week, open-label treatment phase with escitalopram 10 mg or 20 mg daily, were randomized o continuation of escitalopram at their same dose, or to placebo, for up to 36 weeks of observation for relapse. Response during the open-label phase was defined by having a decrease of the MADRS total score to \leq 12. Relapse during the double-blind phase was defined as an increase of the MADRS total score to \geq 22, or discontinuation due to insufficient clinical response. Patients receiving continued escitalopram experienced a statistically significant longer time to relapse compared to those receiving placebo.

Pediatric Patients 12 years of age and older The efficacy of escitalopram as a treatment for major depressive disorder in pediatric patients 12 to 17 years was stablished in an 8-week, flexible-dose, placebo-controlled study that compared escitalopram tablets (10 mg to 20 mg daily) to placebo in outpatients 12 to 17 years of age inclusive who met DSM-IV criteria for major depressive disorder (MDD). The primary outcome was change from baseline to endpoint in the Children's Depression Rating Scale - Revised (CDRS-R). In this study, escitalopram showed statistically significant greater mean improvement compared to placebo on the CDRS-R. The efficacy of escitalopram in the treatment of major depressive disorder in pediatric patients 12 to 17 years was established, in part, on the basis of extrapolation from the 8-week, flexible-dose, placebo-controlled study

with racemic citalopram 20 mg to 40 mg daily. In this outpatient study in pediatric patients 7 to 17 years of age who met DSM-IV criteria for major depressive disorder, citalopram treatment showed statistically significant greater mean improvement from baseline, compared to placebo, on the CDRS-R; the positive results for this rial largely came from the 12 to 17 year subgroup. Two additional flexible-dose, placebo-controlled MDD studies (one escitalopram study in patients ages 7

to 17 years and one citalopram study patients 13 to 18 years) did not demonstrate efficacy. The safety and effectiveness of escitalopram have not been established in pediatric patients less than 12 years of age with MDD.

14.2 Generalized Anxiety Disorde

The efficacy of escitalopram in the treatment of generalized anxiety disorder (GAD) in adults was demonstrated in three, 8-week, multicenter, flexible-dose, placebo-controlled studies that compared escitalopram tablets (10 mg to 20 mg daily) to placebo in outpatients between 18 and 80 years of age who met DSM-IV criteria for GAD. In all three studies, escitalopram showed statistically significant greater mean improvement compared to placebo on the Hamilton Anxiety Scale (HAM-A). There were too few patients in differing ethnic and age groups to adequately assess whether or not escitalopran

has differential effects in these groups. There was no difference in response to escitalopram between men and Additional pediatric use information is approved for AbbVie Inc.'s LEXAPRO® (escitalopram) tablets. However, due to AbbVie Inc.'s marketing exclusivity rights, this drug product is not labeled with that information.

How Supplied

Escitalopram tablets, USP 5 mg are white to off-white, round, biconvex, film coated tablets debossed with '135' on one side and '5' on other side.

Bottles of 1000 NDC 82009-035-10 Escitalopram tablets. USP 10 mg are white to off-white, round, biconvex, film coated tablets debossed with

break line on one side, separating '11' and '36' on one side, and '10' on other side. Bottles of 1000 NDC 82009-036-10 Escitalopram tablets, USP 20 mg are white to off-white, round, biconvex, film coated tablets debossed with break line on one side, separating '11' and '37' on one side, and '20' on other side,

Bottles of 1000 NDC 82009-037-10 Storage and Handling

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

, their families and caregivers to look for the emergence of suicidal ideation and behavior, especially during treatment and when the dose is adjusted up or down, and instruct them to report such symptoms to their healthcare provider [see Boxed Warning and Warnings and Precautions (5.1)]. Serotonin Syndrome

Caution patients about the risk of serotonin syndrome, particularly with the concomitant use of escitalopram with other serotonergic drugs including triptans, tricyclic antidepressants, opioids, lithium, tryptophan, buspirone, amphetamines, and St. John's Wort, and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid). Instruct patients to contact

Discontinuation Syndrome Advise patients not to abruptly discontinue escitalopram tablets and to discuss any tapering regimen with Do not start taking an MAOI for at least 14 days heir healthcare provider. Inform patients that adverse reactions can occur when escitalopram tablets are discontinued [see Warnings and Precautions (5.3)].

Activation of Mania or Hypomania Advise patients and their caregivers to observe for signs of activation of mania/hypomania and instruct them to report such symptoms to the healthcare provider [see Warnings and Precautions (5.5)].

Increased Risk of Bleeding Inform patients about the concomitant use of escitalopram with NSAIDs, aspirin, warfarin, other antiplatelet drugs, or other anticoagulants because the combined use has been associated with an increased risk of bleeding. Advise patients to inform their healthcare providers if they are taking or planning to take any prescription or over-the-counter medications that increase the risk of bleeding [see Warnings and Precautions (5.7)]. Angle Closure Glaucoma

Advise patients that taking escitalopram tablets can cause mild pupillary dilation, which in susceptible individuals, can lead to an episode of angle closure glaucoma. Pre-existing glaucoma is almost always openangle glaucoma because angle closure glaucoma, when diagnosed, can be treated definitively with iridectomy. Open-angle glaucoma is not a risk factor for angle closure glaucoma. Patients may wish to be examined to determine whether they are susceptible to angle closure, and have a prophylactic procedure (e.g., iridectomy), Sexual Dysfunction

Advise patients that use of escitalopram may cause symptoms of sexual dysfunction in both male and female patients. Inform patients that they should discuss any changes in sexual function and potential management Concomitant Medications

Since escitalopram is the active isomer of racemic citalopram (Celexa), the two agents should not be coadministered. Patients should be advised to inform their physician if they are taking, or plan to take, any prescription or over-the-counter drugs, as there is a potential for interactions. Interference with Psychomotor Performance

Because psychoactive drugs may impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that escitalopram tablets therapy does not affect their ability to engage in such activities.

Patients should be told that, although escitalopram has not been shown in experiments with normal subjects to increase the mental and motor skill impairments caused by alcohol, the concomitant use of escitalopram and alcohol in depressed patients is not advised.

Pregnanc Advise pregnant women to notify their healthcare providers if they become pregnant or intend to become pregnant during treatment with escitalopram tablets. Advise patients that escitalopram use later in pregnancy may lead to increased risk for neonatal complications

requiring prolonged hospitalization, respiratory support, tube feeding, and/or persistent pulmonary hypertension (PPHN) of the newborn [see Use in Specific Populations (8.1)]. Advise women that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to escitalopram during pregnancy [see Use in Specific Populations (8.1)].

Lactation Advise breastfeeding women using escitalopram to monitor infants for excess sedation, restlessness, agitation, poor feeding and poor weight gain and to seek medical care if they notice these signs [see Use in Specific Populations (8.2)

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provider about the best way to feed the baby during escitalopram tablets. • If you or your child breastfeed during escitalopram tablets, call your healthcare pro

MEDICATION GUIDE Escitalopram (es" sye tal' oh pram) Table What is the most important information I should kn escitalopram tablets?

- or when the dose is changed. Depression or other mental illnesses
- important causes of suicidal thoughts o How can I watch for and try to prevent suici actions?
- Pay close attention to any changes, e changes in mood, behavior, thoughts, or t or your child develop suicidal thoughts of very important when an antidepressant me
- or when the dose is changed. • Call your healthcare provider right away sudden changes in mood, behavior, thou
- or if you or your child develop suicidal the Keep all follow-up visits with your health scheduled and call your healthcare provid
- if you are worried about symptoms. Call your healthcare provider or get emergency m

away if you or your child have any of the follow especially if they are new, worse, or worry you: attempts to commit suicide acting on

- impulses acting aggressive, being thoughts • angry or violent dying
- new or worse depression new or v ٠
 - anxiety feeling v restless
- new or worse irritability trouble s an extreme increase in other uni

activity or talking (mania)

- Do not take escitalopram tablets if you or your chil are taking, or have stopped taking within the medicine called a monoamine oxidase inhibitor the antibiotic linezolid or intravenous methylene
- are taking the antipsychotic medicine pimozide are allergic to escitalopram or citalopram or any in escitalopram tablets. See the end of this Medic
- complete list of ingredients in escitalopram table Ask your healthcare provider or pharmacist if you you or your child take an MAOI, including the antib intravenous methylene blue.

child have stopped treatment with escitalopram ta

Before taking escitalopram tablets, tell your hea about all your medical conditions, including if you

- have or had seizures or convulsions have, or have a family history of bipolar disc hypomania
- have low blood sodium levels have or had bleeding problems

Escitalopram Tablets, USP	COUNTRY : US_Quallent	LOCATION : Dahej			Supersedes A/W No.:	
Outsert	NO. OF COLORS: 1	REMARK :	REMARK :			V. No. : 01
Back Side	PANTONE SHADE NOS.:	SUBSTRATE : 28	8 g/m ² Bible Pape	er		
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S/S		Reviewed By	Pkg. Dev.			
09-10-2024	Font Size 6.5 pt_Med. 10 pt	Approved By	Quality			

Note: Pharma code/ Bar code and adjacent text must be visible on folded leaflet.

These details can be moved by printed to arrange pharma code/ Bar code and adjacent text visible on folded leaflet.

MEDICATION GUIDE Escitalopram (es" sye tal' oh pram) Tablets, USP What is the most important information I should know about escitalopram tablets? Escitalopram tablets may cause serious side effects, including: Increased risk of suicidal thoughts or actions. Escitalopram tablets and other antidepressant medicines increase the risk of suicidal thoughts and actions in people 24 years of age and younger, especially within the first few months of treatment or when the dose is changed. O Depression or other mental illnesses are the most important causes of suicidal thoughts or actions. How can I watch for and try to prevent suicidal thoughts and actions? Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts, or feelings, or if you or your child develop suicidal thoughts or actions. This is very important when an antidepressant medicine is started or when the dose is changed. Call your healthcare provider right away to report new or sudden changes in mood, behavior, thoughts, or feelings or if you or your child develop suicidal thoughts or actions. Keep all follow-up visits with your healthcare provider as scheduled and call your healthcare provider between visits if you are worried about symptoms. Call your healthcare provider or get emergency medical help right away if you or your child have any of the following symptoms, especially if they are new, worse, or worry you: a attempts to commit suicide acting aggressive, being angry or violent new or worse eirritability angry or violent new or worse eirritability panic att	 medicines used to treat mood, anxiety, psychotic or thought disorders, including selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) diuretics medicines that can affect blood clotting such as aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs) and warfarin Ask your healthcare provider if you are not sure if you or your child are taking any of these medicines. Your healthcare provider can tell you if it is safe to take escitalopram tablets with your other medicines. Do not start or stop any other medicines during treatment with escitalopram tablets suddenly may cause you or your child to have serious side effects. See, "What are the possible side effects of Escitalopram tablets?" Know the medicines you or your child take. Keep a list of them to show your healthcare provider and pharmacist when you get new medicine. How should I take Escitalopram tablets? Take escitalopram tablets varity as prescribed. Your healthcare provider may need to change the dose of escitalopram tablets until it is the right dose for you or your child. Take escitalopram tablets with or without food. If you or your child take too much escitalopram tablets, call your healthcare provider or Poison Help Line at 1-800-222-1222, or go to the nearest hospital emergency room right away. What should I avoid while taking escitalopram tablets? Do not drive, operate heavy machinery, or do other dangerous activities until you know how escitalopram tablets? Do not drive, operate heavy machinery, or do other dangerous activities until you know how escitalopram tablets? Do not drive, aperate heavy machinery, or to other dangerous activities until you know how escitalopram tablets? Escitalopram tablets can cause sleepiness or may affect your ability to make decisions, think clearly, or react quickly.	 Sexual problems (dysfunction). Taking escitalopram tablets may cause sexual problems. Symptoms in males may include: delayed ejaculation or inability to have an ejaculation decreased sex drive decreased sex drive delayed orgasm or inability to have an orgasm Talk to your healthcare provider if you develop any changes in your sexual problems during treatment with escitalopram. There may be treatments your healthcare provider can suggest. The most common side effects of escitalopram tablets include: trederess descip decreased sex drive delayed orgasm or inability to have an orgasm Tak to your healthcare provider can suggest. The most common side effects of escitalopram tablets include: trouble sleeping sweating decreased sex drive delayed orgasm or inability to have an orgasm nausea sleepiness Height and weight changes in children may happen during treatment with escitalopram tablets. These are not all the possible side effects of escitalopram tablets. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. How should 1 store escitalopram tablets? Store escitalopram tablets and all medicines out of the reach of children. General information about the safe and effective use of escitalopram tablets. Any 77°F (20°C to 25°C). Keeg escitalopram tablets and all medicines out of the reach of children. General information about the safe and effective use of escitalopram tablets. For a 20°C to 25°C
 intravenous methylene blue. Do not start taking an MAOI for at least 14 days after you or your child have stopped treatment with escitalopram tablets. Before taking escitalopram tablets, tell your healthcare provider about all your medical conditions, including if you or your child: have or had seizures or convulsions have, or have a family history of bipolar disorder, mania, or hypomania have low blood sodium levels have nad bleeding problems have high pressure in the eye (glaucoma) have had pressure in the eye (glaucoma) have had bleeding, to diver your child the uning the third trimester of pregnancy may cause the baby to have withdrawal symptoms, or breathing, temperature control, feeding, or other problems after birth. Talk to your healthcare provider about the risks to the baby if you or your child take escitalopram tablets during pregnancy. Tell your healthcare provider right away if you or your child become pregnant or think you may be pregnant during treatment with escitalopram tablets. There is a pregnancy registry for females who are exposed to escitalopram tablets during pregnancy. The purpose of the registry is to collect information about the health of females exposed to escitalopram tablets and their baby. If you or your child become pregnant during treatment with escitalopram tablets. There is a pregnancy Registry for Antidepressants at 1-844-405-6185 or visit online at https://womensmentalhealth.org/ research/pregnancyregistry/antidepressants. are breastfieding or plan to breastfied. Escitalopram passes into breast milk and may harm the baby during treatment with escitalopram tablets. If you or your child breastfeed during treatment with escitalopram tablets. of for your or your child breastfeed during treatment with escitalopram tablets. if you or your child breastfeed during treatment with escitalopram tablets. if you or	 tablets may cause you or your child to have serious side effects. Your heathcare provider may want to decrease the dose slowly. Symptoms may include: changes in mood headache irritability and agitation tiredness dizziness problems sleeping electric shock sensation (paresthesia) hypomania anxiety confusion seizures Seizures (convulsions). Manic episodes. Manic episodes may happen in people with bipolar disorder who take escitalopram tablets. Symptoms may include: greatly increased energy severe trouble sleeping racing thoughts excessive happiness or inritability talking more or faster than usual Low sodium levels in the blood (hyponatremia). Low sodium levels in the blood that may be serious and may cause death can happen during treatment with escitalopram tablets. Elderly people and people who take certain medicines may be at greater risk for developing low sodium levels in the blood. Signs and symptoms may include: headache problems concentrating or thinking weakness or feeling unsteady which can lead to falls confusion memory problems Inmore severe or more sudden cases, signs and symptoms include: seizures coma stopping breathing (respiratory arrest) Increased risk of bleeding: Taking escitalopram tablets with aspirin, NSAIDS, warfarin, or other blood thinners may add to this risk. Tell your healthcare provider if you are at risk and receive preventative treatment if you are at risk and receive preventative treatment if you are. Call your healthcare provider if you or your child have: eye pain changes in vision swelling or redness in or around the eye 	<text><text><text><text><text></text></text></text></text></text>

