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AbbVie Pipeline

Global Medical Affairs,
Research and Development

Investigational Compounds and Off-Label Uses Discussed

- Some of the AbbVie compounds discussed in this presentation are investigational new drugs.
- This material also contains information on uses of MAVYRET® (glecaprevir/pibrentasvir), ORILISSA® (elagolix), RINVOQ™ (upadacitinib), SKYRIZI™ (risankizumab-rzaa), VENCLEXTA® (venetoclax), VRAYLAR® (cariprazine), and BOTOX® (onabotulinumtoxin A) that have not been approved by the U.S. Food and Drug Administration.
- Glecaprevir/pibrentasvir, elagolix, upadacitinib, risankizumab-rzaa, venetoclax, cariprazine, onabotulinumtoxin A, ABBV-951, navitoclax, and atogepant are under investigation in various stages of clinical trials and the information in this presentation relates to uses and/or indications that have not been approved by a regulatory agency and neither the safety nor effectiveness of the products have been established. This information is being provided solely to assist in the planning and budgeting for future coverage and/or reimbursement decisions before FDA approval.
- AbbVie in no way intends to suggest that any investigational drugs discussed are safe or effective for the purposes for which they are under investigation or to recommend or imply that MAVYRET (glecaprevir/pibrentasvir), ORILISSA (elagolix), RINVOQ (upadacitinib), SKYRIZI (risankizumab-rzaa), VENCLEXTA (venetoclax), VRAYLAR (cariprazine), BOTOX (onabotulinumtoxin A), ABBV-951, navitoclax, or atogepant should be used for unapproved uses.

MAVYRET (glecaprevir/pibrentasvir) Prescribing Information Overview

Indication and Usage	• **MAVYRET (glecaprevir/pibrentasvir or G/P)** is a direct-acting antiviral (DAA) indicated for the treatment of adults and pediatric patients 12 years and older or weighing at least 45 kg with chronic hepatitis C virus (HCV) genotypes 1 through 6 (GT1-6) without cirrhosis or with compensated cirrhosis (Child-Pugh A). G/P is also indicated for treatment of patients with GT1 HCV who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.
Dosage and Administration	• **G/P is a fixed-dose combination product** containing glecaprevir 100 mg and pibrentasvir 40 mg in each tablet. • **The recommended oral dosage of G/P is three tablets taken at the same time once daily with food** (total daily dose: glecaprevir 300 mg and pibrentasvir 120 mg).
Boxed Warning	• **Risk of Hepatitis B Virus Reactivation in Patients Coinfected with HCV and Hepatitis B Virus (HBV):** Test all patients for evidence of current or prior HBV infection before initiating treatment with G/P. HBV reactivation has been reported in HCV/HBV co-infected patients who were undergoing or had completed treatment with HCV DAAs and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Monitor HCV/HBV co-infected patients for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated.
Contraindications	• **Moderate to severe hepatic impairment (Child-Pugh B or C) or those with any history of prior hepatic decompensation** • **Atazanavir and rifampin**
Warnings and Precautions	• **Risk of Hepatic Decompensation/Failure in Patients with Evidence of Advanced Liver Disease:** Hepatic decompensation and hepatic failure, including fatal outcomes, have been reported mostly in patients with cirrhosis and baseline moderate or severe liver impairment (Child-Pugh B or C). Cases typically occurred within the first 4 weeks of treatment. In patients with compensated cirrhosis (Child-Pugh A) or evidence of advanced liver disease, monitor for clinical and laboratory evidence of hepatic decompensation/failure. • **Risk of Reduced Therapeutic Effect Due to Concomitant Use:** Carbamazepine, efavirenz, and St. John's Wort may significantly decrease plasma concentrations of G/P and reduce its therapeutic effect. The use of these agents with G/P is not recommended.
Adverse Reactions	• Most commonly reported adverse reactions (>10%) included headache and fatigue.

Review MAVYRET full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

MAVYRET [package insert]. North Chicago, IL: AbbVie, Inc. 2020.

ORILISSA® (elagolix) Prescribing Information Overview

Indication and Usage	• **ORILISSA (elagolix)** is a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the management of moderate to severe pain associated with endometriosis.
Dosage and Administration	• **Normal liver function or mild hepatic impairment:** 150 mg once daily for up to 24 months or 200 mg twice daily for up to 6 months. • **Moderate hepatic impairment:** 150 mg once daily for up to 6 months.
Contraindication	• **Pregnancy** • **Known osteoporosis** • **Severe hepatic impairment** • **Strong organic anion transporting polypeptide (OATP) 1B1 inhibitors**
Warnings and Precautions	• **Bone Loss:** Dose- and duration-dependent decreases in bone mineral density (BMD) that may not be completely reversible. Assess BMD in women with additional risk factors for bone loss. • **Reduced Ability to Recognize Pregnancy:** ORILISSA may alter menstrual bleeding, which may reduce the ability to recognize pregnancy. Perform testing if pregnancy is suspected. Discontinue if pregnancy is confirmed. • **Suicidal Ideation and Mood Disorders:** Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes. • **Hepatic Transaminase Elevations:** Dose-dependent elevations in serum alanine aminotransferase (ALT). Counsel patients on signs and symptoms of liver injury. • **Potential for Reduced Efficacy with Estrogen-Containing Contraceptives:** Use non-hormonal contraception during treatment and for one week after discontinuing ORILISSA.
Adverse Reactions	• Most common adverse reactions (>5%) in clinical trials included hot flushes and night sweats, headache, nausea, insomnia, amenorrhea, anxiety, arthralgia, depression-related adverse reactions and mood changes.

Review ORILISSA full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

ORILISSA [package insert]. North Chicago, IL: AbbVie, Inc. 2018.

RINVOQ™ (upadacitinib) Indication & Important Safety Considerations

Indication & Usage

- RINVOQ is a Janus kinase (JAK) inhibitor indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.
- Limitation of Use: Use of RINVOQ in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Boxed Warning

WARNING: SERIOUS INFECTIONS, MALIGNANCY, AND THROMBOSIS

- Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving RINVOQ.
- If a serious infection develops, interrupt RINVOQ until the infection is controlled.
- Prior to starting RINVOQ, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting RINVOQ
- Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative.
- Lymphoma and other malignancies have been observed in patients treated with RINVOQ.
- Thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with Janus kinase inhibitors used to treat inflammatory conditions.

Contraindication

- **None**

Warnings and Precautions

- **Serious Infections:** Avoid use of RINVOQ in patients with active, serious infection, including localized infections.
- **Malignancy:** Consider the risks and benefits of RINVOQ treatment prior to initiating therapy in patients with a known malignancy.
- **Thrombosis:** Consider the risks and benefits prior to treating patients who may be at increased risk of thrombosis. Promptly evaluate patients with symptoms of thrombosis and treat appropriately.
- **Gastrointestinal Perforations:** Use with caution in patients who may be at increased risk.
- **Laboratory Monitoring:** Recommended due to potential changes in lymphocytes, neutrophils, hemoglobin, liver enzymes and lipids.
- **Embryo-Fetal Toxicity:** RINVOQ may cause fetal harm based on animal studies. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
- **Vaccinations:** Avoid use of RINVOQ with live vaccines.

Review RINVOQ full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

RINVOQ [package insert]. North Chicago, IL: AbbVie, Inc.; 2020.

Skyrizi® (risankizumab-rzaa) Indication & Important Safety Considerations

Indication and Usage	SKYRIZI is an interleukin-23 antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy
Dosage and Administration	150 mg SKYRIZI (two 75mg injections) administered by subcutaneous injection at week 0, week 4, and every 12 weeks thereafter.
Contraindications	None
Warnings and Precautions	**Infections:** SKYRIZI may increase the risk of infection. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If such an infection develops, discontinue SKYRIZI until the infection resolves. • **Tuberculosis (TB):** Evaluate for TB prior to initiating treatment with SKYRIZI. • Avoid use of live vaccines in SKYRIZI patients
Adverse Reactions	Most common adverse reactions (≥ 1%) are upper respiratory infections, headache, fatigue, injection site reactions, and tinea infections

Review SKYRIZI full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

SKYRIZI [package insert]. North Chicago, IL: AbbVie, Inc.; 2020.

VENCLEXTA® (venetoclax) Indication and Safety Overview for AML/CLL

Indication and Usage

VENCLEXTA is a BCL-2 inhibitor indicated:

- For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- In combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults:
  - 75 years or older, or
  - who have comorbidities that preclude use of intensive induction chemotherapy.

Dosage and Administration

Dosing in CL/SLL

- **5-Week Dose Ramp-Up Schedule:** Administer VENCLEXTA according to the 5-week ramp-up dosing schedule to the recommended dosage of 400 mg orally once daily – VENCLEXTA Daily Dose: 20 mg (Week 1), 50 mg (Week 2), 100 mg (Week 3), 200 mg (Week 4), and 400 mg (Week 5 and beyond).
- **VEN+G:** For VENCLEXTA in combination with obinutuzumab, start obinutuzumab administration on Cycle 1 Day 1. Administer for a total of 6 cycles. On Cycle 1 Day 22, start VENCLEXTA according to the 5-week ramp-up dosing schedule. After completing the ramp-up phase on Cycle 2 Day 28, continue VENCLEXTA at a dose of 400 mg orally once daily from Cycle 3 Day 1 until the last day of Cycle 12.
- **VEN+R:** For VENCLEXTA in combination with rituximab, start rituximab after completion of the 5-week ramp-up dosing schedule for VENCLEXTA. Continue VENCLEXTA 400 mg orally once daily for 24 months from Cycle 1 Day 1 of rituximab.

Dosing in AML

- **3-Day Ramp-Up Dosing Schedule for Combination with Azacitidine (AZA) or Decitabine (DEC):** Initiate therapy with VENCLEXTA at 100 mg (Day 1), 200 mg (Day 2), 400 mg (Day 3), 400 mg (Day 4 and beyond) once daily. Initiate the AZA or DEC on Day 1.
- **4-Day Ramp-Up Dosing Schedule for Combination with Low Dose Cytarabine (LDAC):** Initiate therapy with VENCLEXTA at 100 mg (Day 1), 200 mg (Day 2), 400 mg (Day 3), 600 mg (Day 4 and beyond) once daily. Initiate the LDAC on Day 1.
- Continue VENCLEXTA, in combination with AZA or DEC or LDAC, until disease progression or unacceptable toxicity.
- **Dose modifications required for administration with CYP3A and P-gp inhibitors.**

- **Oral, Once Daily Dosing:** VENCLEXTA tablets should be taken orally once daily with a meal and water. Do not chew, crush, or break tablets.
- **Perform prophylaxis and monitoring for tumor lysis syndrome (TLS).**

Review full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110 or go to abbviemedinfo.com.

BCL-2=B-cell lymphoma-2 protein

Venetoclax [package insert]. North Chicago, IL: AbbVie, Inc. and South San Francisco, CA: Genentech, Inc.: Nov 2020.

VENCLEXTA® (venetoclax) Indication and Safety Overview for AML/CLL (cont'd)

Contraindication

- Concomitant use with **strong CYP3A inhibitors** at initiation and during ramp-up phase in patients with CLL/SLL is contraindicated.

Warnings and Precautions

- **TLS:** Tumor lysis syndrome (TLS), including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA. Anticipate TLS; assess risk in all patients. Premedicate with anti-hyperuricemics and ensure adequate hydration. Employ more intensive measures (intravenous hydration, frequent monitoring, hospitalization) as overall risk increases.
- **Neutropenia:** Monitor blood counts. Interrupt dosing and resume at same or reduced dose. Consider supportive care measures.
- **Infections:** Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with VENCLEXTA. Monitor for signs and symptoms of infection and treat promptly. Withhold for Grade 3 and 4 infection until resolution and resume at same or reduced dose.
- **Immunization:** Do not administer live attenuated vaccines prior to, during, or after treatment with VENCLEXTA until B-cell recovery.
- **Embryo-Fetal Toxicity:** May cause embryo-fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
- **Increased mortality in patients with multiple myeloma (MM) when VENCLEXTA is added to bortezomib and dexamethasone.** In a randomized trial in patients with relapsed or refractory MM, the addition of VENCLEXTA to bortezomib plus dexamethasone, a use for which VENCLEXTA is not indicated, resulted in increased mortality. Treatment of patients with MM with VENCLEXTA in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

Adverse Reactions

- In **CLL/SLL,** the most common adverse reactions (≥20%) for VENCLEXTA when given in combination with obinutuzumab or rituximab or as monotherapy were neutropenia, thrombocytopenia, anemia, diarrhea, nausea, upper respiratory tract infection, cough, musculoskeletal pain, fatigue, and edema.
- In **AML,** the most common adverse reactions (≥30%) in combination with azacitidine or decitabine or low-dose cytarabine were nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, fatigue, vomiting, edema, pyrexia, pneumonia, dyspnea, hemorrhage, anemia, rash, abdominal pain, sepsis, musculoskeletal pain, dizziness, cough, oropharyngeal pain, and hypotension.

Review full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110 or go to abbviemedinfo.com.

Venetoclax [package insert]. North Chicago, IL: AbbVie, Inc. and South San Francisco, CA: Genentech, Inc.: Nov 2020.

VRAYLAR® (cariprazine) Prescribing Information Overview

WARNINGS: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS; and SUICIDAL THOUGHTS and BEHAVIORS

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. VRAYLAR is not approved for the treatment of patients with dementia-related psychosis.**
- **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. Safety and effectiveness of VRAYLAR have not been established in pediatric patients.**

Indications & Usage	VRAYLAR is an atypical antipsychotic indicated for the: • Treatment of schizophrenia in adults • Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults • Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults
Contraindication	VRAYLAR is contraindicated in patients with history of a hypersensitivity reaction to cariprazine. Reactions have ranged from rash, pruritus, urticaria, and events suggestive of angioedema (eg, swollen tongue, lip swelling, face edema, pharyngeal edema, and swelling face)
Warnings and Precautions	• **Cerebrovascular Adverse Reactions, Including Stroke**: In clinical trials with antipsychotic drugs, elderly subjects with dementia had a higher incidence of cerebrovascular adverse reactions, including fatalities vs placebo. VRAYLAR is not approved for the treatment of patients with dementia-related psychosis.

Review VRAYLAR full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

VRAYLAR® (cariprazine) [package insert]. Madison, NJ: Allergan USA, Inc. May 2019.

VRAYLAR® (cariprazine) Prescribing Information Overview (cont'd)

Warnings and Precautions (Cont'd)

- **Neuroleptic Malignant Syndrome (NMS)**: NMS, a potentially fatal symptom complex, has been reported with antipsychotic drugs. NMS may cause hyperpyrexia, muscle rigidity, delirium, and autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.
  Manage with immediate discontinuation, intensive symptomatic treatment, and monitoring.
- **Tardive Dyskinesia (TD)**: Risk of developing TD (a syndrome of potentially irreversible, involuntary, dyskinetic movements) and the likelihood it will become irreversible may increase with the duration of treatment and the cumulative dose. The syndrome can develop after a relatively brief treatment period, even at low doses, or after treatment discontinuation. If signs and symptoms of TD appear, drug discontinuation should be considered.
- **Late-Occurring Adverse Reactions**: Adverse events may first appear several weeks after initiation of VRAYLAR, probably because plasma levels of cariprazine and its major metabolites accumulate over time. As a result, the incidence of adverse reactions in short-term trials may not reflect the rates after longer term exposures. Monitor for adverse reactions, including extrapyramidal symptoms (EPS) or akathisia, and patient response for several weeks after starting VRAYLAR and after each dosage increase. Consider reducing the dose or discontinuing the drug.
- **Metabolic Changes**: Atypical antipsychotics have caused metabolic changes, such as:
  - **Hyperglycemia and Diabetes Mellitus:** Hyperglycemia, in some cases associated with ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics. Assess fasting glucose before or soon after initiation of treatment, and monitor periodically during long-term treatment.
  - **Dyslipidemia:** Atypical antipsychotics cause adverse alterations in lipids. Before or soon after starting an antipsychotic, obtain baseline fasting lipid profile and monitor periodically during treatment.
  - **Weight Gain:** Weight gain has been observed with VRAYLAR. Monitor weight at baseline and frequently thereafter.
- **Leukopenia, Neutropenia, and Agranulocytosis**: Leukopenia/neutropenia have been reported with antipsychotics, including VRAYLAR. Agranulocytosis (including fatal cases) has been reported with other antipsychotics. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/ neutropenia. Discontinue VRAYLAR at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Review VRAYLAR full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

VRAYLAR® (cariprazine) [package insert]. Madison, NJ: Allergan USA, Inc. May 2019.

VRAYLAR® (cariprazine) Prescribing Information Overview (cont'd)

Warnings and Precautions (Cont'd)

- **Orthostatic Hypotension and Syncope**: Atypical antipsychotics cause orthostatic hypotension and syncope, with the greatest risk during initial titration and with dose increases. Monitor orthostatic vital signs in patients predisposed to hypotension and in those with cardiovascular/cerebrovascular diseases.
- **Falls**: VRAYLAR may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures, or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotics and recurrently for patients on long-term therapy.
- **Seizures**: Use VRAYLAR with caution in patients with history of seizures or with conditions that lower the seizure threshold.
- **Potential for Cognitive and Motor Impairment**: Somnolence was reported with VRAYLAR. Caution patients about performing activities requiring mental alertness (eg, operating hazardous machinery or a motor vehicle).
- **Body Temperature Dysregulation**: Use VRAYLAR with caution in patients who may experience conditions that increase body temperature (eg, strenuous exercise, extreme heat, dehydration, or concomitant anticholinergics).
- **Dysphagia**: Esophageal dysmotility and aspiration have been associated with antipsychotics. Antipsychotic drugs, including VRAYLAR, should be used cautiously in patients at risk for aspiration.
- **Drug Interactions**: Strong CYP3A4 inhibitors increase VRAYLAR concentrations, so VRAYLAR dose reduction is recommended. Concomitant use with CYP3A4 inducers is not recommended.
- **Adverse Reactions**: In clinical trials, the most common adverse reactions (≥5% and at least twice the rate of placebo) are listed below:
  - **Schizophrenia**: The incidences within the recommended dose range (VRAYLAR 1.5 – 3 mg/day and 4.5 – 6 mg/day vs placebo) were: EPS (15%, 19% vs 8%) and akathisia (9%, 13% vs 4%).
  - **Bipolar mania**: The incidences within the recommended dose range (VRAYLAR 3 – 6 mg/day vs placebo) were: EPS (26% vs 12%), akathisia (20% vs 5%), vomiting (10% vs 4%), dyspepsia (7% vs 4%), somnolence (7% vs 4%), and restlessness (7% vs 2%).
  - **Bipolar depression**: The incidences within the recommended doses (VRAYLAR 1.5 mg/day or 3 mg/day vs placebo) were: nausea (7%, 7% vs 3%), akathisia (6%, 10% vs 2%), restlessness (2%, 7% vs 3%), and EPS (4%, 6% vs 2%).

Review VRAYLAR full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

VRAYLAR® (cariprazine) [package insert]. Madison, NJ: Allergan USA, Inc. May 2019.

BOTOX® (onabotulinumtoxin A) Approved Indications for Use

BOTOX® (onabotulinumtoxin A) is indicated:	
Overactive Bladder	BOTOX is indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication.
Urinary Incontinence	BOTOX is indicated for the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)] in adults who have an inadequate response to or are intolerant of an anticholinergic medication.
Chronic Migraine	BOTOX is indicated for the prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer).
Spasticity	BOTOX is indicated for the treatment of spasticity in patients 2 years of age and older.
Cervical Dystonia	BOTOX is indicated for the treatment of cervical dystonia in adult patients, to reduce the severity of abnormal head position and neck pain.
Hyperhidrosis	BOTOX is indicated for the treatment of severe axillary hyperhidrosis that is inadequately managed by topical agents in adult patients.
Blepharospasm	BOTOX is indicated for the treatment of blepharospasm associated with dystonia in patients 12 years of age and older.
Strabismus	BOTOX is indicated for the treatment of strabismus in patients 12 years of age and older.
Boxed Warning	**WARNING: DISTANT SPREAD OF TOXIN EFFECT** • Postmarketing reports indicate that the effects of Botox® and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity, but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and spasticity and at lower doses.

Review BOTOX full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

BOTOX [package insert]. Madison, NJ: Allergan, Inc.; 2020.

Important Safety Considerations BOTOX® (onabotulinumtoxin A)

Contraindications

BOTOX is contraindicated:

- In patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.
- In the presence of infection at the proposed injection site(s).
- For intradetrusor injection in patients with a urinary tract infection; or in patients with urinary retention or post-void residual (PVR) urine volume >200 mL who are not routinely performing clean intermittent self-catheterization (CIC).

Warnings and Precautions

- **Spread of Toxin Effect:** Postmarketing safety data from BOTOX and other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection (See Box Warning).
- **Lack of Interchangeability between Botulinum Toxin Products:** The potency Units of BOTOX are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of BOTOX cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method [see Description (11)].
- **Serious Adverse Reactions with Unapproved Use:** Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported. The safety and effectiveness of BOTOX for unapproved uses have not been established.
- **Hypersensitivity Reactions:** Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea.
- **Increased Risk of Clinically Significant Effects with Pre-Existing Neuromuscular Disorders:** Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis or neuromuscular junction disorders should be monitored when given botulinum toxin. Patients with known or unrecognized neuromuscular disorders or neuromuscular junction disorders may be at increased risk of clinically significant effects.
- **Dysphagia and Breathing Difficulties:** Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications.
- **Pulmonary Effects of BOTOX in Patients with Compromised Respiratory Status Treated for Spasticity or for Detrusor Overactivity Associated with a Neurologic Condition:** Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

Review BOTOX full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

BOTOX [package insert]. Madison, NJ: Allergan, Inc.; 2020.

Important Safety Considerations BOTOX® (onabotulinumtoxin A)

Warnings and Precautions

- **Pulmonary Effects of BOTOX in Patients with Compromised Respiratory Status Treated for Spasticity or for Detrusor Overactivity Associated with a Neurologic Condition:** Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.
- **Corneal Exposure and Ulceration in Patients Treated with BOTOX for Blepharospasm:** Reduced blinking from BOTOX injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.
- **Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity:** Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units-360 Units total dose), compared to placebo (1%). In pediatric patients treated for upper limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (17% at 6 Units/kg and 10% at 3 Units/kg) compared to placebo (9%).
- **Autonomic Dysreflexia in Patients Treated for Detrusor Overactivity Associated with a Neurologic Condition:** Autonomic dysreflexia associated with intradetrusor injections of BOTOX could occur in patients treated for detrusor overactivity associated with a neurologic condition and may require prompt medical therapy.
- **Urinary Retention in Patients Treated for Bladder Dysfunction:** Due to the risk of urinary retention, treat only patients who are willing and able to initiate catheterization post-treatment, if required, for urinary retention. In patients who are not catheterizing, post-void residual (PVR) urine volume should be assessed within 2 weeks post-treatment and periodically as medically appropriate up to 12 weeks.
- **Overactive Bladder:** BOTOX increases the incidence of urinary tract infection. Use of BOTOX for the treatment of overactive bladder in patients with more than 2 UTIs in the past 6 months and those taking antibiotics chronically due to recurrent UTIs, and in patients with multiple recurrent UTIs during treatment should only be considered when the benefit is likely to outweigh the potential risk.
- **Urinary Retention in Patients Treated for Bladder Dysfunction:** Due to the risk of urinary retention, treat only patients who are willing and able to initiate catheterization post-treatment, if required, for urinary retention.
- **Human Albumin and Transmission of Viral Diseases:** This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Review BOTOX full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

BOTOX [package insert]. Madison, NJ: Allergan, Inc.; 2020.

Investigational Assets and Existing Therapies Being Studied for Potential New Indications

Existing Therapies Being Studied in Important New Areas

Risankizumab-rzaa	Psoriatic Arthritis, Atopic Dermatitis, Crohn's Disease, Hidradenitis Suppurativa, Ulcerative Colitis
Upadacitinib	Atopic Dermatitis, Crohn's Disease, Psoriatic Arthritis, Ulcerative Colitis, Ankylosing Spondylitis, Giant Cell Arteritis
Venetoclax	Acute Myeloid Leukemia (fit), Mantle Cell Lymphoma, Multiple Myeloma, Myelodysplastic Syndrome, Solid Tumors
Elagolix	Polycystic Ovary Syndrome
Cariprazine	Adjunctive Treatment in Major Depressive Disorder
Onabotulinumtoxin A	Atrial Fibrillation

Investigational Assets

Navitoclax

- Myelofibrosis

ABBV-951

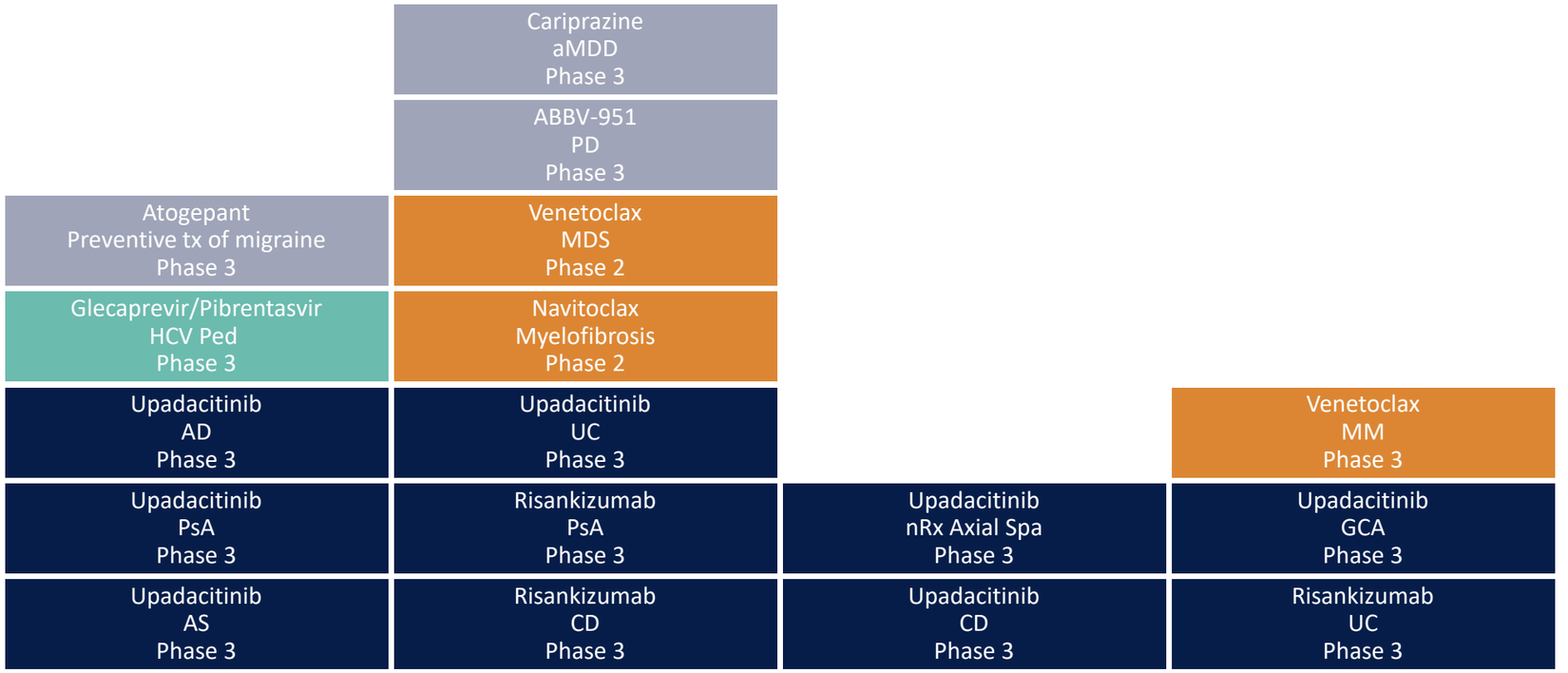
- Parkinson's Disease - Subcutaneous delivery system for levodopa/carbidopa prodrug

ABBV-323

- Ulcerative Colitis

Some of the AbbVie compounds discussed in this presentation are investigational new drugs.
This material also contains information on uses ORILISSA® (elagolix), RINVOQ™ (upadacitinib), SKYRIZI™ (risankizumab-rzaa), VENCLEXTA® (venetoclax), VRAYLAR® (cariprazine), and BOTOX® (onabotulinumtoxin A) that have not been approved by the U.S. Food and Drug Administration.
Elagolix, upadacitinib, risankizumab-rzaa, venetoclax, cariprazine, onabotulinumtoxin A, navitoclax, ABBV-951, and ABBV-323 are under investigation in various stages of clinical trials and the information in this presentation relates to uses and/or indications that have not been approved by a regulatory agency and neither the safety nor effectiveness of the products have been established. This information is being provided solely to assist in the planning and budgeting for future coverage and/or reimbursement decisions before FDA approval.
AbbVie in no way intends to suggest that any investigational drugs discussed are safe or effective for the purposes for which they are under investigation or to recommend or imply that ORILISSA (elagolix), RINVOQ (upadacitinib), SKYRIZI (risankizumab-rzaa), VENCLEXTA (venetoclax), VRAYLAR (cariprazine), BOTOX (onabotulinumtoxin A), navitoclax, ABBV-951, or ABBV-323 should be used for unapproved uses.

AbbVie Pipeline Development



These are AbbVie assets in clinical development. There is no guarantee that any of these clinical compounds will be approved by the FDA or other global regulatory health authorities. Safety and efficacy have not been established for unapproved uses. Current as of 3/11/2021

Some of the AbbVie compounds discussed in this presentation are investigational new drugs.
This material also contains information on uses MAVYRET® (glecaprevir/pibrentasvir), RINVOQ™ (upadacitinib), SKYRIZI™ (risankizumab-rzaa), VENCLEXTA® (venetoclax), and VRAYLAR® (cariprazine), that have not been approved by the U.S. Food and Drug Administration.
Glecaprevir/pibrentasvir, upadacitinib, risankizumab-rzaa, venetoclax, cariprazine, onabotulinumtoxin A, ABBV-951, navitoclax, and atogepant are under investigation in various stages of clinical trials and the information in this presentation relates to uses and/or indications that have not been approved by a regulatory agency and neither the safety nor effectiveness of the products have been established. This information is being provided solely to assist in the planning and budgeting for future coverage and/or reimbursement decisions before FDA approval.
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AD=atopic dermatitis. aMDD=adjuntive major depressive disorder. AS=ankylosing spondylitis. CD=Crohn's disease. GCA=giant cell arteritis. HCV=hepatitis C virus. MDS=myelodysplastic syndromes. MM-multiple myeloma. NDO=neurogenic detrusor overactivity. nRx Axial SpA=non-radiographic axial spondylarthropy. PD=Parkinson's disease. Ped=pediatrics. PsA=psoriatic arthritis. Tx=treatment. UC=ulcerative colitis. ULS=upper limb spasticity.


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