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**Janssen to Present Data from Six Compounds Including Daratumumab and Ibrutinib at the
2016 American Society of Clinical Oncology (ASCO) Annual Meeting**

- Janssen portfolio to be featured in 16 abstracts on topics including blood cancers and solid tumors, as well as the treatment of blood clots in patients with cancer
- Phase 3, pivotal results for daratumumab combination therapy to be featured in the ASCO Press Program and Plenary Session
- Clinical data for ibrutinib spanning approved and investigational uses to be presented
- Updated Phase 2 safety and efficacy results on the use of abiraterone acetate plus prednisone in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) to be presented

RARITAN, NJ, May 18, 2016 – At the [American Society of Clinical Oncology \(ASCO\) 2016 Annual Meeting](#), Janssen Research & Development, LLC will present new data for both approved and investigational oncology and cardiovascular compounds, spanning 10 disease areas. Sixteen company-sponsored abstracts have been accepted for presentation, including for daratumumab, ibrutinib, abiraterone acetate, trabectedin, rivaroxaban and apalutamide. Most notably, Phase 3 data for the immunotherapy daratumumab in combination with standard therapy have been selected for inclusion in the Plenary Session on Sunday, June 5th and will be featured in the ASCO Press Program.

“We are bringing to life medicines that may help to reshape the future of cancer treatment and these data show the paradigm-changing potential of both new and mature compounds in our portfolio,” said Peter F. Lebowitz, M.D., Ph.D., Oncology Therapeutic Area Head, Janssen Research & Development. “We are only beginning to

unlock the full potential of our therapies and we will continue to explore areas where our compounds may benefit patients in need, especially those with hard-to-treat cancers with limited treatment options.”

Key data presentations from our oncology pipeline, include:

- **daratumumab:** Findings from the CASTOR (MMY3004) trial will provide the first look at Phase 3 data assessing the activity of daratumumab in combination with bortezomib and dexamethasone in multiple myeloma patients with at least one prior line of therapy. These pivotal data will serve as the basis for potential regulatory submissions in the U.S. and EU later this year ([Abstract LBA4](#)).
 - These data will be featured in an ASCO Press Briefing from 8:00 – 9:00 a.m. CDT and will be presented in the Plenary Session from 3:10 – 3:25 p.m. CDT on Sunday, June 5th.
- **ibrutinib:** Two-year follow-up data from the Phase 3 HELIOS (CLL3001) study will provide an in-depth look into the use of ibrutinib as a combination therapy in relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL). These data were included in the [May 9th update](#) to the ibrutinib U.S. Prescribing Information ([Abstract 7525](#)). Separately, an analysis of the Phase 3 RESONATE™ (PCYC-1112) and RESONATE™-2 (PCYC-1115) trials will uncover additional information specific to outcomes in CLL/SLL patients based on when they initiate therapy ([Abstract 7520](#)).
 - These data will be presented in a Poster Session from 8:00 – 11:30 a.m. CDT on Monday, June 6th.
- **ibrutinib:** Phase 3 data from the RAY (MCL3001) study will provide insights into the mechanisms of primary and acquired resistance in previously treated mantle cell lymphoma (MCL), for which ibrutinib is currently approved in patients who have received at least one prior therapy ([Abstract 7570](#)).
 - These data will be presented in a Poster Session from 8:00 – 11:30 a.m. CDT on Monday, June 6th.
- **abiraterone acetate:** A safety and efficacy update from the Phase 2 IMAAGEN (Impact of Abiraterone Acetate in Prostate-Specific Antigen) trial will highlight secondary endpoint results on the use of abiraterone acetate plus prednisone in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) ([Abstract 5061](#)).
 - These data will be presented in a Poster Session from 1:00 – 4:30 p.m. CDT on Saturday, June 4th.

A full list of company-sponsored abstracts to be presented at the meeting follows below:

<u>Abstract No.</u>	<u>Title</u>	<u>Date/Time</u>
daratumumab		
Abstract #LBA4	Phase 3 randomized controlled study of daratumumab, bortezomib, and dexamethasone (DVd) versus bortezomib and dexamethasone (Vd) in patients (pts) with relapsed or refractory multiple myeloma (RRMM): CASTOR study.	Plenary Session Sunday, June 5 th 3:10 – 3:25 p.m. CDT
Abstract #TPS8071	An open-label, dose-escalation Phase 1b study of subcutaneous daratumumab with recombinant human hyaluronidase in patients with relapsed or refractory multiple myeloma (PAVO). (Trial in Progress)	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT

ibrutinib

Abstract #7525	Ibrutinib (I) plus bendamustine and rituximab (BR) in previously treated chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL): A 2-year follow-up for the HELIOS study.	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT
Abstract #7570	Sequence variants in patients with primary and acquired resistance to ibrutinib in the Phase 3 MCL3001 (RAY) trial.	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT
Abstract #7520	Outcomes with ibrutinib by line of therapy and outcomes after ibrutinib discontinuation in patients with CLL/SLL: Analyses from Phase 3 data.	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT

abiraterone acetate

Abstract #5061	IMAAGEN trial safety and efficacy update: Effect of abiraterone acetate and low-dose prednisone on prostate-specific antigen and radiographic disease progression in patients with nonmetastatic castration-resistant prostate cancer.	Poster Session Saturday, June 4 th 1:00 – 4:30 p.m. CDT
Abstract #5024	The prostate cancer registry: Do patients with metastatic castration-resistant prostate cancer differ according to metastatic status at diagnosis?	Poster Session Saturday, June 4 th 1:00 – 4:30 p.m. CDT
Abstract #5038	Prostate cancer enhanced mRNA detection assay in whole blood as prognostic biomarker for treatment response to ar-targeted therapies for men with metastatic castration-resistant prostate cancer.	Poster Session Saturday, June 4 th 1:00 – 4:30 p.m. CDT
Abstract #5036	Association of androgen receptor variant 9 (AR-V9) in metastatic tissue with resistance to abiraterone acetate/prednisone.	Poster Session Saturday, June 4 th 1:00 – 4:30 p.m. CDT
Abstract #5078	Assessment of central nervous system and dose reduction events in patients treated with abiraterone acetate plus prednisone or enzalutamide.	Poster Session Saturday, June 4 th 1:00 – 4:30 p.m. CDT

trabectedin

Abstract #11060	Cardiac safety analysis of trabectedin (T) vs. dacarbazine (D) in patients (pts) with advanced leiomyosarcoma (LMS) or liposarcoma (LPS) after prior anthracycline chemotherapy.	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT
Abstract #11061	Patient-reported outcomes from randomized, phase 3 study of trabectedin (T) vs. dacarbazine (D) in advanced leiomyosarcoma (LMS) or liposarcoma (LPS).	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT
Abstract #11064	Trabectedin (T)-related liver toxicity: Results of a pharmacokinetic study with T in patients with hepatic dysfunction (OVC1004) and experience from a Phase 3 clinical trial (SAR3007).	Poster Session Monday, June 6 th 8:00 – 11:30 a.m. CDT

rivaroxaban

Abstract #10024	Recurrent VTE in cancer patients treated with anticoagulation.	Poster Session Monday, June 6 th 1:00 – 4:30 p.m. CDT
Abstract #10112	Duration of anticoagulant therapy and VTE recurrence in patients with cancer.	Poster Session Monday, June 6 th

		1:00 – 4:30 p.m. CDT
apalutamide		
Abstract #TPS5087	ATLAS: A randomized, double-blind, placebo-controlled, Phase 3 trial of apalutamide (ARN-509) in patients with high-risk localized or locally advanced prostate cancer receiving primary radiation therapy. (Trial in Progress)	Poster Session Saturday, June 4 th 1:00 – 4:30 p.m. CDT

About DARZALEX® (daratumumab)

DARZALEX® (daratumumab) injection for intravenous use is the first CD38-directed monoclonal antibody (mAb) approved anywhere in the world.¹ CD38 is a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.² Daratumumab is believed to induce tumor cell death through multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), as well as through apoptosis, in which a series of molecular steps in a cell lead to its death.^{1,3,4} Daratumumab is also believed to induce tumor cell death through immunomodulatory effects, according to a study recently presented at the 57th Annual Meeting and Exposition of the American Society of Hematology (ASH).⁵ Five Phase 3 clinical studies with daratumumab in relapsed and frontline settings are currently ongoing. Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant diseases on which CD38 is expressed, such as smoldering myeloma and non-Hodgkin's lymphoma. DARZALEX is the first mAb to receive regulatory approval to treat relapsed or refractory multiple myeloma.¹

In [August 2012](#), Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize DARZALEX. DARZALEX is commercialized in the U.S. by Janssen Biotech, Inc. For more information, visit www.DARZALEX.com.

DARZALEX® (daratumumab) Important Safety Information

CONTRAINDICATIONS - None

WARNINGS AND PRECAUTIONS

Infusion Reactions - DARZALEX can cause severe infusion reactions. Approximately half of all patients experienced a reaction, most during the first infusion. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing an infusion. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, and hypertension. Signs and symptoms may include respiratory symptoms, such as cough, wheezing, larynx and throat tightness and irritation, laryngeal edema, pulmonary edema, nasal congestion, and allergic rhinitis. Less common symptoms were hypotension, headache, rash, urticaria, pruritus, nausea, vomiting, and chills.

Pre-medicate patients with antihistamines, antipyretics and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt infusion for reactions of any severity and institute medical management as needed.

Permanently discontinue therapy for life-threatening (Grade 4) reactions. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients the first and second day after all infusions. Patients with a history of obstructive pulmonary disorders may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with obstructive pulmonary disorders.

Interference with Serological Testing - Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX. Type and screen patients prior to starting DARZALEX.

Interference with Determination of Complete Response - Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both, the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Adverse Reactions - The most frequently reported adverse reactions (incidence $\geq 20\%$) were: fatigue, nausea, back pain, pyrexia, cough, and upper respiratory tract infection.

Serious adverse reactions were reported in 51 (33%) patients. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%).

DRUG INTERACTIONS - No drug interaction studies have been performed.

About IMBRUVICA® (ibrutinib)

IMBRUVICA® was one of the first therapies to receive U.S. approval after having received the FDA's Breakthrough Therapy Designation. IMBRUVICA works by blocking a specific protein called Bruton's tyrosine kinase (BTK).⁶ The BTK protein transmits important signals that tell B cells to mature and produce antibodies and is needed by specific cancer cells to multiply and spread.^{6,7} IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.⁶ For more information, visit www.IMBRUVICA.com.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA®.

The mechanism for the bleeding events is not well understood. IMBRUVICA® may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies and patients should be monitored for signs of bleeding. Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and postsurgery depending upon the type of surgery and the risk of bleeding.

Infections - Fatal and nonfatal infections have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 14% to 29% of patients. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA®. Evaluate patients for fever and infections and treat appropriately.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 19% to 29%), thrombocytopenia (range, 5% to 17%), and anemia (range, 0% to 9%) based on laboratory measurements occurred in patients treated with single agent IMBRUVICA®. Monitor complete blood counts monthly.

Atrial Fibrillation - Atrial fibrillation and atrial flutter (range, 6% to 9%) have occurred in patients treated with IMBRUVICA®, particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (eg, palpitations, lightheadedness) or new-onset dyspnea should have an ECG performed. Atrial fibrillation should be managed appropriately and if it persists, consider the risks and benefits of IMBRUVICA® treatment and follow dose modification guidelines.

Hypertension - Hypertension (range, 6% to 17%) has occurred in patients treated with IMBRUVICA® with a median time to onset of 4.6 months (range, 0.03 to 22 months). Monitor patients for new-onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA®. Adjust existing antihypertensive medications and/or initiate antihypertensive treatment as appropriate.

Second Primary Malignancies - Other malignancies (range, 5% to 16%) including non-skin carcinomas (range, 1% to 4%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4% to 13%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been infrequently reported with IMBRUVICA® therapy. Assess the baseline risk (eg, high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity - Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise women to avoid becoming pregnant while taking IMBRUVICA® and for 1 month after cessation of therapy. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

ADVERSE REACTIONS

The most common adverse reactions ($\geq 20\%$) in patients with B-cell malignancies (MCL, CLL/SLL, and WM) were neutropenia* (64%), thrombocytopenia* (63%), diarrhea (43%), anemia* (41%), musculoskeletal pain (30%), rash (29%), nausea (29%), bruising (29%), fatigue (27%), hemorrhage (21%), and pyrexia (21%).

*Based on adverse reactions and/or laboratory measurements (noted as platelets, neutrophils, or hemoglobin decreased).

The most common Grade 3 or 4 non-hematologic adverse reactions ($\geq 5\%$) in MCL patients were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%).

Approximately 6% (CLL), 14% (MCL), and 11% (WM) of patients had a dose reduction due to adverse reactions.

Approximately 4%-10% (CLL), 9% (MCL), and 6% (WM) of patients discontinued due to adverse reactions. Most frequent adverse reactions leading to discontinuation were pneumonia, hemorrhage, atrial fibrillation, rash and neutropenia (1% each) in CLL patients and subdural hematoma (1.8%) in MCL patients.

DRUG INTERACTIONS

CYP3A Inhibitors - Avoid coadministration with strong and moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA® dose.

CYP3A Inducers - Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment - Avoid use in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA® dose.

Please see [Full Prescribing Information](#).

About ZYTIGA® (abiraterone acetate)

ZYTIGA® (abiraterone acetate) is indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC). ZYTIGA blocks CYP17-mediated androgen production – which fuels prostate cancer growth – at three sources: in the testes, adrenals and the prostate tumor tissue – and has proven efficacy in patients with mCRPC who have progressed on androgen deprivation therapy.

Since its first approval in the U.S. in 2011, ZYTIGA has been approved in more than 100 countries. More than 239,000 men worldwide have received treatment with it, and it is quickly becoming one of the cornerstones of treatment for metastatic castration-resistant prostate cancer (mCRPC).

Janssen is committed to supporting access to ZYTIGA for appropriate patients who are prescribed this medicine. ZytigaOne™ Support provides enhanced support to physician offices and personalized care coordination services to patients, including the ZytigaOne™ Instant Savings Program, which can help eligible commercially insured patients with out-of-pocket co-pays and coinsurance. For more information on ZytigaOne™ Support, contact 1-855-ZYTIGA-1.

For more information about ZYTIGA, visit www.ZYTIGA.com.

IMPORTANT SAFETY INFORMATION

Contraindications - ZYTIGA® (abiraterone acetate) is not indicated for use in women. ZYTIGA® can cause fetal harm (Pregnancy Category X) when administered to a pregnant woman and is contraindicated in women who are or may become pregnant.

Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess - Use with caution in patients with a history of cardiovascular disease or with medical conditions that might be compromised by increases in blood pressure, hypokalemia, or fluid retention. ZYTIGA® may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Safety has not been established in patients with LVEF <50% or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2) because these patients were excluded from these randomized clinical trials. Control hypertension and correct hypokalemia before and during treatment. Monitor blood pressure, serum potassium, and symptoms of fluid retention at least monthly.

Adrenocortical Insufficiency (AI) - AI was reported in patients receiving ZYTIGA® in combination with prednisone, after an interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of AI if prednisone is stopped or withdrawn, if prednisone dose is reduced, or if the patient experiences unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA®. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Hepatotoxicity - Monitor liver function and modify, withhold, or discontinue ZYTIGA® dosing as recommended (see Prescribing Information for more information). Measure serum transaminases [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] and bilirubin levels prior to starting treatment with ZYTIGA®, every two weeks for the first three months of treatment, and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt ZYTIGA® treatment and closely monitor liver function.

Adverse Reactions - The most common adverse reactions ($\geq 10\%$) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection and contusion.

The most common laboratory abnormalities ($>20\%$) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT and hypokalemia.

Drug Interactions - Based on in vitro data, ZYTIGA® is a substrate of CYP3A4. In a drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during ZYTIGA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA® dosing frequency only during the co-administration period [see Dosage and Administration (2.3)]. In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug interaction trial in healthy subjects, the AUC of pioglitazone, a CYP2C8 substrate, was increased by 46% when administered with a single dose of ZYTIGA®. Patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA®.

Use in Specific Populations - Do not use ZYTIGA® in patients with baseline severe hepatic impairment (Child-Pugh Class C).

About YONDELIS® (trabectedin)

YONDELIS® (trabectedin) is a synthetically produced anti-tumor agent, originally derived from the sea squirt *Ecteinascidia turbinata*. It works by binding to the DNA of cancer cells and disrupting their normal cell activity, which causes cell death. More information, including the full prescribing information, is available at www.YONDELIS.com.

YONDELIS is approved in nearly 80 countries in North America, Europe, South America and Asia. In [October 2015](#), YONDELIS was FDA approved for the treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline containing regimen.

Under a licensing agreement with PharmaMar, Janssen Products, LP has the rights to develop and sell YONDELIS globally except in Europe, where PharmaMar SA holds the rights, and in Japan, where PharmaMar has granted a license to Taiho Pharmaceutical Co., Ltd.

Important Safety Information

CONTRAINDICATIONS - YONDELIS® is contraindicated in patients with known severe hypersensitivity, including anaphylaxis, to trabectedin.

WARNINGS AND PRECAUTIONS

Neutropenic sepsis, including fatal cases, can occur. In Trial 1, the incidence of Grade 3 or 4 neutropenia, based on laboratory values, was 43% (161/378). Median time to the first occurrence of Grade 3 or 4 neutropenia was 16 days (range: 8 days to 9.7 months). Median time to complete resolution of neutropenia was 13 days (range: 7 days to 5.0 months). Febrile neutropenia (fever $\geq 38.5^{\circ}\text{C}$ with Grade 3 or 4 neutropenia) occurred in 18 patients (5%). Ten patients (2.6%) experienced neutropenic sepsis, 5 of whom had febrile neutropenia, which was fatal in 4 patients (1.1%). Assess neutrophil count prior to administration of each dose of YONDELIS and periodically throughout the treatment cycle. Withhold YONDELIS for neutrophil counts of less than 1500 cells/microliter on the day of dosing. Permanently reduce the dose of YONDELIS for life-threatening or prolonged, severe neutropenia in the preceding cycle.

Rhabdomyolysis - YONDELIS can cause rhabdomyolysis and musculoskeletal toxicity. In Trial 1, rhabdomyolysis leading to death occurred in 3 (0.8%) of the 378 patients. Elevations in creatine phosphokinase (CPK) occurred in 122 (32%) of the 378 patients receiving YONDELIS, including Grade 3 or 4 CPK elevation in 24 patients (6%), compared to 15 (9%) of the 172 patients receiving dacarbazine with any CPK elevation, including 1 patient (0.6%) with Grade 3 CPK elevation. Among the 24 patients receiving YONDELIS with Grade 3 or 4 CPK elevation, renal failure occurred in 11 patients (2.9%); rhabdomyolysis with the complication of renal failure occurred in 4 of these 11 patients (1.1%). Median time to first occurrence of Grade 3 or 4 CPK elevations was 2 months (range: 1 to 11.5 months). Median time to complete resolution was 14 days (range: 5 days to 1 month). Assess CPK levels prior to each administration of YONDELIS. Withhold YONDELIS for serum CPK levels more than 2.5 times the upper limit of normal. Permanently discontinue YONDELIS for rhabdomyolysis.

Hepatotoxicity, including hepatic failure, can occur. Patients with serum bilirubin levels above the upper limit of normal or AST or ALT levels $> 2.5 \times \text{ULN}$ were not enrolled in Trial 1. In Trial 1, the incidence of Grade 3-4 elevated liver function tests (defined as elevations in ALT, AST, total bilirubin, or alkaline phosphatase) was 35% (134/378). Median time to development of Grade 3-4 elevation in ALT or AST was 29 days (range: 3 days

to 11.5 months). Of the 134 patients with Grade 3 to 4 elevations in LFTs, 114 (85%) experienced complete resolution with the median time to complete resolution of 13 days (range: 4 days to 4.4 months). In Trial 1, the incidence of drug-induced liver injury (defined as concurrent elevation in ALT or AST of more than three times the upper limit of normal, alkaline phosphatase less than two times the upper limit of normal, and total bilirubin at least two times the upper limit of normal) was 1.3% (5/378). ALT or AST elevation greater than eight times the ULN occurred in 18% (67/378) of patients. Assess LFTs prior to each administration of YONDELIS. Manage elevated LFTs with treatment interruption, dose reduction, or permanent discontinuation based on severity and duration of LFT abnormality

Cardiomyopathy including cardiac failure, congestive heart failure, ejection fraction decreased, diastolic dysfunction, or right ventricular dysfunction can occur. In Trial 1, patients with a history of New York Heart Association Class II to IV heart failure or abnormal left ventricular ejection fraction (LVEF) at baseline were ineligible. In Trial 1, cardiomyopathy occurred in 23 patients (6%) receiving YONDELIS and in four patients (2.3%) receiving dacarbazine. Grade 3 or 4 cardiomyopathy occurred in 15 patients (4%) receiving YONDELIS and 2 patients (1.2%) receiving dacarbazine; cardiomyopathy leading to death occurred in 1 patient (0.3%) receiving YONDELIS and in none of the patients receiving dacarbazine. The median time to development of Grade 3 or 4 cardiomyopathy in patients receiving YONDELIS was 5.3 months (range: 26 days to 15.3 months). Assess left ventricular ejection fraction (LVEF) by echocardiogram or multigated acquisition (MUGA) scan before initiation of YONDELIS and at 2- to 3-month intervals thereafter until YONDELIS is discontinued. Withhold YONDELIS for LVEF below lower limit of normal. Permanently discontinue YONDELIS for symptomatic cardiomyopathy or persistent left ventricular dysfunction that does not recover to lower limit of normal within 3 weeks

Extravasation Resulting in Tissue Necrosis - Extravasation of YONDELIS, resulting in tissue necrosis requiring debridement, can occur. Evidence of tissue necrosis can occur more than 1 week after the extravasation. There is no specific antidote for extravasation of YONDELIS. Administer YONDELIS through a central venous line.

Embryofetal Toxicity - Based on its mechanism of action, YONDELIS can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during therapy and for at least 2 months after the last dose of YONDELIS. Advise males with female partners of reproductive potential to use effective contraception during therapy and for at least 5 months after the last dose of YONDELIS

Adverse Reactions - The most common ($\geq 20\%$) adverse reactions are nausea (75%), fatigue (69%), vomiting (46%), constipation (37%), decreased appetite (37%), diarrhea (35%), peripheral edema (28%), dyspnea (25%), headache (25%)

The most common ($\geq 5\%$) grades 3-4 laboratory abnormalities are: neutropenia (43%), increased ALT (31%), thrombocytopenia (21%), anemia (19%), increased AST (17%), and increased creatine phosphokinase (6.4%)

DRUG INTERACTIONS

Effect of Cytochrome CYP3A Inhibitors - Avoid use of strong CYP3A inhibitors (e.g., oral ketoconazole, itraconazole, posaconazole, voriconazole, clarithromycin, telithromycin, indinavir, lopinavir, ritonavir, boceprevir, nelfinavir, saquinavir, telaprevir, nefazodone, conivaptan) in patients taking YONDELIS. Avoid taking grapefruit or grapefruit juice. If a strong CYP3A inhibitor for short-term use (i.e., less than 14 days) must be used, administer the strong CYP3A inhibitor 1 week after the YONDELIS infusion, and discontinue it the day prior to the next YONDELIS infusion.

Effect of Cytochrome CYP3A Inducers - Avoid administering strong CYP3A inducers (e.g., rifampin, phenobarbital, St. John's wort) to patients who are taking YONDELIS.

WHAT IS XARELTO® (rivaroxaban)?

XARELTO® (rivaroxaban) is a prescription medicine used to reduce the risk of stroke and blood clots in people with atrial fibrillation, not caused by a heart valve problem. For patients currently well managed on warfarin, there is limited information on how XARELTO and warfarin compare in reducing the risk of stroke.

XARELTO is also a prescription medicine used to treat deep vein thrombosis and pulmonary embolism, and to help reduce the risk of these conditions occurring again.

XARELTO is also a prescription medicine used to reduce the risk of forming a blood clot in the legs and lungs of people who have just had knee or hip replacement surgery.

IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO®?

- **For people taking XARELTO® for atrial fibrillation:**

People with atrial fibrillation (an irregular heart beat) are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. XARELTO® lowers your chance of having a stroke by helping to prevent clots from forming. If you stop taking XARELTO®, you may have increased risk of forming a clot in your blood.

Do not stop taking XARELTO® without talking to the doctor who prescribes it for you. Stopping XARELTO® increases your risk of having a stroke.

If you have to stop taking XARELTO®, your doctor may prescribe another blood thinner medicine to prevent a blood clot from forming.

- **XARELTO® can cause bleeding**, which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner medicine that reduces blood clotting. While you take XARELTO® you are likely to bruise more easily and it may take longer for bleeding to stop.

You may have a higher risk of bleeding if you take XARELTO® and take other medicines that increase your risk of bleeding, including:

- Aspirin or aspirin-containing products
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Warfarin sodium (Coumadin®, Jantoven®)
- Any medicine that contains heparin
- Clopidogrel (Plavix®)
- Selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs)
- Other medicines to prevent or treat blood clots

Tell your doctor if you take any of these medicines. Ask your doctor or pharmacist if you are not sure if your medicine is one listed above.

Call your doctor or get medical help right away if you develop any of these signs or symptoms of bleeding:

- Unexpected bleeding or bleeding that lasts a long time, such as:
 - Nosebleeds that happen often
 - Unusual bleeding from gums
 - Menstrual bleeding that is heavier than normal, or vaginal bleeding
- Bleeding that is severe or that you cannot control
- Red, pink, or brown urine
- Bright red or black stools (looks like tar)
- Cough up blood or blood clots
- Vomit blood or your vomit looks like “coffee grounds”
- Headaches, feeling dizzy or weak
- Pain, swelling, or new drainage at wound sites

Spinal or epidural blood clots (hematoma): People who take a blood thinner medicine (anticoagulant) like XARELTO®, and have medicine injected into their spinal and epidural area, or have a spinal puncture, have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). Your risk of developing a spinal or epidural blood clot is higher if:

- A thin tube called an epidural catheter is placed in your back to give you certain medicine
- You take NSAIDs or a medicine to prevent blood from clotting
- You have a history of difficult or repeated epidural or spinal punctures
- You have a history of problems with your spine or have had surgery on your spine

If you take XARELTO® and receive spinal anesthesia or have a spinal puncture, your doctor should watch you closely for symptoms of spinal or epidural blood clots. Tell your doctor right away if you have back pain, tingling, numbness, muscle weakness, (especially in your legs and feet), or loss of control of the bowels or bladder (incontinence).

XARELTO® is not for patients with artificial heart valves.

WHO SHOULD NOT TAKE XARELTO®?

Do not take XARELTO® if you:

- Currently have certain types of abnormal bleeding. Talk to your doctor before taking XARELTO® if you currently have unusual bleeding.
- Are allergic to rivaroxaban or any of the ingredients of XARELTO®.

WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO®?

Before taking XARELTO®, tell your doctor if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Have any other medical condition
- Are pregnant or plan to become pregnant. It is not known if XARELTO® will harm your unborn baby. Tell your doctor right away if you become pregnant while taking XARELTO®. If you take XARELTO® during pregnancy, tell your doctor right away if you have bleeding or symptoms of blood loss.
- Are breastfeeding or plan to breastfeed. It is not known if XARELTO® passes into your breast milk. You and your doctor should decide if you will take XARELTO® or breastfeed.

Tell all of your doctors and dentists that you are taking XARELTO®. They should talk to the doctor who prescribed XARELTO® for you before you have any surgery, medical or dental procedure.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO® works. Certain medicines may increase your risk of bleeding. **See “What is the most important information I should know about XARELTO®?”**

Especially tell your doctor if you take:

- Ketoconazole (Nizoral®)
- Itraconazole (Onmel™, Sporanox®)
- Ritonavir (Norvir®)
- Lopinavir/ritonavir (Kaletra®)
- Indinavir (Crixivan®)
- Carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol®-XR, Teril™, Epitol®)
- Phenytoin (Dilantin-125®, Dilantin®)
- Phenobarbital (Solfoton™)
- Rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®)
- St. John's wort (*Hypericum perforatum*)

Ask your doctor if you are not sure if your medicine is one listed above. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE XARELTO®?

Take XARELTO® exactly as prescribed by your doctor.

Do not change your dose or stop taking XARELTO® unless your doctor tells you to.

- Your doctor will tell you how much XARELTO® to take and when to take it.
- Your doctor may change your dose if needed.

If you take XARELTO® for:

- **Atrial Fibrillation:** Take XARELTO® 1 time a day with your evening meal.
If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
- **Blood clots in the veins of your legs or lungs:**
 - Take XARELTO® once or twice a day as prescribed by your doctor.
 - Take XARELTO® with food at the same time each day.
 - If you miss a dose of XARELTO®:
 - **and take XARELTO® 2 times a day:** Take XARELTO® as soon as you remember on the same day. You may take 2 doses at the same time to make up for the missed dose. Take your next dose at your regularly scheduled time.
 - **and take XARELTO® 1 time a day:** Take XARELTO® as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
- **Hip or knee replacement surgery:** Take XARELTO® 1 time a day with or without food. If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.

- If you have difficulty swallowing the tablet whole, talk to your doctor about other ways to take XARELTO®.
- Your doctor will decide how long you should take XARELTO®. Do not stop taking XARELTO® without talking to your doctor first.
- Your doctor may stop XARELTO® for a short time before any surgery, medical or dental procedure. Your doctor will tell you when to start taking XARELTO® again after your surgery or procedure.
- Do not run out of XARELTO®. Refill your prescription for XARELTO® before you run out. When leaving the hospital following a hip or knee replacement, be sure that you have XARELTO® available to avoid missing any doses.
- If you take too much XARELTO®, go to the nearest hospital emergency room or call your doctor right away.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

Please see “What is the most important information I should know about XARELTO®?”

Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You are also encouraged to report side effects to the FDA: visit <http://www.fda.gov/medwatch> or call 1-800-FDA-1088. You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please click [here](#) for full Prescribing Information, including Boxed Warnings, and Medication Guide.

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About the Janssen Pharmaceutical Companies

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of [OPCO] and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in new product research and development, including uncertainty of clinical success and obtaining regulatory approvals; uncertainty of commercial success for new products; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2016, including in Exhibit 99 thereto, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

¹ DARZALEX Prescribing Information, November 2015.

² Fedele, G et al. CD38 Ligation in Peripheral Blood Mononuclear Cells of Myeloma Patients Induces Release of Protumorigenic IL-6 and Impaired Secretion of IFN γ Cytokines and Proliferation. *Mediators Inflamm.* 2013;2013:564687.

³ Jansen, JH et al. *Blood.* 2012; 120:2974.

⁴ Michel de Weers, M et al. Daratumumab, a Novel Therapeutic Human CD38 Monoclonal Antibody, Induces Killing of Multiple Myeloma and Other Hematological Tumors. *The Journal of Immunology.* February 1, 2011. Vol. 186, No. 3 1840-1848. Available from: <https://ash.confex.com/ash/2015/webprogram/Paper79122.html>. Accessed May 2016.

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⁶ IMBRUVICA Prescribing Information, May 2016.

⁷ Genetics Home Reference. Isolated growth hormone deficiency. Available from: <http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency>. Accessed May 2016.