Prescribing and adverse event reporting information can be found on the last page of this document.
This is intended to be viewed as an electronic document and should not be printed.

Do you have a patient with 2+ enlarged lymph node sites and no clear diagnosis? – think iMCD

Idiopathic Multicentric Castleman Disease (iMCD)

- A rare and severe subset of Castleman Disease (CD) with unknown aetiology which is **difficult to identify**[1–4]
- A **progressive disease** which can lead to organ failure and death[1]

Patients with iMCD have **poorer outcomes than many cancers** including Stage II colon cancer, Stage III breast cancer, and progressive non-Hodgkin's lymphoma[4]

In a real-world, retrospective analysis, in the US:*[3]

the **incidence** of iMCD was

3.1–3.4
cases per mil.

the **prevalence** of iMCD was

6.9–9.7
cases per mil.

*Claims data. Given the methodology used in this study, the incidence likely reflects the incidence of individuals with a new diagnosis, and the prevalence likely reflects the prevalence of individuals with a diagnosis currently listed in their medical record.

Patients can be any age and present with a range of non-specific symptoms and laboratory abnormalities[1,3,4]

Diagnosis

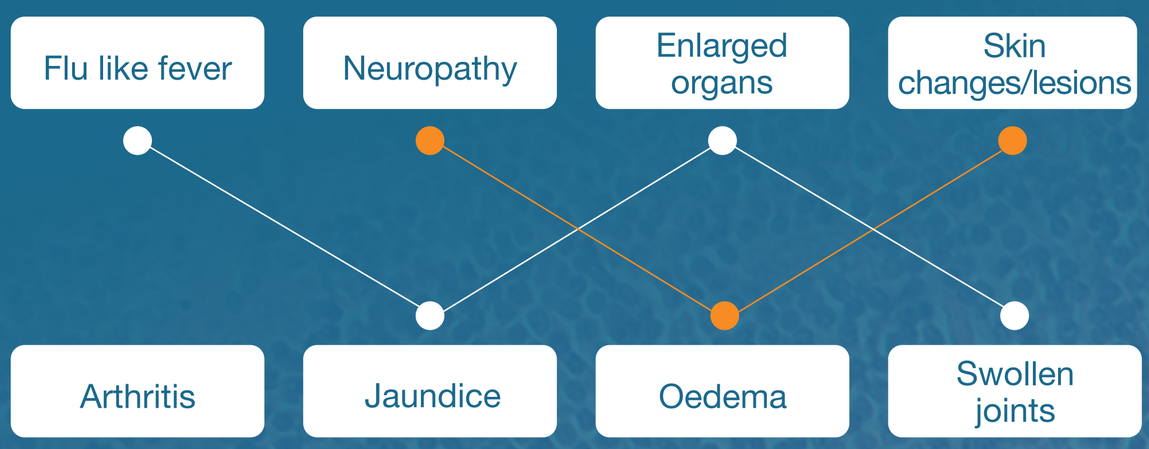
An **excisional lymph node biopsy** is required to confirm a diagnosis of iMCD[1]

Remember to tell pathology colleagues that you ***"suspect Castleman Disease"***.

Symptoms

A patient with iMCD will have a mix of symptoms which can look like an infection, autoimmune/autoinflammatory disease, and/or malignancy[1]

Patients can often present with…



● **Example patient 1** ● **Example patient 2**

Please note, not all iMCD patients will exhibit all of the symptoms described here. See the diagnostic guidelines for more information.[1]

A retrospective claims analysis[3]

The most prevalent minor criteria in patients with iMCD were...

- **89.0%** **Constitutional symptoms** (226/254)
- **68.5%** **Anaemia** (174/254)
- **58.3%** **Oedema and effusion** (148/254)
- **33.5%** **Renal dysfunction** (85/254)
- **24.0%** **Hepatosplenomegaly** (61/254)
- **18.9%** **Thrombocytopenia** (48/254)

US claims data.

Abbreviations: CD, Castleman Disease; **EU,** European Union; **iMCD,** idiopathic Multicentric Castleman Disease; **MCD,** Multicentric Castleman Disease; **US,** United States.

References: 1. Fajgenbaum DC, *et al. Blood.* 2017; 129: 1646–57. **2.** Dispenzieri A and Fajgenbaum DC. *Blood.* 2020; 135: 1353–64. **3.** Mukherjee S, *et al. Blood Adv.* 2022; 6: 359–67. **4.** Sitenga J, *et al. Patient Relat Outcome Meas.* 2018; 9: 35–41.

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IE-SYL-0091. May 2025.

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Additional guidance available online

For more information scan this code

www.thinkimcd.co.uk

Please contact your Recordati Rare Diseases representative to request replacements

UK & IRELAND PRESCRIBING INFORMATION
SYLVANT®▼ (siltuximab) 100mg and 400mg powder for concentrate for solution for infusion

Prescribers should refer to the Summary of Product Characteristics before prescribing.

PRESENTATION: Siltuximab, 100 mg or 400 mg freeze-dried white powder for concentrate. **INDICATION:** Treatment of adult patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV8) negative. **POSOLOGY & ADMINISTRATION:** This medicinal product should be administered by qualified healthcare professionals and under appropriate medical supervision. **Adults:** Recommended dose 11mg/kg siltuximab given over 1 hour as an intravenous infusion administered every 3 weeks until treatment failure. Haematology laboratory tests should be performed prior to each dose for first 12 months, then every third cycle. Consider delaying treatment if: absolute neutrophil count <1.0x10^9/L; platelet count <75x10^9/L for first administration or <50x10^9/L for subsequent administration; or haemoglobin ≥170g/L (10.6 mmol/L). Withhold treatment if severe infection or any severe non-haematological toxicity. Restart at the same dose after recovery. Discontinue if severe infusion-related reaction, anaphylaxis, severe allergic reaction or cytokine release syndrome. Consider discontinuation if more than 2 dose delays due to treatment-related toxicities during first 48 weeks. **SPECIAL POPULATIONS: Elderly Patients:** No dose adjustment required. **Renal & Hepatic impairment:** No studies. **Paediatric population:** The safety and efficacy of siltuximab in children aged 17 years and younger has not been established. No data available. **CONTRAINDICATIONS:** Severe hypersensitivity to active substance or any excipient. **SPECIAL WARNINGS & PRECAUTIONS: Traceability:** In order to improve the traceability of biological medicinal products, the tradename and the batch number of the administered product should be clearly recorded. **Concurrent active serious infections:** Infections, including localised infections, should be treated prior to administering SYLVANT. Serious infections, including pneumonia and sepsis, were observed during clinical studies. Hypoglobulinaemia was observed in 4% to 11.3% of patients in the clinical study. Two cases of reactivated hepatitis B have been reported on concomitant use with high dose dexamethasone, and bortezomib, melphalan and prednisone. Monitor for serious infections as SYLVANT may mask signs and symptoms of acute inflammation, including suppression of fever and acute-phase reactants such as C-reactive protein (CRP). **Vaccinations:** Do not administer live, attenuated vaccines concurrently or within 4 weeks prior to initiating SYLVANT. **Lipid parameters:** Triglyceride and cholesterol elevations observed, manage as per current guidelines for hyperlipidaemia. **Infusion reactions and hypersensitivity:** Mild to moderate infusion reactions may improve following slowing of or stopping the infusion. Upon resolution, reinitiating the infusion at a lower infusion rate and therapeutic administration of antihistamines, paracetamol, and corticosteroids may be considered. Discontinue in patients who have severe infusion related hypersensitivity reactions (e.g., anaphylaxis).The management of severe infusion reactions should be dictated by the signs and symptoms of the reaction. Appropriate personnel and medicinal product should be available to treat anaphylaxis if it occurs. **Malignancy:** Immunomodulatory medicinal products may increase the risk of malignancy. On the basis of limited experience with siltuximab the present data do not suggest any increased risk of malignancy. **Gastrointestinal perforation:** Gastrointestinal (GI) perforation has been reported in siltuximab clinical trials. Use with caution in patients at increased risk of GI perforation. Promptly evaluate patients presenting with symptoms that may be associated with or suggestive of GI perforation. **Hepatic impairment:** Transient or intermittent mild to moderate elevation of hepatic transaminase levels or other liver function tests have been reported. Monitor patients with known hepatic impairment or elevated transaminase or bilirubin levels. **INTERACTIONS:** Binding bioactive IL-6 by siltuximab may result in increased metabolism of CYP450 substrates. It is recommended to monitor the effect or concentration of CYP450 substrates that have a narrow therapeutic index (e.g., warfarin, cyclosporine or theophylline). Exercise caution when siltuximab is co-administered with medicinal products that are CYP3A4 substrates where a decrease in effectiveness would be undesirable (e.g., oral contraceptives). **WOMEN OF CHILDBEARING POTENTIAL:** Effective contraception must be used during and up to 3 months after treatment. **PREGNANCY:** Not recommended. **BREAST-FEEDING:** No data. Risk to newborn / infant cannot be excluded. **FERTILITY:** Effects on fertility have not been evaluated in humans. **ADVERSE REACTIONS: Very common (≥1/10):** Upper respiratory tract infection, urinary tract infection, nasopharyngitis, neutropenia, thrombocytopenia, hypertriglyceridaemia, hyperuricaemia, dizziness, headache, oropharyngeal pain, hypertension, nausea, abdominal pain, vomiting, constipation, diarrhoea, gastroesophageal reflux disease, mouth ulceration, rash, pruritus, eczema, arthralgia, pain in extremity, renal impairment, localised oedema, weight increased. **Common (≥1/100 to <1/10):** Anaphylactic reaction, hypercholesterolaemia. **Prescribers should refer to the summary of product characteristics in relation to other adverse reactions. LEGAL CLASSIFICATION:** POM. **PRESENTATIONS, PACK SIZES, MARKETING AUTHORISATION NUMBER(S):** SYLVANT 100 mg powder for concentrate for solution for infusion, 1 vial per pack: PLGB 44185/0006 (UNITED KINGDOM), EU/1/14/928/001 (REPUBLIC OF IRELAND). SYLVANT 400mg powder for concentrate for solution for infusion, 1 vial per pack: PLGB 44185/0007 (UNITED KINGDOM), EU/1/14/928/002 (REPUBLIC OF IRELAND). **UK BASIC NHS COST:** SYLVANT 100 mg powder for concentrate for solution for infusion, 1 vial per pack: £502.15. SYLVANT 400mg powder for concentrate for solution for infusion, 1 vial per pack: £2009.81. **MARKETING AUTHORISATION HOLDER (UNITED KINGDOM):** Recordati UK Ltd., Breakspear Park, Breakspear Way, Hemel Hempstead, HP2 4TZ, United Kingdom. **MARKETING AUTHORISATION HOLDER (REPUBLIC OF IRELAND):** Recordati Netherlands B.V., Beechavenue 54, 1119PW Schiphol-Rijk, Netherlands. FURTHER INFORMATION IS AVAILABLE UPON REQUEST FROM: Recordati UK Ltd, Breakspear Park, Breakspear Way, Hemel Hempstead, HP2 4TZ, United Kingdom. **DATE PRESCRIBING INFORMATION LAST REVISED:** December 2024 (version 3.0).

Adverse events should be reported. (UK) Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/. (Ireland) Healthcare professionals are requested to report suspected adverse reactions to HPRA via their website https://www.hpra.ie/. Adverse events should also be reported to Recordati UK Ltd by telephone: +44 (0)1491 414 333 or email: RRDpharmacovigilance@recordati.com.

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