UHL Guidance on Management of MGUS in Primary Care

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0 INTRODUCTION

- ✓ A paraprotein band is an abnormal immunoglobulin or immunoglobulin light chain that is produced in excess by the clonal proliferation of plasma cells.
- ✓ Paraproteins can be detected in the serum of about 1% of the population, and are frequently detected as a result of a myeloma screen.
- ✓ Monoclonal gammopathy of undetermined significance (MGUS) is defined as the presence of a serum monoclonal protein (M protein) at a concentration of less than 30 g/L, the absence of CRAB features (i.e., hypercalcemia, renal insufficiency, anaemia, and bone lesions) related to the M protein and less than 10% monoclonal plasma cells in the bone marrow.

0.1. Purpose and Intended use of procedure

This policy gives guidance to clinicians and outlines the next follow up steps when a new paraprotein band is detected.

0.2. Responsibility

All staff involved in the caring for patients with a new paraprotein band, whether clinical or laboratory must adhere to this policy.

0.3. Clinical Significance

Risk stratification for MGUS

- ✓ Monoclonal gammopathy of undetermined significance (MGUS) occurs in approximately 3% of persons 50 years of age or older and in 5.3% of those 70 years of age or older.
- ✓ MGUS can be classified into two major subtypes, IgM and non-IgM (IgG and IgA), because the nature of progression differs between these two types.
- ✓ IgM MGUS is associated with a risk of progression to lymphoma or Waldenström's macroglobulinemia more typically. In contrast, non-IgM MGUS is associated with a risk of progression to multiple myeloma. Both disease types can progress to AL amyloidosis.
- ✓ If a new paraprotein is detected, the Laboratory will automatically send the sample for Serum Free Light Chains (SFLC) analysis. This result takes up to 3 weeks to be reported and a comment with clinical guidance will be issued to the GP at this stage.
- ✓ Two risk factors determine the risk of progression from MGUS to Myeloma over time: (1. An abnormal serum free light-chain ratio and 2. High serum monoclonal protein ≥15 g/L),
- ✓ Among patients with non-IgM MGUS, the risk of progression at 20 years was 30% among those who had two risk factors, 20% among those who had one risk factor, and only 7% among those who had neither risk factor.
- ✓ Among patients with IgM MGUS, the presence of the two risk factors was associated with a risk of progression at 20 years of 55%, as compared with 41% among patients who had one risk factor and 19% among patients who had neither risk factor.
- ✓ Please note that any patient with symptoms, signs or results suggestive of myeloma, other lymphoproliferative disorders or AL amyloidosis need to be dealt with outside of this stratification listing, and need to be seen by a Consultant Haematologist.
- ✓ Patients with a high and intermediate risk of progression should be referred to a Consultant Haematologist for further assessment (See Algorithm below).
- ✓ Patients with a low risk of progression: The majority of patients can be managed in the community as detailed below, without the need for a Consultant referral. Comments and

recommendations will be added to the results; alternatively you can establish whether your patient falls into this group yourself (See Algorithm below), or contact one of the Consultant Haematologists for advice on the further management of the patient.

- ✓ If a new IgD, IgE, Free Kappa only or Free Lambda only paraprotein is detected, the patient should be referred to a Consultant Haematologist. (See Algorithm below).
- ✓ Urgent Haematology Referral is recommended if a new paraprotein with a concentration ≥ 30g/L is detected and/or in the case of a Serum Free Light Chain Ratio (SFLCr) ≥ 100 (Serum involved / uninvolved free light chain ratio i.e. involved free light chain either kappa or lambda, is the one that is above the normal reference range; the uninvolved free light chain is the one that is typically in, or below, the normal range). (See Algorithm below).

Management of low risk patients in Primary Care or patients discharged back for monitoring to Primary Care

Patients should be re-assessed 6 monthly or annually depending on Paraprotein type and concentration (see Algorithm below).

They should specifically be asked about bone pain and episodes of infection. The following blood tests should be carried out prior to each assessment:

• Full blood count (FBC)
• Renal, liver and bone function tests
• Serum protein electrophoresis (SPE) and paraprotein quantification
• Serum immunoglobulins

Re-Referral

Patients should be re-referred to the Consultant Haematologist if they develop any of the following:

• New symptoms including significant fatigue, recurrent infections (>2 significant bacterial infections within 12 months), unexplained bleeding, weight loss and particularly bone-related pain.
• Anaemia Hb <10g/dL or 2g/dL below reference range.
• The paraprotein level increases by >25% (minimum increase of 5 g/L) or become >15 g/L
• The development of abnormal renal function (>25% increase in creatinine OR creatinine > 173 µmol/L without any other cause)
• Hypercalcaemia (>25% increase in adjusted calcium OR adjusted calcium > 2.75 mmol/L without any other cause)

If IgM paraprotein, re-refer patients with any new symptoms of weight loss, night sweats, fever, lymphadenopathy or organomegaly.

0.4. Abbreviations

SPE	Serum Protein Electrophoresis
SFLC	Serum Free Light Chains

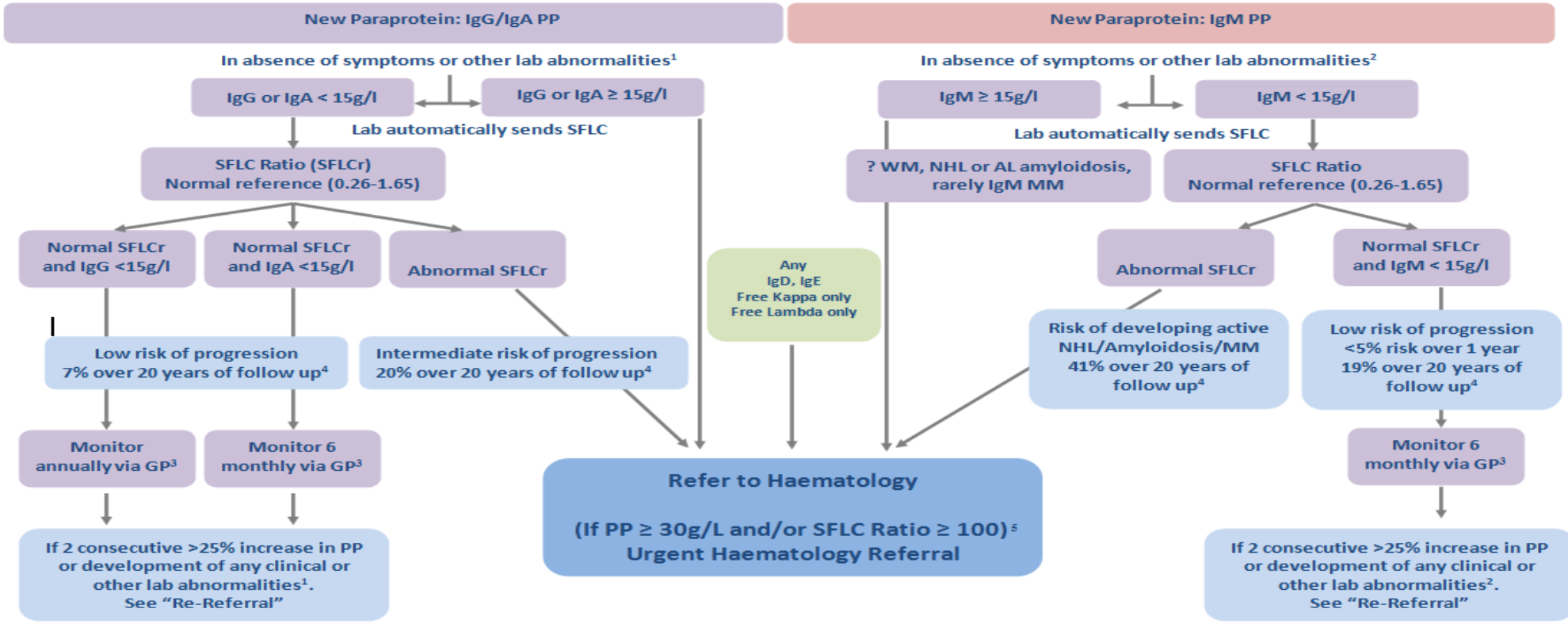
0.5. References

a) "Long-Term Follow-up of Monoclonal Gammopathy of Undetermined Significance"
Robert A. Kyle, M.D., Dirk R. Larson, M.S., Terry M. Therneau, Ph.D., Angela Dispenzieri, M.D., Shaji Kumar, M.D., James R. Cerhan, M.D., Ph.D., and S. Vincent Rajkumar, M.D.
N Engl J Med 2018;378:241-9. DOI: 10.1056/NEJMoa1709974

b) NICE Guidelines August 2015 "Myeloma in adults: diagnosis and management"

1 PROCEDURE

1.1. Algorithm: UHL Guidance on Management of MGUS in Primary Care.



[1]Clinical symptoms: bone pain, anaemia, renal impairment, hypercalcaemia, neuropathy, lymphadenopathy.
[2]Clinical symptoms: Bruising, bone pain, anaemia, renal impairment, hypercalcaemia, neuropathy, lymphadenopathy.
[3] Lab monitoring: FBC/Renal/Liver/Bone/Immunoglobulins/SPEP and PP.
[4] Kyle et al, NEJM, 2018 Long term follow-up of Monoclonal Gammopathy of Undetermined Significance.
[5]Serum involved / uninvolved free light chain ratio ≥ 100 (involved free light chain, either kappa or lambda, is the one that is above the normal reference range; the uninvolved free light chain is the one that is typically in, or below, the normal range)