

## Guidance on what to do when a paraprotein is found

### Presentation

- Broadly, immunoglobulins are requested in patients with unexplained anaemia, renal failure, hypercalcaemia, a raised total protein or raised plasma viscosity.
- 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 or MGUS is the presence of a monoclonal protein (also known as a paraprotein), in the serum or urine of an individual with no evidence of multiple myeloma, AL amyloidosis, Waldenstrom macroglobulinaemia or other related disorder.

### Diagnostic criteria for MGUS

- Paraprotein in serum <30g/L.
- Bone marrow clonal plasma cells <10% and low level plasma cell infiltration in a trephine biopsy.
- No myeloma-related organ or tissue impairment (including bone lesions or symptoms).
- No evidence of other B-cell lymphoproliferative disorder or light chain associated amyloidosis or other light chain, heavy chain or immunoglobulin-associated tissue damage.

### Clinical Findings

#### Risk stratification for MGUS

- MGUS is uncommon below the age of 50 years and the prevalence increases with age. It is important to identify and monitor those patients at highest risk of progression to significant disease, whilst avoiding unnecessary follow-up of patients at low risk of progression.
- Population studies show the risk of MGUS is approximately: 3% in people over 50 years old, 5% in people over 70 and 7.5% in people over 85.
- Three parameters can separate patients with MGUS into those with low, intermediate and high risks of developing multiple myeloma.
- They are the serum paraprotein level, the immunoglobulin (Ig) isotype and the free light chain (FLC) ratio.
- The Intermediate grouping is further subdivided into “low-intermediate” and “high-intermediate”.
- 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.

Risk Group	20 year risk of progression to myeloma (%)
<b>Low risk</b> Serum Paraprotein <15g/L IgG isotype Appropriate FLC ratio	5%
<b>Low-intermediate risk</b> Presence of an IgA or IgM isotype (NB: Paraprotein must be less than 10g/L) OR Inappropriate FLC ratio	21%
<b>High-intermediate risk</b> Presence of an IgA or IgM isotype (NB: Paraprotein must be less than 10g/L) AND Inappropriate FLC ratio	37%
<b>High risk</b> If IgG, Paraprotein >15g/L If IgA or IgM, Paraprotein >10g/L Inappropriate FLC ratio	58%

## Further Assessment

### Low Risk Group

Given this group has the lowest transformation rate the majority of patients can be managed in the community as detailed below, without the need for further invasive testing or a Consultant referral. You can establish whether your patient falls into this group yourself, or alternatively write/telephone one of the haematologists for advice on the further management of the patient.

### Intermediate and High Risk Groups

These patients should to be referred to haematology if appropriate for further assessment. These patients may be discharged back to your care for monitoring (as detailed below).

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

Patients should be assessed every 3 to 4 monthly initially. If these are stable the interval can be increased to every 6-12 months. They should specifically be asked about bone pain and episodes of infection. Blood tests should be carried out prior to each assessment as follows:

- Full blood count
- Renal, liver and bone function tests
- Serum electrophoresis and paraprotein quantification
- Serum immunoglobulins
- Serum free light chains

## Referral

Patients should be re-referred to the consultant clinic if they develop any of the following:

- New symptoms including fatigue, recurrent infections, unexplained bleeding, weight loss and particularly bone-related pain.
- The paraprotein level increases by >25% (minimum increase of 5 g/l)
- The development of abnormal renal function
- Hypercalcaemia

## References

- 1) UK Myeloma Forum (UKMF) and Nordic Myeloma Study Group (NMSG): guidelines for the investigation of newly detected M-proteins and the management of monoclonal gammopathy of undetermined significance (MGUS). Bird J et al. British Journal of Haematology, 147, 22-42.