Orphan Diseases Industry Group

Ensuring access to appropriate medicines for the treatment of patients with orphan diseases in the UK.
ODIG (Orphan Diseases Industry Group) is a group of orphan drug manufacturers working together to ensure the NHS provides patients with the medicines they need.

ODIG is working closely with Rare Disease UK – an alliance of patient groups and other engaged stakeholders – to develop a strategic approach to treating rare diseases in the UK.

Who is ODIG?

In order to be granted orphan drug status by the European Union, manufacturers must demonstrate that:

- The disease or conditions for which the medicinal product would be administered, affects not more than five in 10,000 persons in the Community at the time at which the application for designation is submitted.
- The disease or condition should be of a life-threatening or chronically debilitating nature.
- Without incentives it is unlikely that the marketing of the medicinal product in the Community would generate sufficient return to justify the necessary investment.
- There exists no satisfactory method of diagnosis, prevention or treatment of the condition in question, or if such method exists that the medicinal product will be of significant benefit to those affected by that condition.

Many patients with rare, or orphan, diseases do not receive the medicines they need

The medicines used to treat rare conditions are classified as orphan drugs, which is an official designation of the European Union (EU). Orphan drugs are defined as innovative treatments in an area of unmet need for rare but serious conditions.

Unfortunately, treatment is not yet available for many rare conditions. However, where treatment is available it often does not receive funding for provision on the NHS.

According to the NHS Constitution, everyone has an equal right to appropriate medicine and care for their condition – and this includes people with rare diseases.¹

In the UK around 5.7% of the population are affected by a rare disease at any one time.² Challenges continue to exist in accessing treatments that can help.

One of the main reasons why patients do not have access to orphan medicines is that current health technology appraisal (HTA) processes are not appropriate for them (see page 4).

• Even though European marketing authorisation has been granted for 50 orphan drugs, only 3 have been recommended by NICE.

• In Scotland, the Scottish Medicines Consortium (SMC) uses HTA to determine whether orphan medicines should receive funding. As of May 2010, the SMC had appraised 46 orphan medicines and issued the following guidance:
  18 have been recommended
  17 were rejected
  11 have been recommended for restricted use only³

• Despite the addition of modifiers to the SMC process, which give special consideration to rare or terminal illness treatments, there has been minimal impact on the positive appraisal of orphan medicines.

Commissioning processes at local level are not appropriate for funding orphan medicines. ODIG welcomes the National Framework being developed by the Department of Health and looks forward to working with stakeholders to ensure patients receive the treatments they need.
Health technology appraisals and commissioning processes are not appropriate for evaluating medicines for orphan diseases

There are no consistent funding routes for orphan medicines. Many orphan medicines are not evaluated through the HTA process, and the few that are appraised are often rejected on the basis of their high estimated cost per QALY.

- Cost-effectiveness measures do not take into account the low commercial viability of orphan medicines; small patient populations also mean a small potential market.

- Small patient populations make it difficult to conduct the research which would fulfil specific HTA requirements for evidence. NICE’s evidence requirements and methods rely on randomised clinical trials with large numbers of patients to generate sufficient data to prove cost-effectiveness. The current process in isolation is not appropriate as it fails to take into account appropriate recognition of the rarity of the disease.

- The assessment criteria currently used do not capture the full benefit and innovative nature of these medicines, particularly benefits to carers and society.

- The current QALY/ICER cost-effectiveness tool is not appropriate for the appraisal of orphan medicines because it fails to give appropriate recognition of the rarity of the disease and hence the size of patient population.

Traditionally, commissioning processes have also failed to provide access to orphan medicines. Regional Specialist Commissioning teams predominantly consider services rather than medicines, while there is no national framework to guide regional teams, meaning any services that are commissioned at this level vary considerably across the country.

There are limitations in the current commissioning processes, particularly at a local level, which mean a number of patients do not get access to the treatment they need.
Recent developments have attempted to, but fallen short of, addressing some of these issues:

In 2009, Sir Ian Kennedy recommended that NICE should incentivise innovation and development of products for rare diseases. In response, NICE has proposed that Appraisal Committees should adjust their processes to demonstrate that they have considered the innovative characteristics of a new product.

But standard HTA methods continue to be applied to orphan medicines. The cost-effectiveness data that NICE requires will continue to be unavailable for orphan medicines owing to their small patient populations. As a result, these changes bring us no closer to better access for patients who need orphan medicines.

In addition, the Innovation Pass proposed by the OLS will not improve access to orphan medicines in the longer term. After three years of limited funding through the Pass, these medicines will then still be subject to NICE appraisal, at which time the same limitations of the HTA process will apply.

The Department of Health has recently proposed replacing the National Commissioning Group with the National Commissioning Advisory Group, but the commissioning powers of this group will still be restricted to conditions with 500 or fewer patients, and with a maximum of 4 treatment centres around the country.4 These criteria will exclude many diseases that have bigger patient populations than 500 in England but are still classified as rare conditions.

ODIG welcomes the acknowledgement in the Chief Medical Officers Annual Report 2009 of the importance of treating patients with orphan diseases.5 Such recommendations should be reviewed and implemented as part of the national strategy for rare diseases being developed by RDUK.
Access to orphan medicines should be driven by equity for patients, taking into account the EU criteria for orphan drug designation.

Although orphan medicines have a low impact on the overall NHS budget, they can significantly distort the local budget of PCTs. As such, ODIG believes funding for orphan medicines should be organised nationally from a central source.

We believe that orphan medicines should still be subject to evaluation, but processes should be refined for orphan medicines to take into account the difficulties of collecting data for small populations. Evaluation should primarily be based on the benefits to the patient. Societal preferences suggest that severity and degree of unmet need should inform these decisions.

The UK could learn from the approach of other European countries:

- EU health ministers, including those from the UK, have agreed that countries need to institute national strategies on rare diseases to make sure patients receive the right treatment.  
- Five European countries have already adopted national plans on rare diseases. France instituted its first national plan for treating patients with rare diseases in 2005.  

We need a radical review of how orphan medicines are evaluated and funded

- A recent report from the Office of Health Economics, Access to Orphan Drugs: A Comparative Study of Selected European Countries, found that the majority of orphan medicines are available through public health systems in other comparable European countries.

The most pressing issue is to ensure that patients have access to the medicines they need. The UK must develop a strategy which ensures patients with rare diseases get equity of access to orphan medicines. ODIG supports the work that Rare Disease UK is doing to bring together stakeholders to define such a strategy.

A coordinated UK strategy should:

- Include a National Framework for delivery of specialised services.
- Ensure that any HTA processes for the evaluation of orphan medicines address all aspects of value provided by these innovative treatments.
**Case studies**

**Vidaza**

Vidaza (Azacitidine) is the only drug licensed for the treatment of myelodysplastic syndrome (MDS), a group of rare blood cancers. Patients with MDS have a very poor prognosis and will suffer extreme fatigue and the inability to carry out the simplest tasks in everyday life. For approximately 5%, there is a small chance of cure through stem cell transplantation. Many patients are offered chemotherapy, but this has not been shown to consistently prolong survival. The only other option is supportive care which manages the symptoms, not the underlying disease, and does not prolong life.

Currently there are no other licensed and NICE-approved treatments available on the NHS to treat the higher risk forms of the illness meaning azacitidine represents the only innovative treatment option for this patient group. A study published in *The Lancet Oncology* showed that patients who are treated with azacitidine have a 50% greater chance of being alive after two years than patients treated with painkillers and blood transfusions – which is part of the supportive care regimen for MDS. NICE has accepted this evidence yet plans to issue a final guidance denying patients access to this drug on the basis that it is not cost-effective. The decision is under appeal.

The drug has faced two key challenges during the appraisal process. Firstly, the choice of comparator treatment in the appraisal strongly influenced the cost per QALY. Secondly, the drug has been disadvantaged in this appraisal because data are collected from a small patient population meaning that NICE's strict evidence criteria can not fully be met, and cost-effectiveness is more difficult to demonstrate.

Prepared by Celgene Ltd

**Mepact**

Mepact (mifamurtide) is used to treat high grade, resectable non-metastatic osteosarcoma, the most frequent primary malignant bone cancer, in children, adolescents and young adults under the age of 30. Non-metastatic osteosarcoma is a very rare condition, with an estimated 1,200 cases in Europe every year. Less than 100 of those are in the UK.

Mepact is currently going through Health Technology Appraisals by both NICE in England & Wales and the SMC in Scotland to assess its cost and clinical effectiveness for use in the UK. Both of these bodies have acknowledged the potential clinical benefits for patients, and have noted the fact that it is a one-off course of therapy and not a treatment that patients are required to take for the rest of their lives. The primary issue, perhaps unsurprisingly, is the cost.

As an (ultra) orphan medicine, Mepact exceeds the standard cost effectiveness threshold used by both NICE and the SMC. However, because there are so few cases in the UK every year, and each of these would require just one course of the treatment, the actual cost to the NHS is minimal. The availability of this medicine to patients in the UK depends on recognition of this fact.

Prepared by Takeda UK Ltd

**Kuvan**

Kuvan (sapropterin dihydrochloride) is a treatment for Phenylketonuria (PKU), a rare inherited disorder that affects approximately 1 in 10,000 people. Patients with PKU are unable to break down Phenylalanine (Phe), an amino acid found in food proteins. Without dietary management, the disorder leads to irreversible damage of the developing brain. Currently, a very strict protein-restricted diet is the only treatment available on the NHS but compliance can be poor, risking neurological damage. Addition of sapropterin decreases blood phenylalaine levels in responding patients and potentially may allow the diet to be relaxed in some patients.

Although NICE decided not to prioritise sapropterin for appraisal, the SMC and AWMSG sought to assess it. There is a lack of published trials or observational studies on the effectiveness of current treatment i.e. restricted diet, particularly on the long-term consequences of the disease. It was therefore difficult to put together a reasonable model of comparative cost-effectiveness without great uncertainty. It was decided in discussion with the AWMSG and SMC that it was best to opt for a non-submission. The HTA bodies could therefore not recommend the use of sapropterin.

At a NICE appraisal committee the views of patient groups and clinical experts are given great consideration in the decision-making process; however it is difficult for such groups representing individuals with orphan diseases to fully contribute. Little or no UK experience exists to give an informed opinion of the drug and without funding that experience cannot be gained.

Currently the only route left to patients in the UK to obtain sapropterin is through individual funding requests and for this process you need to demonstrate exceptionality. The UK needs to evaluate its methods and processes for assessing such drugs if patients with rare diseases are going to get fair and equitable access to treatment in comparison to more common conditions.

Prepared by Merck Serono Ltd
References

3. Data on file
6. EU Council, Recommendation on an action in the field of rare diseases (2009)