

## SILDENAFIL

### Use

Sildenafil is being used experimentally as a pulmonary artery vasodilator in children with primary and post-surgical pulmonary hypertension, to treat persistent pulmonary hypertension of the newborn, and to wean term babies from treatment with inhaled nitric oxide (q.v.) for this condition.

### Pharmacology

Sildenafil citrate, a phosphodiesterase 5 inhibitor, first came onto the market in 1998 as an oral treatment for male erectile dysfunction. There is a lot of this enzyme present in the lung, so it is not surprising that sildenafil was soon shown to relax the pulmonary arteries by slowing down the degradation of cyclic guanosine monophosphate in a dose that did not cause troublesome systemic vasodilatation. As a result the drug was soon put to use in the management of pulmonary hypertension in adults, and in the management of post-operative pulmonary hypertension in children with congenital heart disease. Oral treatment is now also starting to be used experimentally in the management of babies with severe persisting pulmonary hypertension of the newborn, especially where there is also a diaphragmatic hernia. The drug is quite rapidly absorbed when given by mouth and then metabolised to the inactive *N*-desmethyl metabolite in the liver before excretion in the faeces and, to a lesser extent, in the urine (the terminal half life in adults being 4 hours). Clearance in the first year of life has not yet been studied in any detail. Only about half the ingested dose gets into the systemic circulation because of 'first-pass' metabolism in the liver.

While an increasing number of case reports of neonatal use have now started to appear, cases where treatment was successful will be more likely to have found their way into print, and there are, as yet, almost no published reports of the successful use of sildenafil in the preterm baby. High dose treatment could certainly do more harm than good, and combined use with other vasodilators has sometimes increased ventilation-perfusion mismatch in animal studies. There have, however, now been several small structured studies of the drug's neonatal use, first to wean term babies off the need for further treatment with inhaled nitric oxide (q.v.) and also, more recently, to see if use may sometimes make the need for such expensive treatment unnecessary. Clinical reports also suggest that judicious use can improve cardiac output and cerebral blood flow. Obstetric use is now undergoing assessment. The effect of maternal use during pregnancy or lactation on the baby is unknown, but high molecular weight makes significant transfer unlikely.

### Treatment

**Oral treatment:** Start by giving 300 micrograms/kg once every 6 hours and increase, as required, to no more than 2 mg/kg once every 4 hours. There are a few reports of babies who respond being offered, and benefiting from, sustained oral treatment for several weeks or even months.

**IV treatment:** Start by giving 200 micrograms/kg IV over 2 minutes. Very little is yet known about sustained use if such a loading dose proves effective, but a continuing infusion of 100 micrograms/kg per hour has sometimes been used.

### Supply

While tablets are available on prescription, the IV preparation is only available for research purposes on direct application from the manufacturers. A liquid for oral use containing 1 mg/ml can be made by dissolving one 25 mg tablet (which costs £4.10) in 25 ml of water (and this can be used for a month if kept refrigerated).

### References

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